Complex network approach to the neuroscience of psychedelic phenomena

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Introduction

Ayahuasca is a brew from the Amazonian indigenous culture made out of two main ingredients: the leaves of *Psychotria viridis*, containing *N,N*-Dimethyltryptamine (DMT); and the vine *Banisteriopsis caapi*, which contains monoamine oxidase inhibitors (MAOi). The DMT molecule is a serotonergic agonist similar to LSD and mescaline, but it is rapidly metabolized by the human body. The MAOi act by slowing down the degradation process, allowing for the DMT to cross the blood-brain barrier and produce a profound *psychedelic experience*. Recent studies have been piling up evidence of the therapeutic effects of psychedelic substances in treating mental illnesses such as depression,[1] making imperative the need for research on the neuroscience of psychedelic phenomena.

Figure 1: *Banisteriopsis caapi* vine containing MAOi alkaloids are combined with the DMT-containing leaves of *Psychotria viridis* to make ayahuasca (bottom), originally used within indigenous culture and, more recently, in clinical settings highlighting the potential therapeutic effects of psychedelics.

fMRI data

Ten healthy adult volunteers were submitted to an awake resting-state fMRI scan 40 minutes before and after ingestion of 120-200 mL of ayahuasca containing 0.8 mg/mL of DMT and 0.21 mg/mL of harmine.[2] The subjects' brain's images were parcellated into 110 cortical regions (Harvard-Oxford Atlas). The time series of pairs of regions were Pearson-correlated to give a cross-correlation 104×104 matrix C with elements $0 \leq c_{ij} \leq 1$.

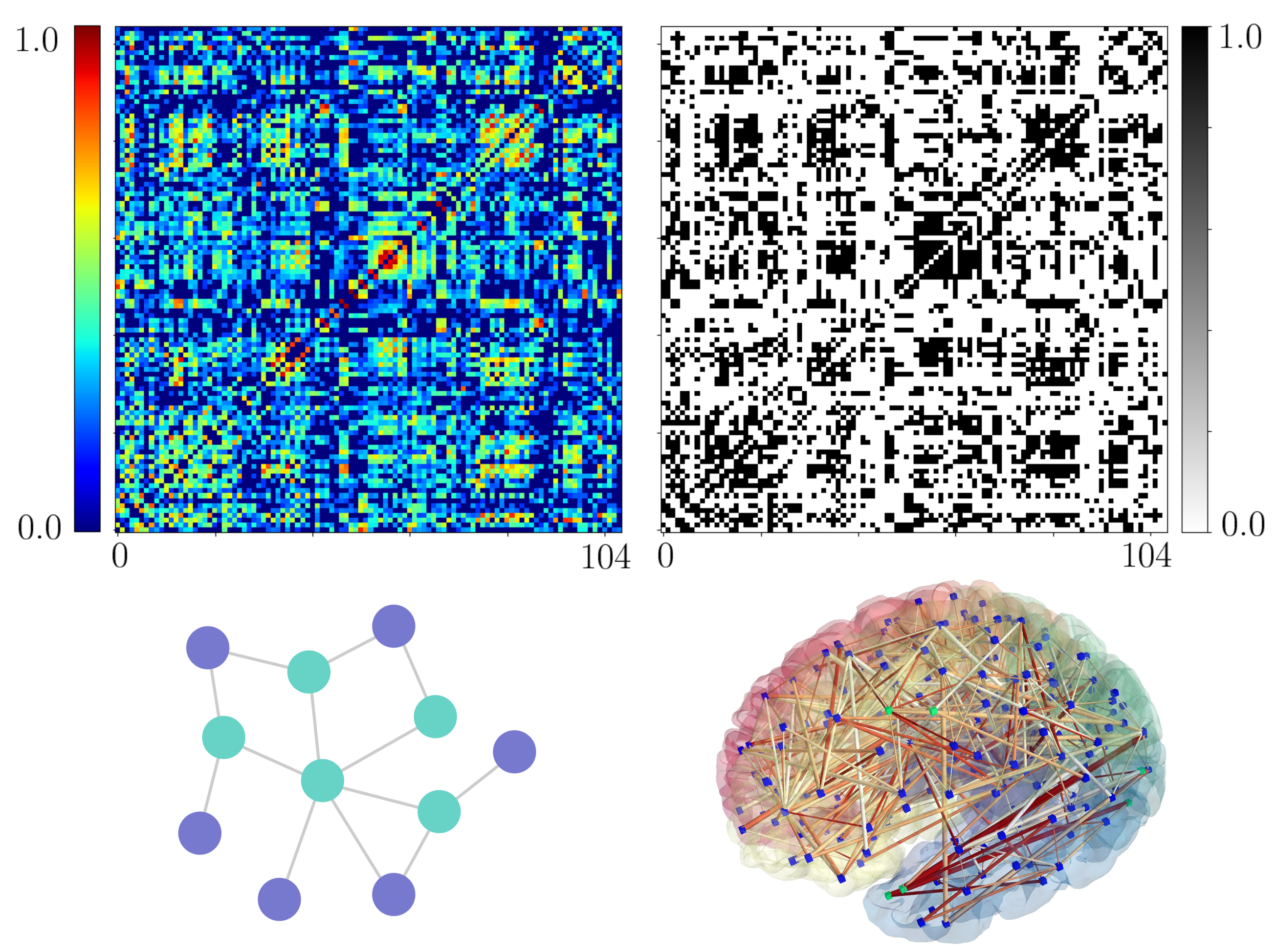

Figure 2: Correlation matrix (upper left) and its thresholded, adjacency matrix (upper right), which admits a network representation (bottom left) capturing the functional connectivity of the human brain (bottom right, adapted from *Connectome Viewer Toolkit*).

Complex networks

Given a correlation matrix C, an adjacency matrix A with elements $a_{ij} = 0$ or 1 is obtained through a *thresholding* procedure, such that a network representation is admitted. Null a_{ij} are construed as disconnected pairs i, j ($a_{ij} = 1$ being the opposite). A degree k_i denotes the number of connections of the i-th node. The geodesic distance d_{ij} measures the minimal distance between a pair i, j. A neighborhood radius r associates connected nodes around i, accordingly.

Entropy

Taking the degree distribution $\mathcal{P}(k)$ of a network and the geodesic distance distribution $\mathcal{D}_i(r)$ of each node i, one can define the Shannon's entropies functionals

$$S[\mathcal{P}] = -\sum_{k}^{k_{max}} \mathcal{P}(k) \ln \mathcal{P}(k)\,, \qquad S[\mathcal{D}_i] = -\frac{1}{N}\sum_{i}^{N}\sum_{r}^{r_{max}} \mathcal{D}_i(r) \ln \mathcal{D}_i(r)\,,$$

in which the former quantifies constraints imposed by the network degree distribution, while latter measures the information due to intrinsic configuration of the network structure.

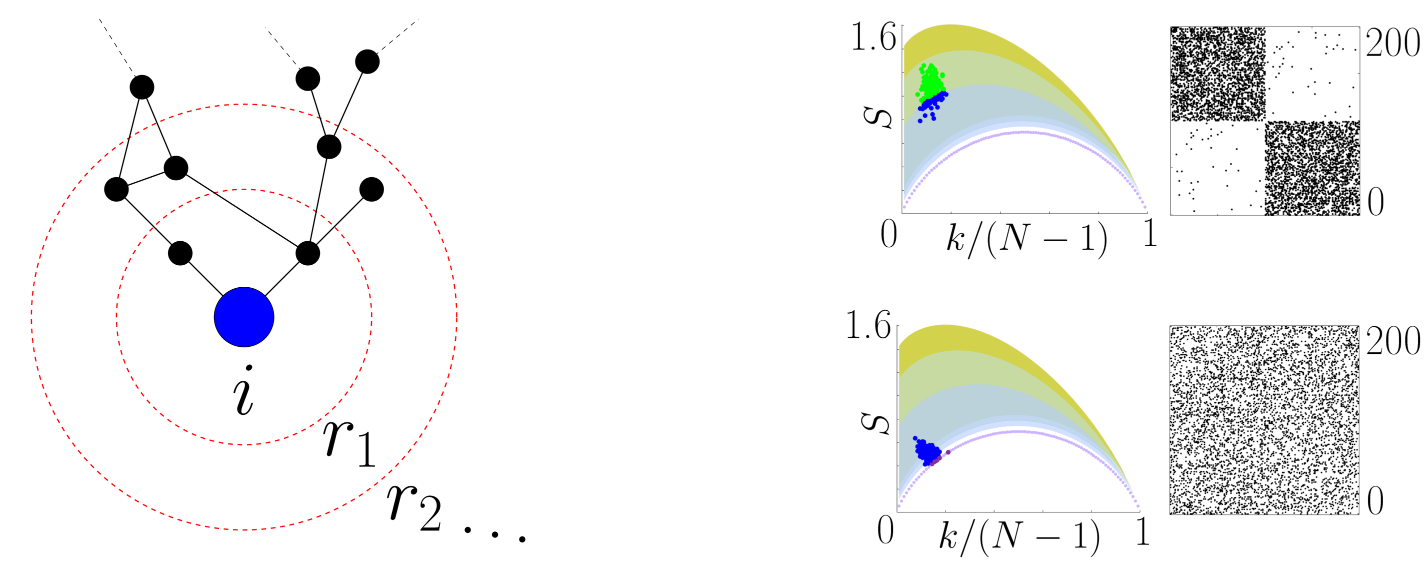

Figure 3: A node i with its immediate radii $r_1, r_2, \ldots, r_{max}$ around it (left). Entropy-degree diagram of a random network of $N = 200$ nodes (right).

Results: increased entropy after ayahuasca ingestion

Entropies $S[\mathcal{P}]$ and $S[\mathcal{D}_i]$ increased after ayahuasca intake, corroborating Carhart-Harris' entropic brain hypothesis[3] that the psychedelic state is associated to a higher entropy when compared to ordinary states of consciousness.

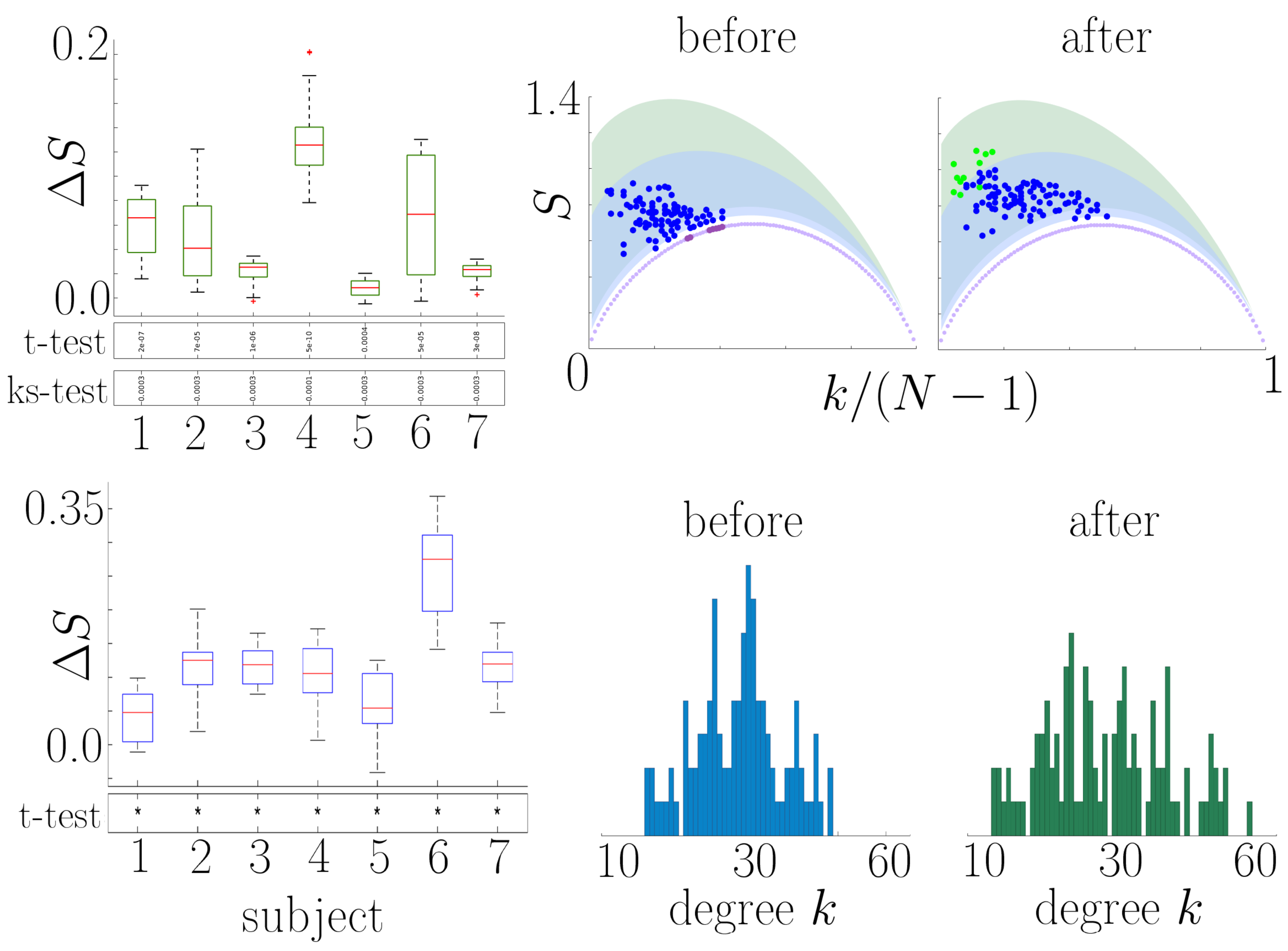

Figure 4: Entropy degree-diagram and characteristic geodesic entropy such that $\Delta S = S_{\text{after}} - S_{\text{before}} > 0$ for all subjects (top). Degree histogram and entropy of the degree distribution such that $\Delta S > 0$ for all subjects (bottom).

References

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[2] Viol A., Palhano-Fontes F., Onias H., de Araujo D.B., Viswanathan G.M. (2014) Shannon entropy of brain functional complex networks under the influence of the psychedelic Ayahuasca. *Scientific Reports* **7**; Viol A., Palhano-Fontes F., Onias H., de Araujo D.B., Hövel P., Viswanathan G.M. (2019) Characterizing Complex Networks Using Entropy-Degree Diagrams: Unveiling Changes in Functional Brain Connectivity Induced by Ayahuasca. *Entropy* **21**(2).

[3] Carhart-Harris R.L., Leech R., Hellyer P., Shanahan M., Feilding A., Tagliazucchi E., Chialvo D., Nutt D. (2014) The entropic brain: a thoery of conscious states informed by neuroimaging research with psychedelic drugs. *Frontiers in Human Neuroscience* **8**.