

Ayahuasca in Adolescence: A Neuropsychological Assessment†

Evelyn Doering-Silveira, M.Sc.*; Enrique Lopez, Psy.D.**; Charles S. Grob, M.D.***;
Marlene Dobkin de Rios, Ph.D.****; Luisa K. Alonso, Ph.D.*****;
Cristiane Tacla, Psy.*****; Itiro Shirakawa, M.D., Ph.D.*****;
Paulo H. Bertolucci, M.D., Ph.D.***** & Dartiu X. Da Silveira, M.D.*****

Abstract—The purpose of the study was to evaluate neuropsychologically adolescents who use ayahuasca in a religious context. A battery of neuropsychological tests was administered to adolescents who use ayahuasca. These subjects were compared to a matched control group of adolescents who did not use ayahuasca. The controls were matched with regards to sex, age, and education. The neuropsychological battery included tests of speeded attention, visual search, sequencing, psychomotor speed, verbal and visual abilities, memory, and mental flexibility. The statistical results for subjects from matched controls on neuropsychological measures were computed using independent t-tests. Overall, statistical findings suggested that there was no significant difference between the two groups on neuropsychological measures. Even though, the data overall supports that there was not a difference between ayahuasca users and matched controls on neuropsychological measures, further studies are necessary to support these findings.

Keywords—adolescence, ayahuasca, cognition, hallucinogen, neuropsychology, religion

Ayahuasca is a hallucinogenic beverage made essentially of two Amazonian plants. It is prepared by boiling the stems of a vine named *Banisteriopsis caapi* and the leaves of *Psychotria viridis*, although other plants are often mixed in as well. This psychedelic tea has been used for centuries by native Indian and mestizo shamans in Peru,

Colombia, and Ecuador for healing and divination. In the eighteenth century ayahuasca was taken up by the colonists as a result of their proximity to tribal peoples during the Colonial period. The mixing of native contexts with nonnative settings resulted in the incorporation of ayahuasca as a psychoactive ritual sacrament in ceremonies by several

†This research was funded in part with a grant from the Heffter Research Institute, Santa Fe, New Mexico and from the Fundação de Amparo a Pesquisa do Estado de São Paulo, Brazil. Special thanks are due to Dr. Glacus Da Souza Brito and Dr. Otavio Castillo Campos Derrera, who served as liaison between the União do Vegetal Church and the Research Team.

*Neuropsychologist, Addiction Unit (PROAD), Department of Psychiatry, Federal University of São Paulo (UNIFESP), São Paulo, Brazil.

**Clinical Assistant Professor, Department of Psychiatry and Behavioral Sciences, David Geffen School of Medicine at UCLA, Los Angeles, California.

***Director, Division of Child and Adolescent Psychiatry, Harbor/UCLA Medical Center, Torrance, California.

****Associate Clinical Professor, Department of Psychiatry and Human Behavior, University of California, Irvine.

*****Professor, Brasilia Catholic University Graduate School, Brazil.

*****Psychologist, Department of Psychiatry, Federal University of São Paulo (UNIFESP), São Paulo, Brazil.

*****Professor, Department of Psychiatry, Federal University of São Paulo (UNIFESP), Brazil.

*****Professor, Department of Neurology, School of Medicine, Federal University of São Paulo (UNIFESP), Brazil.

*****Professor, Department of Psychiatry, School of Medicine, and Director, Addiction Unit (PROAD), Department of Psychiatry, Federal University of São Paulo (UNIFESP), São Paulo, Brazil.

Please address correspondence and reprint requests to E. Doering-Silveira, Rua Florida 320, 04565-000, São Paulo, Brazil; email:dartiu@psiquiatria.epm.br

different religious movements. In Brazil, ayahuasca is used as sacrament within the context of religious practice by the syncretic churches União do Vegetal (UDV) and Santo Daime, among others; this practice was legally approved in 1987. Churches using ayahuasca in Brazil differ somewhat from one another as to their principles, rituals, and composition of the tea.

According to the laws of the UDV, the use of ayahuasca is restricted to religious ceremonies where multigenerational families meet twice a month for approximately four hours. In sound accordance with the principles of this church (UDV), adolescents are encouraged to voluntarily join their parents and drink the ayahuasca tea during the ritual ceremonies. Adherents commonly believe that ayahuasca is harmless and potentially beneficial for adolescents (e.g., prophylaxis against drug abuse) as long as it is imbibed in a religious context. To date, however, this assumption has never been confirmed by means of controlled studies on the effects of periodic ritual use of ayahuasca by adolescents.

In 1993, a multinational research team composed of American and Brazilian physicians, psychologists and social scientists conducted a comprehensive study with UDV adult members in Manaus, the large capital city of the state of Amazon located in the heart of the Brazilian tropical rainforest. This was the first investigation of what is called the Hoasca Project. Phase I evaluations of pharmacokinetics, neuroendocrine assays, and serotonin function were carried out as well as psychiatric, medical health, and baseline neuropsychological screenings. (Callaway et al. 1999, 1996, 1994; McKenna et al. 1998; Grob et al. 1996). Contrasting the findings from 15 men who had been UDV members for at least 10 years (subjects) with demographically-matched controls who did not belong to the UDV and had never consumed ayahuasca, this pilot investigation concluded that there was no evidence of any injurious effect which could have been induced or caused by or be related to the ritualistic use of ayahuasca. On the contrary, these long-term UDV members reported a marked decline in severe psychiatric disorders, including discontinuation of cigarette, alcohol, and recreational drug use following their entry into this sect. Dramatic improvements in their personal values, behavioral compliance, and sense of purpose were described as well. Neuropsychological testing of long-term adult UDV members and matched controls found the UDV members to have statistically significant superior concentration and short-term memory on some measures, though overall both groups scored well.

Currently, in Brazil, adolescent membership of the UDV is estimated at over 1,200. A thorough investigation of UDV adolescents' cognitive profile is definitely warranted when one considers the slow but ever-growing population that consumes ayahuasca worldwide on a regular basis, and the significant proportion of younger people who are among them.

OBJECTIVE

The primary objective of this study is to assess the effects of long-term use of ayahuasca on adolescent cognitive functioning.

SUBJECTS AND METHOD

Sample

Eighty-four adolescents from three cities in Brazil (São Paulo, Campinas, and Brasilia) voluntarily participated in this study. Ayahuasca-consuming adolescents were randomly selected among participants of three distinct UDV churches, whereas the comparison group included randomly selected adolescents according to pairing criteria. Interviews were conducted by a trained psychiatrist in 2001 in two different Brazilian cities. Four of the adolescents (one subject and three controls) were not paired and as such were automatically excluded from the statistical analysis. As a result two groups of 40 adolescents ($N = 80$) between the ages of 15 and 19, from both sexes, were considered in this study. The first group, hereafter designated as the *subjects*, was composed of 40 adolescents from the Brazilian syncretic church UDV (União do Vegetal) who had drunk ayahuasca within a ritual context at least 24 times during the last two years prior to the neuropsychological assessment. They were 22 males and 18 females, with a mean age of 16.52 years and a standard deviation of 1.34. Most of them were White (78.9%) and their educational level ranged from first year in high school to first year in college. The second group, hereafter designated as the *control group*, was a comparison group composed of 40 adolescents who had never drunk ayahuasca (22 males and 18 females) matched on sex, age, race, and educational level to the subject group, with a mean age of 16.62 years and a standard deviation of 1.00. They were mostly White (82.1%) and their educational level ranged from first year in high school to third year in high school. Both groups had similar social and economic profiles, belonged to the same community, and shared the same environmental influences (although they did not attend the same schools). Subjects were recruited from various public and private schools whereas the comparison group of adolescents was selected from two private schools only.

Procedure

Data collection was accomplished in settings purposefully aimed at enhancing both subjects' and control's maximal motivation and collaborative attitudes as well as safeguarding the neuropsychological assessment against undesirable interferences. Thus, 20 subjects and 20 controls from Brasilia were taken on a four-day stay to a hotel located in a farm near Brasilia. Subjects and controls from São Paulo and Campinas were taken on a two-day stay to a hotel located on a quiet beach near São Paulo during two

consecutive weekends (10 subjects and 10 controls at a time). Having both subjects and controls exposed to the same environmental and psychological conditions allowed for a closer monitoring of possible confounding variables such as cigarette smoking, alcohol and drug use, poor sleeping hours, caffeine ingestion, and use of medicine, among others. Both subject and control tobacco smokers had refrained from cigarette smoking at least one hour before the assessment. Caffeine ingestion was available exclusively during breakfast time. No alcoholic beverages and other drugs were consumed 24 hours before the neuropsychological assessment. Sleeping times ranged from six to eight hours during the nights spent either at the farm hotel or at the beach hotel. Subjects had kept a minimal 20-day interval since last ingestion of ayahuasca on occasion of the neuropsychological assessment. Comfortable, quiet and well lit assessment rooms were provided. Researchers involved in data collection remained “blind” to the identity of participants throughout the study.

All adolescents and their respective parents and/or legal guardians were asked to sign an informed consent before enrollment in the study.

Neuropsychological Assessment

A comprehensive battery of neuropsychological tests was devised to assess the overall level of cognitive functioning of the adolescents. All 40 experimental adolescent subjects and 40 controls were administered a neuropsychological battery. Neuropsychological tests that assessed attention, concentration, intelligence, language, memory, executive functioning, processing speed, visuomotor skills and visuoconstructional abilities were administered. The following measures were administered: Trailmaking Test, Stroop-Victoria version, Rey-Osterrieth Complex Figure Test (ROCF), the Conners' Continuous Performance Test-II (CPT-II), and the World Health Organization/University of California at Los Angeles Auditory Verbal Learning Test (WHO/UCLA Auditory Verbal Learning Test). Additionally, subtests of the Wechsler Adult Scale of Intelligence-III (WAIS-III) were used. The following subtests were administered from the WAIS-III: Digit Span, Digit Symbol, Symbol Search, and Object Assembly. It is important to note that Portuguese versions were administered for verbal measures. For nonverbal measures, instructions were given in Portuguese.

The Trailmaking Test, which measures sequencing, visual attention and scanning, psychomotor speed, and mental flexibility, requires that a connection be made between 25 encircled numbers randomly arranged on a page in proper order using a pencil for Part A and the connection of 25 encircled numbers and letters in alternating order for Part B (Lezak 2004).

The Digit Span subtest is used as one of the measures to calculate Verbal Intelligence and the Working Memory Index of the WAIS-III. It is used to assess verbal attention.

The Digit Span subtest consists of two parts. In the first part, individuals are required to repeat sequences of three to nine digits long (Digit Forward); in the second part, examinees are asked to repeat backwards sequences of two to eight digits long (Digit Backwards). The Digit Symbol and Symbol Search are subtests from the WAIS-III that are used to assess psychomotor speed. They both are used to calculate the Processing Speed Index. The Digit Symbol subtest consists of a series of numbers, each of which is paired with its own corresponding symbol. Using a key, the individual writes the symbol corresponding to its number (Wechsler 1997). In the Symbol Search subtest, individuals scan two groups of symbols and indicate whether the target symbol appears in the search group. In the Object Assembly subtest, examinees are required to assemble puzzles as quickly as possible. It measures visual-spatial constructional abilities.

The Stroop-Victoria version is a test that measures selective attention and cognitive flexibility; it has three separate conditions (Spreen & Strauss 1998). In the first part, individuals are asked to read randomized color blocks (red, green, yellow, and blue). In the second part, the examinees are required to read words printed in different ink colors. In the last condition, individuals are given a card where color names are printed in different colored ink (the printed word never corresponds to the color name); this requires the subjects to name the color of the ink while disregarding the printed word. The Rey-Osterrieth Complex Figure Test is used to measure visuomotor skills, visual-spatial constructional ability, and visual memory (Mitrushina et al. 2005). On this measure, individuals are asked to copy a complex figure and then reproduce the design from memory 30 minutes later.

The Conners' Continuous Performance Test—Second Edition (CPT-II) is a computerized task used to assess abilities such as sustained attention, vigilance, reaction time, and impulsivity (Conners 2005). In this task, individuals are asked to press the space bar for all letters that are displayed on the computer screen except the letter X. There are six blocks, each displaying 60 letters at different interstimulus intervals. The test lasts approximately 14 minutes. A computerized report is generated at the end that includes the total number of omitted letters (omission), number of Xs pressed (commissions), and a variety of other measures related to visual attention (Hit Rate, Hit Rate SE, Variability of SE, D-prime, Beta, Perseverations, Hit RT Block Change, Hit RT SE Block Change, Hit RT ISI Change, and Hit RT SE ISI Change).

The WHO/UCLA Auditory Verbal Learning Test is a verbal memory-list test that assesses verbal learning and memory (Mitrushina et al. 2005). In this measure, examinees are read out loud a list of 15 items (list A) for five consecutive trials, each followed by a free recall test. After the fifth trial, individuals are presented with an interference trial (list B) of 15 items (Trial VI). Immediately

TABLE 1
Neuropsychological Performance of Adolescents Who Drink Ayahuasca Within a Religious Context (N = 40) Compared to a Matched Control Group (N = 40)

	Ayahuasca		Comparison Group		Statistics	
	Mean	SD	Mean	SD	<i>t</i>	<i>p</i>
Trailmaking Test						
Trail A	29.20	8.86	27.25	8.26	1.02	0.31
Trail B	61.38	25.10	56.00	15.82	1.15	0.26
WAIS-III						
Digit Span Forward	9.38	2.32	9.03	2.69	0.62	0.53
Digit Span Backward	6.83	2.26	6.48	1.97	0.74	0.46
Digit Span Total	16.45	4.27	16.00	3.46	0.52	0.61
Digit Symbol (Coding)	77.80	10.07	81.58	18.73	-1.12	0.27
Symbol Search	37.20	6.24	37.83	6.83	-0.43	0.67
Object Assembly	32.35	9.26	34.17	6.18	-1.04	0.30
Stroop-Victoria version						
Stroop I	13.03	2.27	12.60	2.22	0.85	0.40
Stroop II	16.20	3.89	14.75	3.34	1.79	0.08
Stroop III	24.95	7.14	25.05	8.00	-0.06	0.95
Rey-Osterrieth Test						
Rey Figure Copy	34.64	1.46	34.08	2.58	1.20	0.23
Rey Figure Recall	21.89	5.00	21.69	6.79	0.15	0.88
Continuous Performance Test						
CPT Omissions	2.64	4.99	1.65	1.90	1.17	0.24
CPT Commissions	10.37	6.80	10.80	5.97	-2.97	0.77
Hit Rate	406.93	77.43	400.25	73.70	0.40	0.69
Hit Rate SE	6.06	2.72	5.78	2.09	0.50	0.62
Variability of SE	7.49	5.22	7.40	5.05	0.08	0.94
D-prime	0.86	0.40	0.86	0.48	0.00	1.00
Beta	0.84	0.98	0.80	1.03	0.17	0.86
Perseverations	0.62	1.27	0.52	0.93	0.40	0.69
WHO/UCLA AVLT						
Trial I	6.73	2.34	7.20	2.05	-9.64	0.34
Trial II	10.05	2.17	11.55	1.66	-3.47	0.00*
Trial III	11.70	2.09	12.40	1.93	-1.56	0.12
Trial IV	12.48	1.82	13.38	1.23	-2.58	0.01*
Trial V	12.90	1.45	13.23	1.72	-0.92	0.36
Total I-V	53.85	7.5	57.75	5.51	-2.65	0.01*
Interference List (Trial VI)	6.58	1.83	6.83	1.81	-6.13	0.54
Short-delay (Trial VII)	12.15	1.90	12.83	1.58	-1.73	0.09
Long-delay (Trial VIII)	12.40	1.93	12.93	1.55	-1.34	0.18
Recognition (Trial IX)	14.55	0.82	14.78	0.62	-1.39	0.17

*Statistically significant ($p < 0.05$).

following the interference trial, individuals are asked to recall the first list without further presentation (Short Delay Recall, Trial VII). After about a 30-minute delay, individuals are again asked to recall the words from list A (Long Delay Recall, Trial VIII). Finally, a recognition trial (Trial IX) is administered where individuals are to identify words recognized from list A.

Data Analysis

Descriptive statistics were followed by the comparison between ayahuasca-using subjects and control groups. Strength of associations was tested with chi-square for categorical variables, whereas t-test was used for comparing continuous variables.

RESULTS

Overall, no significant differences in performance were found between adolescent ayahuasca users and matched controls on most of the neuropsychological measures. Results of the neuropsychological measures between both ayahuasca users and controls are available in Table 1.

On a neuropsychological measure of visual search, sequencing, visual attention, psychomotor speed, and mental flexibility, there was no difference between the two groups (Trail Making Test A and B, $p < 0.31$ and $p < 0.26$, respectively). On a measure of verbal attention, both subjects and controls did not score significantly different in their total Digit Span scores ($p < 0.61$). Additionally, no difference

was found on Digit Span Forward and Digit Span Backward ($p < 0.53$ and $p < 0.46$, respectively). Ayahuasca users and matched controls did not score significantly different on both subtests that measure processing speed (Digit Symbol, $p < 0.27$; Symbol Search, $p < 0.67$). Again, there was no difference between both groups on the Object Assembly subtest ($p < 0.30$). On all conditions of the Stroop test, both groups did not score significantly differently (Stroop I, II, and III; $p < 0.40$, $p < 0.08$, and $p < 0.95$, respectively). Ayahuasca users and matched controls did not differ in performance on the ROCFT in both the copy and memory conditions ($p < 0.23$, $p < 0.88$, respectively). On all measures of the Continuous Performance Test, the subjects and controls did not differ significantly (p values on all CPT measures ranged from $p < 0.24$ to $p < 1.00$).

Subjects and matched controls scored similarly on most trials of the WHO/UCLA Auditory Verbal Learning Test. However, they seemed to differ on two of the initial trials (Trial II, $p < 0.00$, and Trial IV, $p < 0.01$). Trial I, Trial III, Trial V were not significantly different ($p < 0.34$, $p < 0.12$, and $p < 0.36$, respectively). The total score of all initial trials (Total I-V) was also statistically significant ($p < 0.01$). As expected, performances on Trial VI (interference list) were comparable among groups. Short-delay memory recall (Trial VII), long-delay memory recall (Trial VIII), and recognition recall (Trial IX) were not significantly different ($p < 0.09$, $p < 0.18$, and $p < 0.17$, respectively). Table 1 displays scores on neuropsychological measures for the adolescent ayahuasca users and matched controls.

DISCUSSION

This is the first study to focus on cognition of long-term ayahuasca-using adolescents. To date there is no scientific information on the consequences of this activity, whether beneficial or deleterious, although the Hoasca Project (referred to in the Introduction to this issue of the *Journal of Psychoactive Drugs*) details some of the consequences for adult participants. The primary finding of the present study is that no overall differences in neuropsychological performance were found between the group of ayahuasca-consuming adolescents and the group of adolescents who had never used the substance. Current scientific knowledge places great emphasis on education acting as a protector against brain insults. Since good performance on neuropsychological tests is greatly influenced by educational level the authors considered good academic achievement a central aspect in this study. Both the experimental subjects and controls had maintained good academic levels, which may have contributed to their good performance.

However, it is important to note that both groups performed well and presented similar results in most neuropsychological measures except for two trials from a verbal learning memory list test, with lower scores for the ayahuasca-consuming adolescents. Although two of the initial five trials (Trial II and IV) did show a statistically significant difference between groups on the WHO/UCLA Auditory Verbal Learning Test, the groups differed only on initial trials, which are not truly indicative of memory differences between both groups. The initial trials are more likely to be assessing learning and encoding abilities and strategies (Mitrushina et al. 2005). On memory trials, later trials (Trial VI, Trial VII, and Trial IX), both adolescent groups did not statistically differ.

It is also important to note that the mean raw scores of the initial trials (Trial II and IV) of both subjects and controls were in the average range in regards to normative data among similar aged adolescents on a similar memory list task (Geffen et al. 1990). This indicates that the mean raw scores of both groups did not significantly differ when compared to adolescent normative data.

Even though this data overall supports the theory that there was not a difference between ayahuasca users and matched controls on neuropsychological measures, one can argue that the difference in scores may suggest that ayahuasca users might differ on subtle cognitive abilities (i.e., learning and encoding). Therefore, it is important that further studies elucidate these findings. Additionally, results are limited because of the small sample size and because long-term effects were not addressed. Results may also not generalize among other populations. Again, further studies are necessary.

While additional investigations are recommended, in this pilot research study, the authors found no evidence of injurious effects of ayahuasca on adolescents who participated with their families in ceremonial rituals using psychoactive substances. In Western society, it is indeed a unique phenomenon when young people are permitted to ingest a powerful hallucinogen. We have been allowed access to study the effects and have found, at least in this pilot preliminary investigation, that ayahuasca did not have a toxic or deleterious effect on adolescent neurocognitive functioning. The question arises that since the UDV adolescents use much less alcohol, marijuana and other intoxicants according to data published in this same issue (Doering-Silveira et al. 2005) all of which are known to have negative effects on cognition when used excessively, whether ayahuasca may protect the UDV adolescents from further harm.

REFERENCES

- Callaway, J.C.; McKenna, D.J.; Grob, C.S.; Brito, G.S.; Raymon, L.P.; Poland, R.E.; Andrade, E.N. & Mash, D.C. 1999. Pharmacokinetics of hoasca alkaloids in healthy humans. *Journal of Ethnopharmacology* 65: 243-56.
- Callaway, J.C.; Raymon, L.P.; Hearn, W.L.; McKenna, D.J.; Grob, C.S. & Brito, G.S. 1996. Quantitation of N,N-dimethyltryptamine and harmala alkaloids in human plasma after oral dosing with ayahuasca. *Journal of Analytical Toxicology* 20: 492-97.
- Callaway, J.C.; Airaksinen, M.M.; McKenna, D.J.; Grob, C.S. & Brito, G.S. 1994. Platelet serotonin uptake sites increased in drinkers of ayahuasca. *Psychopharmacology* 116: 385-87.
- Conners, C.K. 2005. *Conners' Continuous Performance Test-II (CPT-II)*. Toronto: Multi-Health Systems Inc.
- Doering-Silveira, E.; Grob, C.S.; De Rios, M.D.; Lopez, E.; Alonso, L.K.; Tacla, C.; Brito, G.S. & Da Silveira, D.X. 2005. Report on psychoactive drug use among adolescents using ayahuasca within a religious context. *Journal of Psychoactive Drugs* 37 (2).
- Geffen, G.; Moar, K.J.; O'Hanlon, A.P.; Clark, C.R. & Geffen, L.B. 1990. Performance measures of 16- to 86-year-old males and females on the Auditory Verbal Learning Test. *Clinical Neuropsychologist* 4 (1): 45-63.
- Grob, C.S.; McKenna, D.J.; Callaway, J.C.; Brito, G.S.; Neves, E.S.; Oberlander, G.; Saide, O.L.; Labigalini, E.; Tacla, C.; Miranda, C.T.; Strassman, R.J. & Boone, K.B. 1996. Human psychopharmacology of Hoasca, a plant hallucinogen used in ritual context in Brazil. *Journal of Nervous and Mental Disorders* 184 (2): 86-94.
- Lezak, M.D. 2004. *Neuropsychological Assessment—Fourth Edition*. New York: Oxford University Press.
- McKenna, D.J.; Callaway, J.C. & Grob, C.S. 1998. The scientific investigation of ayahuasca. A review of past and current research. *Heffter Review of Psychedelic Research* 1: 65-77.
- Mitrushina, M.N.; Boone, K.B.; Razani, J. & D'Elia, L.F. 2005. *Handbook of Normative Data for Neuropsychological Assessment—Second Edition*. New York: Oxford University Press.
- Spreen, O. & Strauss, E. 1998. *A Compendium of Neuropsychological Tests—Second Edition*. New York: Oxford University Press.
- Wechsler, D. 1997. *Manual for the Wechsler Adult Scale of Intelligence—Third Edition (WAIS-III)*. San Antonio, Texas: The Psychological Corporation.

This article was originally published in the *Journal of Psychoactive Drugs* in an issue entitled "Ayahuasca Use in Cross Cultural Perspective." The issue is available from Haight Ashbury Publications, 856 Stanyan Street, San Francisco CA 94117 USA. Phone 415-752-7601 or visit their website at www.drDave.org/journal.