Insight into Ayahuasca's Antidepressant Effects

Research indicates that C-Reactive Protein may play a vital role in combating Treatment-Resistant Depression.

.

Ayahuasca demonstrates great efficacy as a fast-acting, reliable antidepressant.[1] But just how these effects are produced has remained elusive. A recent study published by Galvão-Coelho et al. in the *Journal of Psychopharmacology* proposes that pro-inflammatory components of the immune system are at work in ayahuasca's antidepressant effects.[2]

The Association Between Inflammation and Depression

Elevated levels of C-Reactive Protein (CRP) have been noted in the wider body of research into Treatment-Resistant Depression (TRD). Wium-Anderson, et al., in *JAMA Psychiatry*, noted significantly increased levels of the protein in depressed patients as compared to healthy controls. [3] In addition to this, mutations in genes encoding CRP may play a role not only in the incidence of depression but the efficacy of antidepressant drugs.[4] Likewise, Jun, et al. recently reported in the J*ournal of Affective Disorders* that higher baseline CRP was associated with a worse antidepressant response and that subjects with lower concentrations exhibited greater reductions in depressive symptoms.[5]

Detailing the Study

The Galvão-Coelho et al. research paper describes their double-blind, placebo-controlled study using patients suffering from TRD (n=28) and healthy controls (n=45) who were given ayahuasca or placebo. Prior to ingestion, blood plasma concentrations of CRP were measured, and the Montgomery–Åsberg Depression Rating Scale (MADRS) questionnaire, to assess self-reported symptoms, was administered. Consequently, after 48 hours, CRP levels were measured and the MADRS inventory given again.
Initially, patients with TRD showed higher levels of CRP than did healthy controls. A marked reduction in CRP 48 hours post-ingestion was observed in both depressed patients and controls, but in neither group treated with placebo. Most notably, subjects treated with ayahuasca demonstrated a significant correlation between reductions in CRP and lessening depressive symptoms on the MADRS questionnaire. However, the concentrations

of DMT (dimethyltryptamine) and accessory alkaloids in the materials used, and details describing the preparation of the brew, were not included, posing a potential limitation. The study also analyzed ayahuasca's impact on other proteins involved in inflammatory and anti-inflammatory processes, namely IL (interleukin)-6 and BDNF (Brain-Derived Neurotrophic Factor). No significant correlation between their respective concentrations and depressive symptoms were found. This reiterates that CRP is particularly likely to play a role in the underlying cause of TRD, which ayahuasca is demonstrably apt to address.

Ayahuasca as Practical Medicine

Interestingly, ayahuasca appears especially effective in naïve users, presenting a unique opportunity as a treatment; 80% of first-time users who met the diagnostic criteria for TRD reported reductions in symptoms, persisting for up to 6 months afterward.[6] It was also found that ayahuasca users experienced an increased quality of life, and scored higher for measures of self-transcendence on the SF (Short Form)-36 survey. Again, phytochemical analyses of the materials used, and details of preparation were not included. Hamil, et al. notes that due to ayahuasca's complex pharmacology, it is difficult to consider any one aspect of the brew in isolation and that its many constituents should be studied together.[7]

The Potential for a New Paradigm in Mental Health Treatment

Ayahuasca holds great hope as a treatment, and may provide an alternative to standard antidepressants, whose cessation results in an unpleasant "discontinuation syndrome." The risk of relapsing depressive symptoms is also a prevalent concern accompanying the discontinuance of commonly prescribed antidepressants.[8] Moreover, contrary to the many undesirable side effects associated with typical antidepressant drugs, Barbosa, et al. failed to elucidate any "deleterious effects" of ayahuasca, and even found superior scores on measures of psychosocial status and wellbeing, as compared to those undergoing traditional antidepressant therapy.[9] Fewer struggles with alcoholism and substance abuse, common comorbidities in depressive disorders, were also reported.

La Purga: Side Effect or Essential Element?

While ayahuasca is not without its side-effects, including nausea, vomiting, and diarrhea, these phenomena are only seen as undesirable in a Western medical framework.[10] Many practitioners refer to these reactions as an integral aspect of the experience.[11-13] La purga, or "the purge," is intended to rid the body [and soul] of repressed emotions and negative energy, which are released and expelled, and to ultimately heal what may be ailing the person.[14]

Standard Antidepressants and Ayahuasca--A Dangerous Combination

While side-by-side efficacies of traditional antidepressants and ayahuasca remain to be studied, coadministration of the two leads to adverse reactions.[15] Those taking SSRIs (Selective Serotonin Reuptake Inhibitors) are cautioned against working with ayahuasca for the risk of serotonin syndrome, a potentially fatal interaction between serotonergic drugs, and inhibition of the serotonin reuptake transporter. This interplay leads to the accumulation of serotonin or structurally similar metabolites and may cause physiologically dangerous effects.

Conclusion

The study by Galvão-Coelho, et al. proposes a mechanism by which ayahuasca's antidepressant effects may be mediated and recapitulates the idea that depressive disorders have an inflammatory component. Taken with previous research implicating components of the immune system in TRD, ayahuasca shows great promise in tackling the pathology of the illness at a finer level while remedying the personal aspects that often accompany it.

Cited

1. Galvão-Coelho, N. L., de Menezes Galvão, A. C., de Almeida, R. N., et al. Changes in inflammatory biomarkers are related to the antidepressant effects of Ayahuasca. (2020). *Journal of Psychopharmacology (Oxford, England)*, *34*(10), 1125–1133.https://doi.org/10.1177/0269881120936486
2. Wium-Andersen, M. K., Ørsted, D. D., Nielsen, S. F., et al. Elevated C-Reactive Protein Levels, Psychological Distress, and Depression in 73 131 Individuals. (2013). *JAMA Psychiatry*, *70*(2), 176. https://doi.org/10.1001/2013.jamapsychiatry.102
3. Li, X., Sun, N., Yang, C., et al. C-Reactive Protein Gene Variants in Depressive Symptoms & Antidepressants Efficacy. (2019). *Psychiatry Investigation*, *16*(12), 940–947. https://doi.org/10.30773/pi.2019.0117
4. Zhang, J., Yue, Y., Thapa, A., et al. Baseline serum C-reactive protein levels may predict antidepressant treatment responses in patients with major depressive disorder. (2019). *Journal of Affective Disorders*, *250*, 432–438. https://doi.org/10.1016/j.jad.2019.03.001
5. Jiménez-Garrido, D. F., Gómez-Sousa, M., Ona, G., et al. Effects of ayahuasca on mental health and quality of life in naïve users: A longitudinal and cross-sectional study combination. (2020). *Scientific Reports*, *10*(1). https://doi.org/10.1038/s41598-020-61169-x
6. Hamill, J., Hallak, J., Dursun, S. M., et al. Ayahuasca: Psychological and Physiologic Effects, Pharmacology and Potential Uses in Addiction and Mental Illness. (2019). *Current Neuropharmacology*, *17*(2), 108–128. https://doi.org/10.2174/1570159x16666180125095902
7. Batelaan, N. M., Bosman, R. C., Muntingh, A., et al. Risk of relapse after antidepressant discontinuation in anxiety disorders, obsessive-compulsive disorder, and post-traumatic stress disorder: systematic review and meta-analysis of relapse prevention trials. (2017). *BMJ*, j3927. https://doi.org/10.1136/bmj.j3927
8. Barbosa, P. C. R., Mizumoto, S., Bogenschutz, M. P., et al. Health status of ayahuasca users. (2012). *Drug Testing and Analysis*, *4*(7–8), 601–609. https://doi.org/10.1002/dta.1383
9. Wolff, T. J., Ruffell, S., Netzband, N., et al. A phenomenology of subjectively relevant experiences induced by ayahuasca in Upper Amazon vegetalismo tourism. (2019). *Journal of Psychedelic Studies*, 1–13. https://doi.org/10.1556/2054.2019.007
10. Riba, J., Valle, M., Urbano, G., et al. Human Pharmacology of Ayahuasca: Subjective and Cardiovascular Effects, Monoamine Metabolite Excretion, and Pharmacokinetics. (2003). *Journal of Pharmacology and Experimental Therapeutics*, *306*(1), 73–83. https://doi.org/10.1124/jpet.103.049882
11. Beyer, S. V. *Singing to the plants : a guide to mestizo shamanism in the upper Amazon*. (2010). University Of New Mexico Press.
12. Caiulabate, B., & Henrik Jungaberle. *The internationalization of Ayahuasca*. (2011). Lit-Verlag.
13. Caiulabate, B., Clancy Cavnar, & Springer-Verlag Gmbh. *The Therapeutic Use of Ayahuasca*. (2016). Berlin Springer.
14. Schmid JT. Healing with Ayahuasca: Notes on Therapeutic Rituals and Effects in European Patients Treating Their Diseases. In: Labate BC, Cavnar C, eds. The

Therapeutic Use of Ayahuasca. Springer Heidelberg; 2013: doi:10.1007/978-3-642-40426-40429.

15. Callaway, J. C., & Grob, C. S. Ayahuasca Preparations and Serotonin Reuptake Inhibitors: A Potential Combination for Severe Adverse Interactions. (1998). *Journal of Psychoactive Drugs*, *30*(4), 367–369. https://doi.org/10.1080/02791072.1998.10399712