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Effects of *Ayahuasca* on the human EEG

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Summary

EEG data were recorded under field conditions from 11 members of the Santo Daime Doctrine, a Brazilian shamanistic religion, before and after ingesting the psychoactive alkaloid preparation, *ayahuasca,* or *daime,* as they term it. Post-ingestion, we observed increases in power in the 36 – 44 Hz frequency band ("40 Hz") from the left occipital-temporal-parietal scalp electrodes in the eyes-closed condition, which extended to most of the posterior scalp in the eyes-open condition. The results are consistent with many reports that *ayahuasca* intensifies visual imagery. These results are discussed in terms of a thalamocortical model of the role of 40 Hz activity in brain function and conscious experience. We also noted tendencies toward decreases in the power of slow (theta and alpha) brain rhythms, and increases in the 14 – 30 Hz beta band, in accord with studies reported 30 years ago with other consciousness-altering compounds. Analysis of four *ayahuasca* samples yielded an average composition per ingested dose (75 ml) of 55.6 mg harmine, 43.9 mg tetrahydroharmine, 41.3 mg N,N-dimethyltryptamine (DMT), 4.6 mg harmaline, and 3.1 mg harmol. The DMT appeared to be of sufficient concentration to promote psychoactive effects, while the β-carbolines functioned to supply MAO inhibitors necessary to prevent degradation of DMT and to maintain its oral activity.

Key words: *Ayahuasca, Banisteriopsis caapi, Psychotria viridis,* harmane alkaloids, brain function, psycho activity, EEG-measurements, topographic brain mapping, Brazil, Santo Daime, DMT

Introduction

The main focus of our laboratory is the recording and analysis of brain electrical activity associated with a range of cognitive tasks. However, we have also conducted field research in Brazil, in which we examined brain activity in a variety of mediums, healers, and others attaining altered states of consciousness.

During these studies, the opportunity arose to examine the EEG effects of the psychoactive alkaloid preparation *ayahuasca* or *daime,* in a sample of members of the Brazilian shamanistic religion, the Santo Daime Doctrine. In Brazil, this substance has legal, sacramental status. Both published reports of the effects of hallucinogens on the EEG and reports we received from Brazilian members of Santo Daime suggested the likelihood that some aspects of brain activity during the ritual of *ayahuasca* ingestion were similar to those in our other study populations. Therefore, a sample of Santo Daime subjects was incorporated into our field work.

To our knowledge, no EEG studies of *ayahuasca* effects on the human EEG have been published previously. Furthermore, no human EEG study employing hallucinogenic compounds has appeared in a scientific journal in 30 years.

However, several studies of the pharmacologic and psychological aspects of long-term *ayahuasca* use in Brazil have been published recently. Callaway et al. (1994) reported data on serotonin uptake sites in long-term male users. In that study, an increased number of binding sites (B_{max}) was found, whereas the dissociation constant (K_d) was the same for experimental and control groups. Findings concerning the psychological aspects of *ayahuasca* use (Grob et al., 1996) included remission of psychopathology and overall high functional status of people engaging in sacramental use.

Also, McKenna (1995) discussed *ayahuasca* in a review of the role of natural products in the development of psychopharmacology and CNS-active agents. Callaway et al. (1996) reported the quantitative analysis of N,N-dimethyltryptamine (DMT) and harmala alkaloids in human plasma after oral ingestion. Desmarchelier et al. (1996) reported shamanic practices among the Ese'eja of south-eastern Peru which included the use of *ayahuasca*. Leal and Elisabetsky (1996) investigated the pharmacologic activity of *P. carthagenesis*, sometimes used as a component of *ayahuasca*, along with *P. viridis*. They found *P. carthagenesis* to be devoid of alkaloids.

EEG data were collected at one of twelve centers affiliated with the mother church at Céu do Mapía, located in the upper Amazon. This center was Céu do Mar, located on a mountainside within the city limits of Rio de Janeiro. In addition to the recording of physiological data, a videotape was made of the Santo Daime rituals and the ingestion of *ayahuasca*, or *daime* as the practitioners term it, during these rituals. The *Padrinho*, the spiritual leader of the community, and other leaders of the Center were very supportive of this study; without their help and encouragement it would not have been possible.

The drink is frequently prepared from the vine *Banisteriopsis caapi* (Spruce ex Griseb.) Morton (Malpighiaceae) and the bushy plant *Psychotria viridis* Ruiz & Pav. (Rubiaceae). Preparation of *ayahuasca* by the Santo Daime Doctrine, a process termed *Feitio* (the making), has been described by Richman (1990 – 91). After the ritual harvesting of the two plant components, pots are filled with alternating layers of pulverized leaves and vines. Water is added and boiling is commenced. This is done in silence.

"The person in charge – usually the Padrinho – must concentrate on the daime as it 'comes to life' and on any factors in the astral plane that are affecting its creation" (Richman, 1990–1991)

Although the *Padrinho* informed us that *B. cappi* and *P. viridis* were the two components used, we did not verify this by obtaining plant samples.

The chemical composition of *ayahuasca* is described by McKenna and Towers (1985):

"most mestizo ayahuasca brews contain substantial amounts of β-carbolines and N,N-dimethyltryptamine (DMT). The DMT is a serotonic (5-hydroxytryptamine or 5-HT) agonist. The major β-carbolines are harmine and tetrahydroharmine, with lesser amounts of harmaline ... the hallucinogenic activity of ayahuasca is probably due to DMT ... ."

Harmine and tetrahydroharmine are close biosynthetic relatives of the natural alkaloid harmaline found in these plants. Thus, the DMT is probably responsible for most of the hallucinogenic activity while the β-carbolines supply the MAO inhibitors necessary to maintain the oral activity of DMT.

Strassman et al. (1994) state that 0.2 to 0.4 mg/kg of intravenous DMT:

"elicited the nearly instantaneous onset of visual hallucinatory phenomena, bodily dissociation, and extreme shifts in mood, which totally replaced subject's previously ongoing mental experiences. Lower doses, 0.05 and 0.1 mg/kg, were not hallucinatory; emotional and somasthetic effects predominated."

Also, harmaline and the other β-carbolines are themselves hallucinogenic, although the effects are mild at the concentrations commonly found in *ayahuasca* (1– 3 mg/kg) (Callaway et al., 1994).

Shulgin (1977) discusses the effects of higher doses (5 mg/kg or higher):

"The effective dose range of harmaline in man is 70 – 100 mg i.v., or 300 – 400 mg orally. The initial effects are noted about one hour following oral administration and persist for about six hours following ... . The modality most consistently affected by harmaline is the visual sense. There can be vivid images generated, often in the form of meaningful dream-like sequences, and frequently containing subject matter such as wild animals or jungle scenes."

According to Naranjo (1987):

"... the effects of harmaline are subjectively different from the LSD-like hallucinogens in that this alkaloid causes no depersonalization or perceptual changes in the environment, though it shares with the hallucinogens the effect of eliciting visual imagery with eyes closed."

Naranjo proceeds to discuss this imagery. In an earlier study in which he gave harmaline to 30 naive North American volunteers, the same specific animal imagery was reported as that from South American Indians. Naranjo concluded that:

"traditional ayahuasca imagery is not only confirmatory of tradition but a spontaneous symbolization of a characteristic experience or state of consciousness elicited by the ayahuasca alkaloids."

McKenna and Towers (1985) state that *ayahuasca* is considered by native people to be the:

"healer's passport to supernatural dimensions ... with

which the healer is able to diagnose disease, divine the supernatural causes of illness, predict the future, and see and communicate across distances."

It is therefore understandable that members of religions employing *ayahuasca* as a sacrament would prefer the term "entheogenic" to "hallucinogenic" to describe ayahuasca's mind-altering effects.

EEG effects

Use of the EEG to assess the effect of synthesized drugs on the CNS is known as the "Pharmaco-EEG"; when combined with statistical analytic methods, its use is termed the "Quantified Pharmaco-EEG" or QPEEG. These methods have focused primarily on the effects of these drugs on the frequency and amplitude characteristics of the spontaneous brain rhythms, although stimulus-locked, event related potentials can also be studied. The cumulative evidence suggests that QPEEG changes are valid measures of functional changes in the brain and might be related to pharmacokinetics, dynamics, and bioavailability of these drugs (Fink, 1985). Also, QPEEG methods have been used fruitfully in the study of natural substances in psychiatry (Itil & Martorano, 1995).

Although several hallucinogen studies with human subjects have been approved in recent years, previous federal restrictions have resulted in the absence of human EEG-hallucinogen studies during the previous generation. The earlier human reports are less quantitative and more descriptive than current studies. It is of interest to note Fink's (1978) observation that small samples of 10 – 15 subjects are sufficient to elicit characteristic EEG profiles.

The two major components of *ayahuasca,* the β-carbolines and N,N-dimethyltryptamine (DMT), are reported to desynchronize the EEG and increase the power at high frequencies in animal and human studies. Fuentes and Longo (1971), describing the effects of harmine and harmaline in animal studies, state:

"... the characteristic EEG effects of these two alkaloids is an increase in both frequency and voltage at the cortical and hippocampal level."

Further, in an experiment with six rabbits, they found that three curarized animals had the same EEG response as the three controls, indicating that the augmentation of high frequencies in the EEG was not due to muscle (EMG) activity. Examining for possible EMG activity is essential when studying high frequency electrical activity (over 30 Hz) recorded on the scalp.

Itil (1968) stated that the indole hallucinogens produced "acceleration of all EEG frequencies and desynchronization" in the human EEG, while clinically "they are considered central stimulatory compounds and can produce thought disorders and perceptual disturbances." He also noted a decrease in slow waves after IV administration. The group of drugs tested included LSD-25, mescaline, and cyclocybine, but he generalized this type of EEG as being characteristic of the action of all hallucinogens, which would therefore include also the indolalkylamines psilocybin and DMT.

In concordance with this, Fink (1978) cited Wikler's (1954) earlier findings, and stated:

"... regardless of the nature of the drug administered, EEG synchronization was associated with euphoria, relaxation and drowsiness; EEG desynchronization was associated with anxiety, hallucinations, fantasies, illusions or tremors."

During the 1950s and early 1960s, a predominant tenet in pharmacology was that there was no association between the EEG and behavior. However, Bradley and Fink's (1968) studies of the clinical and EEG effects of psychopharmacologic compounds supported the association of human behavior with EEG patterning, rather than with the chemical structures of these compounds.

Fink (1978) therefore grouped the following hallucinogenic drugs together as "Class IIb," producing decreases in slow (theta and alpha) wave activity and increases in fast (beta) waves: amphetamine, LSD-25, mescaline, methamphetamine, methylphenidate, and psilocybin. Fink summarized the findings of six studies involving three investigators, the first published 1963 and the last in 1969.

As was customary in earlier EEG studies, frequencies above approximately 30 Hz were rarely examined. However, in the past twenty years, there has been increasing evidence of the importance of higher frequencies in brain function and conscious experience, especially in the 36 – 44 Hz ("40 Hz") band of activity (Sheer, 1984; Llinás & Ribary, 1992, 1993). We have therefore selected this frequency band for analysis of high-frequency brain activity.

Methods and Materials

Subjects and Data Collection

Data reported here were collected under field conditions from eleven subjects over a nine-month period during rituals, in four separate data recording sessions. The extended data collection period was due to the fact that the investigators were engaged in other studies in Brazil and their presence at Céu do Mar in Rio de Janeiro was only periodic. Also, the rituals during which *ayahuasca* is ingested occur only twice a month (there are also some other special rituals); therefore, data collection was dependent on the presence of the researchers in Rio de Janeiro on those specific days. Other constraints were the limited number of research personnel,

limited number of Electrocaps used for electrode application, plus the special demands created by work of this type conducted in a field setting. No special rituals were scheduled for this research, nor did the researchers influence the manner or quantity of *ayahuasca* administered.

Two subjects were recorded on our first visit to their Center and three subjects were recorded during the second, third and fourth visits. They ranged in age from early twenties to early fifties (mean = 35.8 years); there were 6 men and 5 women. Their participation in the Center and use of *ayahuasca* varied from four months to 15 years.

All subjects volunteered to participate by having their EEGs recorded and were not paid. The subjects decided to volunteer when they came to the Center for regularly-scheduled rituals and heard that volunteers were needed for the experiment. Informed consent was obtained from all subjects.

Drug Administration

The quantity and concentration of *ayahuasca* given to a participant was at the discretion of the community elders; the researchers provided no input into this process. Therefore, a placebo condition was not possible. All administrations were 75 ml. The participants were weighed on a spring scale so that dosages could be calculated in units of mg/kg. Typically, three or four administrations occurred over the time course of a meeting. Our EEG data were collected before and after the first administration.

Upon analysis, we found that for the three major components of *ayahuasca*, the average doses were as follows:

DMT (average dose = 0.67 mg/kg po)
harmine (average dose = 0.90 mg/kg po)
tetrahydroharmine (average dose = 0.71 mg/kg po).

Materials Used in Chemical Analysis

Dimethyltryptamine (DMT) was obtained from *Virola sebifera* Aubl. (Myristicaceae) (Kawanishi et al., 1985). Harmine, harmol and harmaline were purchased from Sigma Co., U.S.A., and *p*-aminobenzoic acid from Nacalai Tesque Industries, Japan. Tetrahydroharmine (THH) was prepared by the reduction of harmaline with $NaBH_4$ in MeOH solution and confirmed by ^1H NMR, EI and CIMS. Six alkaloids were obtained from *Banisteriopsis caapi*, i.e., harmine-*N*-oxide, harmic acid methyl ester, harmic amide, acetylnorharmine, ketotetrahydronorharmine and harmalinic acid (Hashimoto and Kawanishi, 1975, 1976).

Analyses of Samples

Four different *ayahuasca* samples (Santo 1–4) were obtained from the study site and were representative of those generally used by the study population. These were each frozen and lyophilized. The residues were dissolved in ethanol (1 mg/40 µl), containing *p*-aminobenzoic acid as an internal standard (IS) and centrifuged at 2000 g for 10 min. Each supernatant (4 µl) was subjected to HPLC analysis. The reference alkaloids were separated by HPLC using a model 803C manometric module with a model 811 mixer (Gilson Medical Electronics), and using a Wakopak Wakosil II-5 C-18 RS (column size 4.6 mm i.d. x 150 mm, Wako Pure Chemical Industries Ltd., Japan). The mobile phase was 20 mM phosphate buffer (pH 3.0) (A), to which MeOH (B) was added by a linear gradient: initially, 20% of B for 20 min, followed by 40% of B for 10 min, with a flow rate of 1 ml/min. Alkaloids were detected at 254 nm by Holochrome (Gilson Medical Electronics) and concentrations were calculated by C-R2AX (Shimadzu Corporation, Japan).

LC/APCI-MS was carried out using a Hitachi M-10000H instrument, connected to a Hitachi L-6200 intelligent pump and Hitachi L-4000 UV detector. LC was performed using a Wakopak Wakosil II-5 C-18 RS (4.6 mm i.d. x 150 mm). The mobile phase used was 0.1M $AcONH_4$ (pH 3.8) (A) to which MeOH (B) was added by linear gradient: initially, 20% of B for 10 min, followed by 30% of B for 10 min, 35% of B for 10 min, 40% of B for 15 min, 45% of B for 5 min, and 50% of B for 40 min, with a flow rate of 1 ml/min. Alkaloids were also monitored by UV (254 nm). APCIMS conditions were the following: nebulizer and vaporizer temperatures, 190 °C and 400 °C, respectively. Drift voltage was 45 V. The quasimolecular ions were monitored with the SIM method.

EEG Recording Procedure

Our data were recorded with a NeuroSearch-24 topographic brain mapping system, manufactured by Lexicor Medical Technology, Inc. This system consisted of 19 channels of EEG with four additional auxiliary channels. An electrode cap made by Electrocap Corp. was also used.

Electrode caps were applied to subjects before the rituals began. With some subjects, additional EMG electrodes were used in order to detect the possible presence of scalp muscle activity, which would confound the interpretation of high frequency EEG data. A data sampling rate of 256 EEG samples per sec was used for 8 sessions; EEG data for the remaining sessions were sampled at a rate of 512 EEG samples per sec.

One-hundred second eyes-closed and eyes-open baseline EEGs were recorded. During eyes-open recordings,

subjects fixated on a mark at eye level, one meter distant. The subjects then joined the rituals, and after approximately one-half hour drank the *ayahuasca.* Between 45 minutes and one hour later, the subjects returned to the testing room and had 100 sec eyes-closed and eyes-open EEGs recorded. During typical ceremonies, two or three additional administrations were made at similar time intervals; however, further EEG data were not recorded.

Data Editing and Reduction

Physiological data were digitized on-line and stored on the hard disk of a 486-33 DX transportable computer during the ceremonies. After the ceremony, the data were transferred to a 250-megabyte tape drive. Data editing and reduction were performed off-line. Due to an equipment malfunction, the eyes-open EEG records of two subjects were improperly stored and later discovered to be unusable. All remaining epochs of EEG data were visually inspected for eye movement, obvious muscle tension (EMG), and other artifacts. Epochs containing such artifacts were excluded from further analyses.

Power spectra were computed on the artifact-free EEG epochs by a digital signal-processing chip and associated hardware in the Lexicor NeuroSearch-24. For each of 19 scalp sites, the mean power density in the theta (4 – 8 Hz), alpha (8 –14 Hz), beta (14 – 30 Hz), and "40 Hz" (36 – 44 Hz) frequency bands was computed. A log transform was applied to the spectral data in order to normalize the distributions before statistical analyses were conducted. Visual inspection of the data histograms indicated that this transformation worked as expected and that the log power-density distributions were approximately normal.

Results

EEG Results

The effects of *ayahuasca* on the EEG power spectrum were examined by a series of matched, two-tailed t-tests comparing the pre-drug baseline with the post-ingestion EEG record, for each frequency band and scalp site. Separate statistical analyses were performed on the eyes-closed and eyes-open conditions. These are presented in Table 2.

For the eyes-closed condition, data from all 11 subjects were available for analysis. Drug effects were found only in the 40 Hz band; all t-tests in the lower frequency bands were nonsignificant (all $p > .10$). However, nonsignificant drug effects in the theta, alpha, and beta (14 – 30 Hz) bands were in the direction noted by Fink (1978) in earlier studies. That is, there was a slight decrease in theta and alpha and a slight increase in beta, at most recording sites.

Drug ingestion was associated with significantly enhanced 36 – 44 Hz power at the T5 scalp site overlying the left posterior temporal cortex ($t = 2.43$, $p = .035$, $df = 10$), and the 01 site overlying the left occipital lobe ($t = 2.29$, $p = .045$, $df = 10$). The same trend was observed at P3, Pz, and 02: left parietal, midline parietal, and right occipital areas, respectively (all $p < .10$)

The topographic distribution of *ayahuasca's* effects on 40 Hz power is shown in Figure 1.[1]

As can be seen in the map on the left (Eyes Closed), the sites significantly affected by *ayahuasca* are primarily over the left posterior (occipital, temporal and parietal) areas of the cortex. Similar, but larger and more extensive effects, involving most of the posterior scalp, were observed for the eyes-open condition. These results are depicted on the right-hand topographic map in Figure 1. As previously mentioned, data from only nine subjects were used for this analysis. *Ayahuasca* effects on the lower frequency bands were generally in the same direction as with eyes closed (Table 2) and were again nonsignificant (all $p > .10$). Significant enhancements ($p < .05$) of 40 Hz power were observed at the following eight scalp sites (Table 2): C3 and Cz over the central cortex; P3, P4, Pz over the parietal cortex, 01 and 02 over the occipital cortex, and T6, overlying the right posterior temporal lobe. A trend in this direction was also observed at T5 ($p = .064$).[2]

As seen in the topographic map, the distribution of significant effects observed in the eyes-open condition

[1] The topographic distribution of observed drug effects on 40 Hz power seen in Figure 1 argues against an EMG interpretation of the results for both eyes-open and eyes-closed conditions. The predominantly posterior scalp areas involved are the most distant from the most likely sources of artifact: frontalis and temporalis muscle activity. Moreover, the results of a Principal Components Analysis suggest that the activation of the posterior cortex was a separate process from probable EMG activity, which was seen frontally and fronto-laterally.

[2] Topographic brain mapping has progressed to the point where some investigators are constructing maps from electrodes at hundreds of scalp sites. The more complete the mapping of the electrical fields from the brain, the better the graphical representation and understanding of brain function, and the increasing unlikelihood that any data would remain significant after correction for multiple analysis. Therefore, an alternative approach to this problem is to consider whether the integrity of the maps as a whole reflects the physiological parameters of the experiment. In our experiment, there were 19 t-tests for each of the eyes-open and eyes-closed conditions implicit in our 40 Hz analyses; therefore, the probability of a Type I error may be greater than the specified α-level.

is similar to that observed in the eyes-closed condition, except that the effects are stronger and more widespread, spreading to include most of the posterior regions.

Results of Analyses of ayahuasca

The concentrations of dimethyltryptamine, harmol, tetrahydroharmine, harmaline and harmine in the four samples (Santo 1–4) were calculated and expressed as mg of each major alkaloid per 75 ml of each ayahuasca sample analyzed (the usual amount ingested by the subjects). These data are presented in Table 1. In addition, trace amounts of harmalinic acid, harmine-N-oxide, ketotetrahydronorharmine, harminic acid methyl ester and acetylnorharmine were detected by HPLC/MS analysis in each of the Santo samples. It can be noted that of the four ayahuasca samples the total alkaloid content was greatest in Santo 3 (100%), compared to which the total alkaloid contents of Santos 1, 2, and 4 were 52.8%, 75.9%, and 86.0%, respectively (Table 1).

Table 1. Alkaloid Analyses of Ayahuasca Samples Santo 1–4 (mg/75 ml).

Sample Number	DMT[a]	Harmol	THH[b]	Harmaline	Harmine
Santo 1	41.8	2.79	40.1	3.90	54.6
Santo 2	28.4	1.94	27.4	2.90	39.0
Santo 3	51.7	4.12	58.2	5.88	68.8
Santo 4	43.4	3.34	50.1	5.56	60.1
Mean	41.3	3.05	43.9	4.56	55.6

[a] DMT, N,N-dimethyltryptamine;
[b] THH, tetrahydroharmine

Discussion

EEG findings

Increases in power of the 36 – 44 Hz frequency band ("40 Hz") were observed following ritualistic *ayahuasca* ingestion. In the eyes-closed condition, we observed a predominantly left-posterior distribution of significant *ayahuasca*-induced increases in 40 Hz power. In the eyes-open condition, the effects were similar to those observed in the eyes-closed condition, with the exception that they were stronger and more widespread, involving most of the posterior regions of the cortex. Previous studies have manipulated human 40 Hz EEG either with eyes open (see Bird et al., 1978; Sheer, 1984) or with eyes closed (see Llinás & Ribary, 1993), but none has manipulated 40 Hz under both conditions.

EEG power in the alpha and theta frequency bands tended to decrease, while power in the beta band (14 – 30 Hz) tended to increase. These tendencies are in the direction of studies reported 30 years ago with other hallucinogenic compounds (reviewed by Fink, 1978). The fact that power measurements in these three bands in our data were not significantly different from preingestion baseline values may be due to two potential factors. First, we measured the EEGs before and after the first drug administration. Most subjects ingested three or four doses over the course of the rituals, and therefore, the effects on the EEG may well have been more pronounced following subsequent administrations. Second, the quantitative analysis of the EEG is much easier to accomplish today than it was 30 years ago. In general, the earlier reports were more qualitative, and so comparisons to our data are suggestive, at best.

Table 2. Effects of Ayahuasca on EEG Power Density.

• Nonsignificant EEG effects

EEG Frequencies:	Eyes Closed (n = 11)	Eyes Open (n = 9)
Theta (4 – 8 Hz):	all sites n.s., p >.10	all sites n.s., p >.10
Alpha (8 –14 Hz):	all sites n.s., p >.10	all sites n.s., p >.10
Beta (14 – 28 Hz):	all sites n.s., p >.10	all sites n.s., p >.10

• Significant and near-significant EEG effects

EEG Frequencies:	Eyes Closed (n = 11)	Eyes Open (n = 9)
"40 Hz"	T5; t(10) = 2.43, p = .035	P3; t(8) = 4.08, p = .004
(36 – 44 Hz):	O1; t(10) = 2.29, p = .045	O2; t(8) = 3.51, p = .008
	Pz; t(10) = 2.16, p = .056	O1; t(8) = 3.10, p = .015
	P3; t(10) = 2.09, p = .063	Pz; t(8) = 3.00, p = .017
	02; t(10) = 1.89, p = .088	C3; t(8) = 2.93, p = .019
	all other sites, p >.10	Cz; t(8) = 2.87, p = .021
		P4; t(8) = 2.43, p = .041
		T6; t(8) = 2.39, p = .044
		T5; t(8) = 2.15, p = .064
		all other sites, p >.10

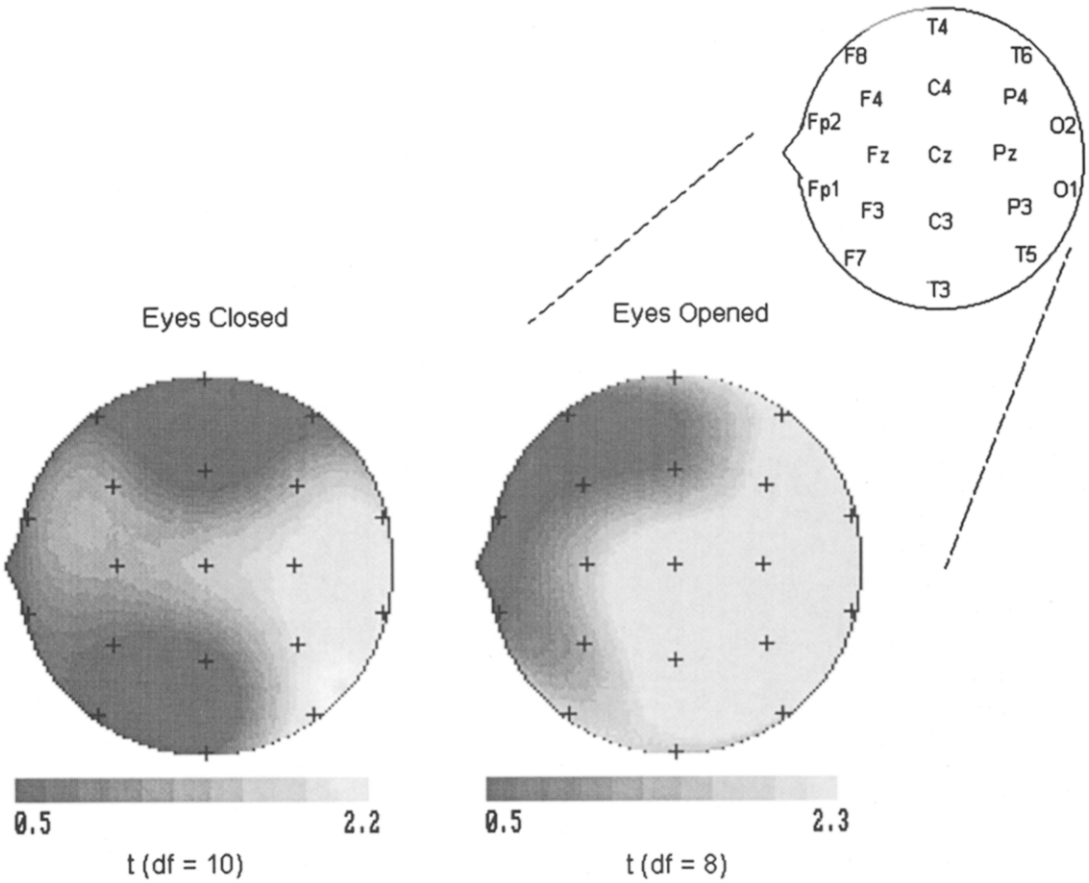

Fig. 1. Topographic brain maps of effects of Ayahuasca on 40 Hz EEG.
The topographic map on the left shows the distribution of drug effects on 40 Hz power in the eyes-closed condition; the map on the right is for the eyes-opened condition. Each map depicts a top-down or "bird's eye" view of the head, facing left (the nose points to the left). These significance probability maps plot the gray-scaled t-statistic from the tests of pre-ingestion vs. post-ingestion EEG power at each of 19 scalp sites, with an interpolation algorithm used for intermediate points on the scalp. The lightest shade of gray indicates a t-score associated with a p-value of .05 or less. The darker shades of gray indicate progressively smaller, and nonsignificant, t-statistics. The schematic diagram in the upper right of the figure shows the International "10-20 System" of electrode placements.

In addition, the study of 40 Hz activity in scalp-recorded EEGs began in the 1970s with the work of Sheer (1984). Clinical EEGs in general, as well as many research studies, still do not investigate frequencies beyond approximately 30 Hz. However, the frequency range above 30 Hz has become increasingly important in the understanding of brain function and conscious experience.

Chemistry

The Santo 3 sample was 15.8% more concentrated than the next most-concentrated sample, Santo 4 (Table 1). Santo 3 was used in the "Star Ceremony," a special healing ritual, in which participants ingested more potent dosages. EEG data from two of our subjects were obtained with the more highly concentrated *ayahuasca*.

The β-carbolines in our samples produced concentrations much less than 5 mg/kg at the ingested dosages. Therefore, according to Shulgin (1977) and Callaway et al. (1994), they probably contributed little to the hallucinogenic effects.

In a recently reported study (Callaway et al., 1996), in which human plasma levels of DMT and the β-carboline alkaloids were quantitated after *ayahuasca* ingestion, the average doses for the major alkaloids (based on ingestion of 2 ml/kg *ayahuasca* by 59 kg individuals) were as follows: harmine, 204.0 mg; harmaline, 24.0 mg; tetrahydroharmine, 128.4 mg; and DMT, 28.8 mg. The amount of *ayahuasca* ingested in this study is approximately 1.5 times that ingested in our study of the Santo Daime practitioners, in which the average doses for the major alkaloids were: harmine, 55.6 mg; harmaline, 4.56 mg; tetrahydrohar-

mine, 43.9 mg; DMT, 41.3 mg; and harmol 3.05 mg. Thus, it can be seen that in the Santo Daime study the dosages of the β-carbolines were significantly lower, while that of DMT was higher, despite the smaller amount of *ayahuasca* consumed.

Phenomenology

Informal, anecdotal reports from our subjects revealed amplification of mental contents, thoughts and feelings from the present and past, and intense, vivid visions. These often were archetypal, such as religious figures like Christ, the Virgin Mary, the Buddha, and other spiritual personages and deities. These visions were most intense with the eyes closed, which is consistent with previous self-reports of mental imagery being elicited when eyes are closed (Naranjo, 1987).

Our subjects' experiences differed from Naranjo's subjects who ingested harmaline and experienced the same animal imagery as Amazonas shamans. These experiential differences between studies may be due to differences between the effects of harmaline and DMT or set and setting factors.

At 0.4 mg/kg IV DMT, subjective reports of research subjects in the investigations of Strassman et al. (1994) differed somewhat from ours. This may have been due partly to effective dosage differences. Also, differences in set and setting may have contributed to experiential variation, since our subjects were members of a religion that uses *ayahuasca* sacramentally, and our measurements were performed at their meeting place. In contrast, the study of Strassman et al. was performed in a laboratory setting with subjects who were "experienced hallucinogen users," not members of a religion.

The activation of the visual cortex and associated posterior brain sites as indicated by the 40 Hz effects in our data is consistent with many reports that *ayahuasca* intensifies visual imagery. However, it should be emphasized that in this study, although we asked our subjects about their phenomenological experiences during *ayahuasca* intoxication, we made no attempt to correlate these subjective reports with simultaneously measured EEG activity. Therefore, we cannot establish one-to-one correspondences between those phenomenological reports and the EEG alterations observed. Nonetheless, the present findings suggest that future studies could fruitfully examine the question of whether or not there is a more systematic relationship between drug-induced phenomenological experiences and EEG effects. For example, it would be interesting to see if the new Hallucinogen Rating Scale, developed by Strassman et al. (1994), could help establish a link between which neurophysiological systems are involved, subjective effects, and dosage levels.

Thalamocortical 40 Hz brain model

Basar (1980), Basar et al. (1984, 1989), propose that 40 Hz EEG, as well as other EEG frequencies, may serve as a means for embodiment of internal sensory and cognitive mental activities. Llinás and Ribary (1992, 1993) interpret a variety of findings dealing with possible mechanisms underlying the elicitation of 40 Hz neuronal oscillations in various states to propose a consciousness-generating mechanism which produces not only the dreaming state (REM sleep), but hallucinations and daydreaming states as well. The model consists of at least two systems, each involving feedback circuits between thalamic nuclei, the thalamic reticular nucleus and the cerebral cortex. These two systems operate in parallel. *System One* consists of the specific thalamic (sensory and motor) nuclei, while *System Two* consists of the nonspecific thalamic nuclei (intralaminar complex), which has more extensive projections to cortical pyramidal cells, going to superficial layers (layer I) of the entire cortex, and to layers V and VI. A hallmark of the operation of System Two is the presence of hyperattentiveness to internal stimuli.

Steriade et al. (1991, 1993) have suggested that for 40 Hz activity to be recorded from scalp electrodes, a large number of cells must be synchronized. One key to achieving this is through the use of inhibitory as well as excitatory circuits. Inhibition serves to help quickly synchronize large populations of pyramidal neurons. According to Steriade et al. (1993) a variety of neurotransmitters, including serotonin (5-HT), are released from various ascending activating systems (brainstem, hypothalamus and basal forebrain). These neurotransmitters abolish low frequency rhythms in thalamocortical systems during waking and REM sleep and promote high frequency oscillation. This increase in frequency is achieved both in the thalamus and in the cortex via depolarization of pyramidal cells. Application of 5-HT produces a selective depolarization in thalamic reticular cells (nucleus reticularis). Since thalamic reticular cells are inhibitory, depolarization of reticular cells should increase the amount of inhibition supplied to thalamic nuclei, and thereby enhance synchronization.

The 40 Hz brain model and *ayahuasca* effects

When subjects have their eyes closed, it is likely that, relative to the baseline condition, the increase in 40 Hz activity may be due to the 5-HT-like effects of *ayahuasca.* These effects would result in enhancing the inhibitory activity within the thalamic reticular nuclei of *System Two* (the non-specific thalamic system), not due to any specific visual input, but reflecting simply an amplification of endogenous brain activity. Perhaps

this activity is sculpted by the structure of the existing neural circuitry and by system biases into the meaningful images experienced by *ayahuasca* users. Hence, we observed increased 40 Hz EEG in the left occipital, temporal, and parietal areas with lesser effects in surrounding tissue.

When subjects opened their eyes, it is likely that *System One* (visual modality) activity heightened, wherein the increased thalamic reticular nuclear inhibition spread the synchronization over a much greater area of the cortex. Thus, we see enhanced 40 Hz EEG over not only the left occipital-parietal areas, but also most of the posterior region.

The differences in EEG topography, between the eyes-closed and eyes-open conditions, suggest that the subjects' conscious experience changed also, particularly visual imagery. Anecdotal accounts we gathered are in accord with this.

Conclusion

Power in the 36 – 44 Hz frequency band ("40 Hz") was significantly increased following ritualistic *ayahuasca* ingestion. The major components of our *ayahuasca* samples were DMT, tetrahydroharmine, and harmine. Although this study was conducted under field conditions and without placebo control, the results are consistent with, and extend, earlier EEG studies of other hallucinogens. Those showed similar increases in high-frequency brain activity but did not examine the 40 Hz band, as we did.

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