

Theme: Cognitive Neuroscience

The effects of ayahuasca on Theory of Mind (ToM) - a crossover multiple dosage fMRI study

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Abstract:

Social cognition has been proposed as a mechanism underlying the therapeutic potential of psychedelics, yet its neural effects in this context remain an emerging area of exploration. This pharmacoinaging study investigated the effects of ayahuasca on Theory of Mind (ToM), focusing on neural network connectivity and related subjective experiences.

Using a crossover, multiple dosage design, 12 healthy, experienced ayahuasca users (mean age: 40±6.6 years; 4 female) underwent three conditions: two ayahuasca dosages (0.5 mg/kg DMT and 0.8 mg/kg DMT), and a placebo, administered with 1–2-month washout intervals. The study was randomized and double-blind, except for the highest dose, which was administered last in a single-blinded manner.

Resting-state fMRI was used to assess intra- and inter-areal connectivity of ToM network, previously defined in a meta-analysis. Visual analog scales measured mentalizing and empathy states experienced during fMRI acquisition.

Significant functional connectivity within the ToM network was observed across all conditions, with no significant intra-network differences. However, the highest dose increased functional connectivity in the posterior superior temporal sulcus (pSTS), enhancing its co-activation with regions involved in visual processing (primary and extrastriate cortices) and motor planning (supplementary motor cortex, SMC). Additionally, effective connectivity analysis showed sensorimotor and visual regions Granger-causally modulated the pSTS. Subjectively, the highest dose also enhanced social cognition states, with a strong positive correlation between pSTS-SMC functional connectivity and the experience of perspective-taking.

These findings suggest a dose-dependent enhancement in the integration of visual and motor-related sensory inputs into ToM brain regions. This increased neural integration may suggest a mechanism by which ayahuasca facilitates perspective-taking and mentalizing, potentially impacting social functioning.

Keywords: Ayahuasca, N,N-Dimethyltryptamine (DMT), Theory of Mind (ToM), pharmacoinaging, fMRI, brain connectivity