Complex network approach to the neuroscience of psychedelic phenomena

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SCIENTIFIC REPORTS [1]

Shannon entropy of brain functional complex networks under the influence of the psychedelic Ayahuasca

A. Viol[1,2,3], Fernanda Palhano-Fontes[4], Heloisa Onias[4], Draulio B. de Araujo[4] & G. M. Viswanathan[1,5]

The entropic brain hypothesis holds that the key facts concerning psychedelics are partially explained in terms of increased entropy of the brain's functional connectivity. Ayahuasca is a psychedelic beverage of Amazonian indigenous origin with legal status in Brazil in religious and scientific settings. In this context, we use tools and concepts from the theory of complex networks to analyze resting state fMRI data of the brains of human subjects under two distinct conditions: (i) under ordinary waking state and (ii) in an altered state of consciousness induced by ingestion of Ayahuasca. We report an increase in the Shannon entropy of the degree distribution of the networks subsequent to Ayahuasca ingestion. We also find increased local and decreased global network integration. Our results are broadly consistent with the entropic brain hypothesis. Finally, we discuss our findings in the context of descriptions of "mind-expansion" frequently seen in self-reports of users of psychedelic drugs.

2

entropy

Characterizing Complex Networks Using Entropy-Degree Diagrams: Unveiling Changes in Functional Brain Connectivity Induced by Ayahuasca

Aline Viol [1,2,*], Fernanda Palhano-Fontes [3], Heloisa Onias [3], Draulio B. de Araujo [3], Philipp Hövel [1,2,4] and Gandhi M. Viswanathan [5,6]

Abstract: With the aim of further advancing the understanding of the human brain's functional connectivity, we propose a network metric which we term the *geodesic entropy*. This metric quantifies the Shannon entropy of the distance distribution to a specific node from all other nodes. It allows to characterize the influence exerted on a specific node considering statistics of the overall network structure. The measurement and characterization of this structural information has the potential to greatly improve our understanding of sustained activity and other emergent behaviors in networks. We apply this method to study how the psychedelic infusion Ayahuasca affects the functional connectivity of the human brain in resting state. We show that the geodesic entropy is able to differentiate functional networks of the human brain associated with two different states of consciousness in the awaking resting state: (i) the ordinary state and (ii) a state altered by ingestion of the Ayahuasca. The functional brain networks from subjects in the altered state have, on average, a larger geodesic entropy compared to the ordinary state. Finally, we discuss why the geodesic entropy may bring even further valuable insights into the study of the human brain and other empirical networks.

[1] A. Viol *et al.*, *Sci. Rep.* **7**: 7388 (2017). DOI: 10.1038/s41598-017-06854-0.

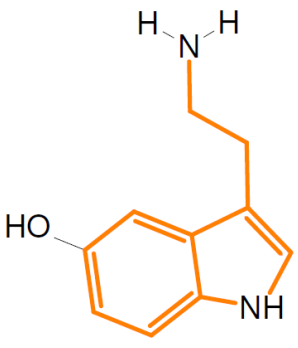
[2] A. Viol *et al.*, *Entropy* **21**: 128 (2019). DOI: 10.3390/e21020128.

H. Osmond (1957):[3]

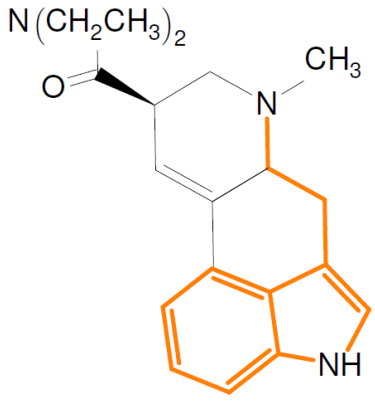
psychedelic = ***psychē*** **(“soul”) + *dēloun* (“to reveal”).**

Psychedelics are agonists of the 5-HT_{2A}.[4]

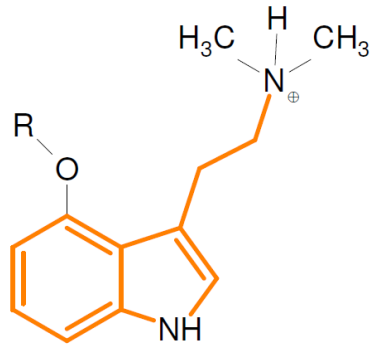
serotonin (5-HT)



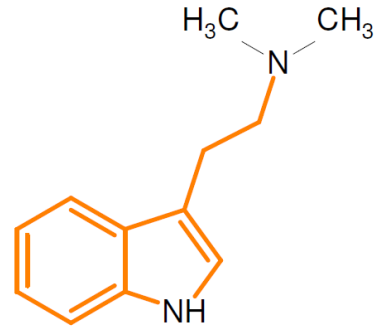
LSD



psilocybin (R = PO_3H^-)



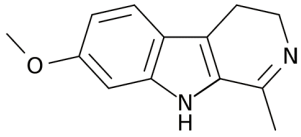
DMT



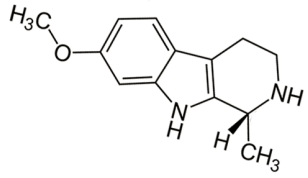
[3] C.C. Bisbee, P. Bisbee, E. Dyck, P. Farrell, *Psychedelic Prophets* (2018).

[4] D.E. Nichols, *Pharmacol. Rev.* **68**: 264 (2016).

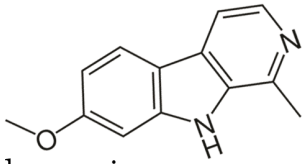
harmaline



tetrahydroharmine

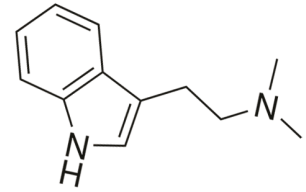


harmine



B. caapi vine (MAOi)

N,N-dimethyltryptamine



P. viridis leaves (DMT)

Therapeutic potential for treatment-resistant depression:[5]

Psychological Medicine

Rapid antidepressant effects of the psychedelic ayahuasca in treatment-resistant depression: a randomized placebo-controlled trial

Fernanda Palhano-Fontes[1,2], Dayanna Barreto[2,3], Heloisa Onias[1,2], Katia C. Andrade[1,2], Morgana M. Novaes[1,2], Jessica A. Pessoa[1,2], Sergio A. Mota-Rolim[1,2], Flávia L. Osório[4,5], Rafael Sanches[4,5], Rafael G. dos Santos[4,5], Luís Fernando Tófoli[6], Gabriela de Oliveira Silveira[7], Mauricio Yonamine[7], Jordi Riba[8], Francisco R. Santos[9], Antonio A. Silva-Junior[9], João C. Alchieri[10], Nicole L. Galvão-Coelho[5,11], Bruno Lobão-Soares[5,12], Jaime E. C. Hallak[4,5], Emerson Arcoverde[2,3,5], João P. Maia-de-Oliveira[2,3,5] and Dráulio B. Araújo[1,2]

[5] F. Palhano-Fontes *et al.*, *Psychol. Med.* **49**: 655 (2019).

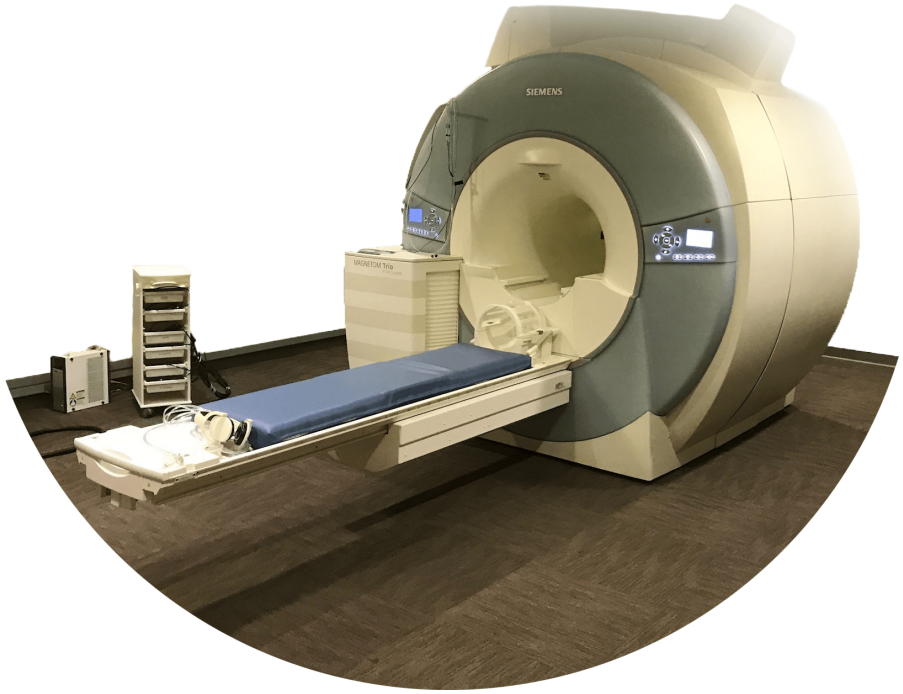
Data and methods

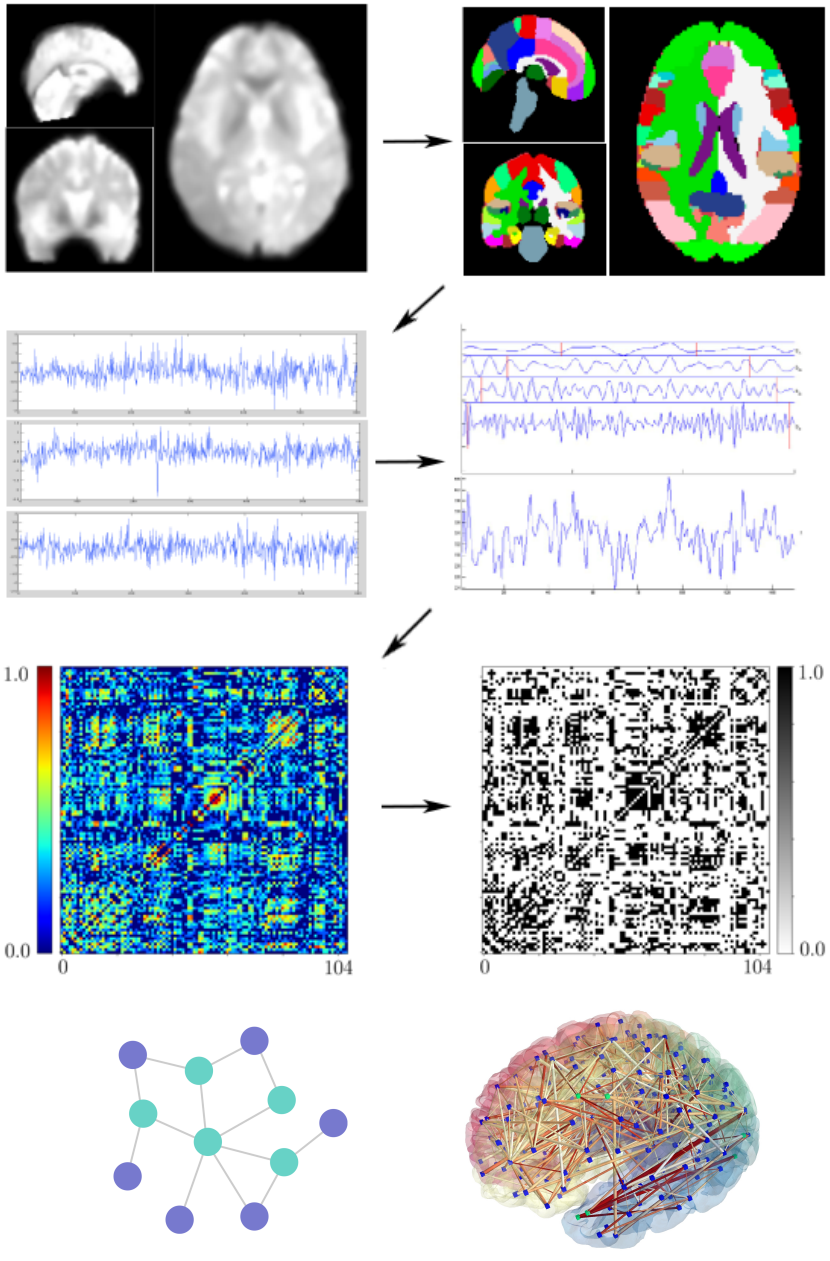
- 7 healthy, right-handed volunteers.

- dosage of 120-200 mL of ayahuasca (0.8 mg/mL DMT + 0.21 mg/mL harmine).

- fMRI scans 40 minutes both before and after ingestion.

- awake resting state.





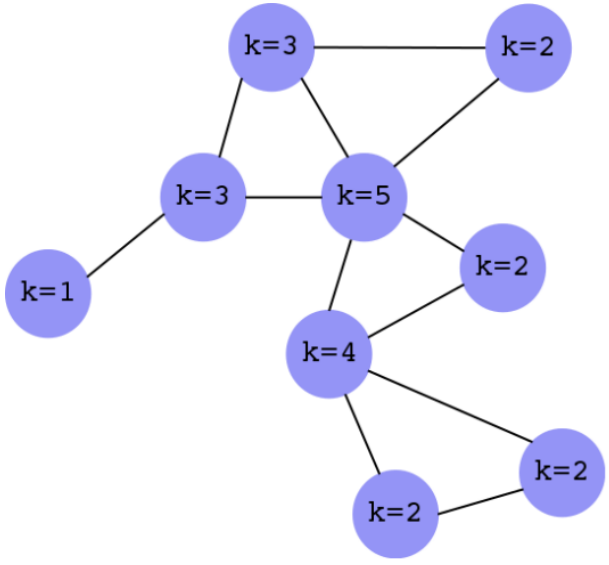
From fMRI to networks:

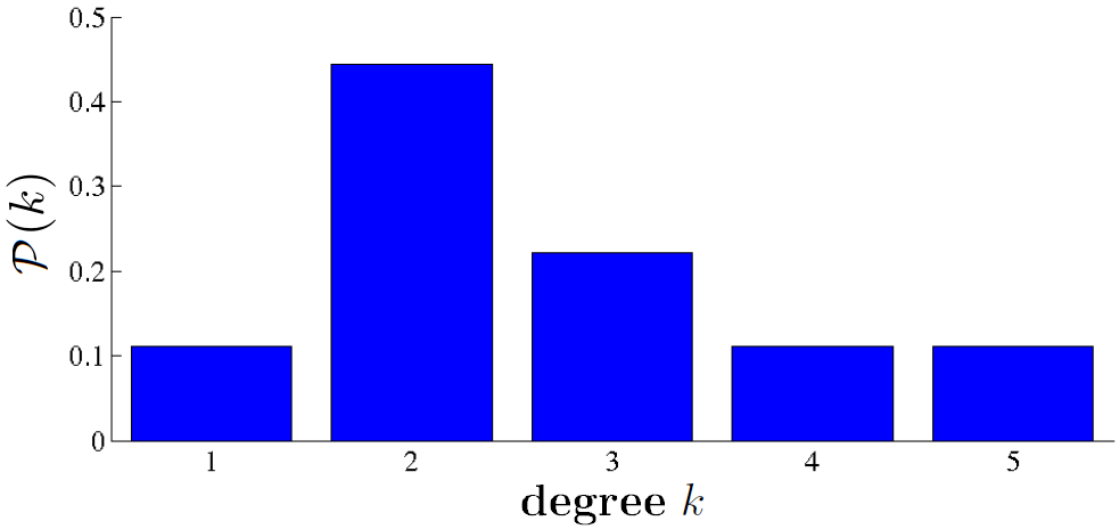
- pre-processing;
- parcellation;
- time-series extraction;
- filtering;
- Pearson correlation

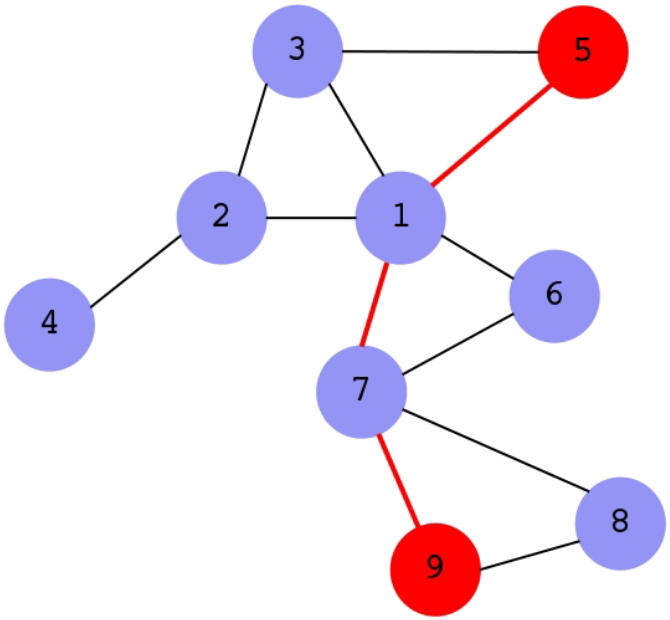
$$c_{xy} = \sum_{k}^{N} \frac{\left(x_k - \langle x \rangle\right)\left(y_k - \langle y \rangle\right)}{\sigma_x \sigma_y};$$

- thresholding.

Degree distribution $\mathcal{P}(k)$:





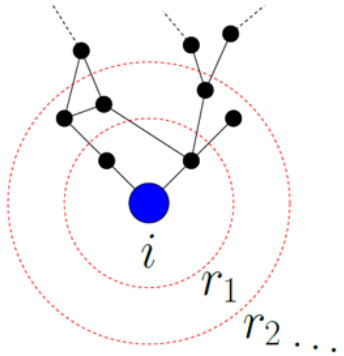


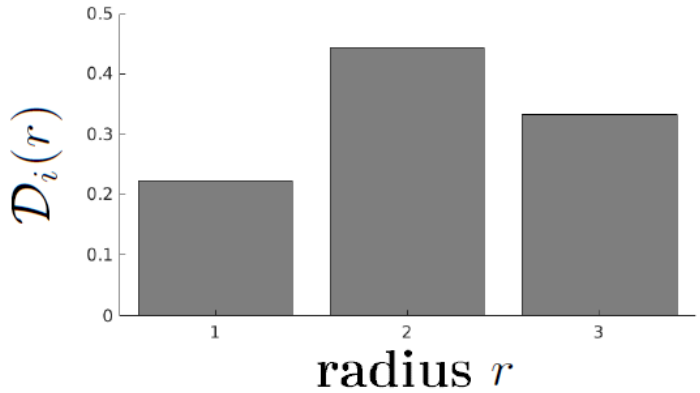
Mean geodesic distance:

$$D(G) = \sum_{i,j}^{N} \frac{d(i,j)}{N(N-1)},$$

for every pair of nodes $i, j \in G$**.**

Define a distribution $\mathcal{D}_i(r)$ **so that***





* $\mathcal{D}_i(r) = \frac{1}{N-1} \sum_{j \in g}^{N} \delta_{r,d(i,j)};\ g = \{j \,|\, j \in G \setminus \{i\}\}.$

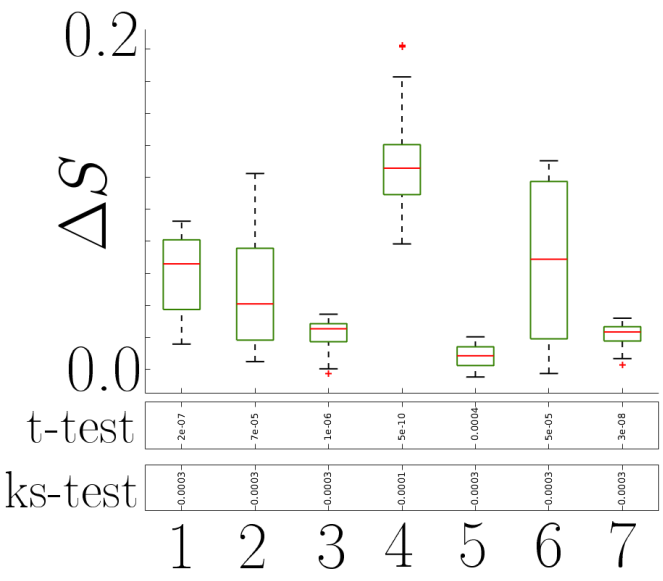
Entropy of the degree distribution $\mathcal{P}(k)$:

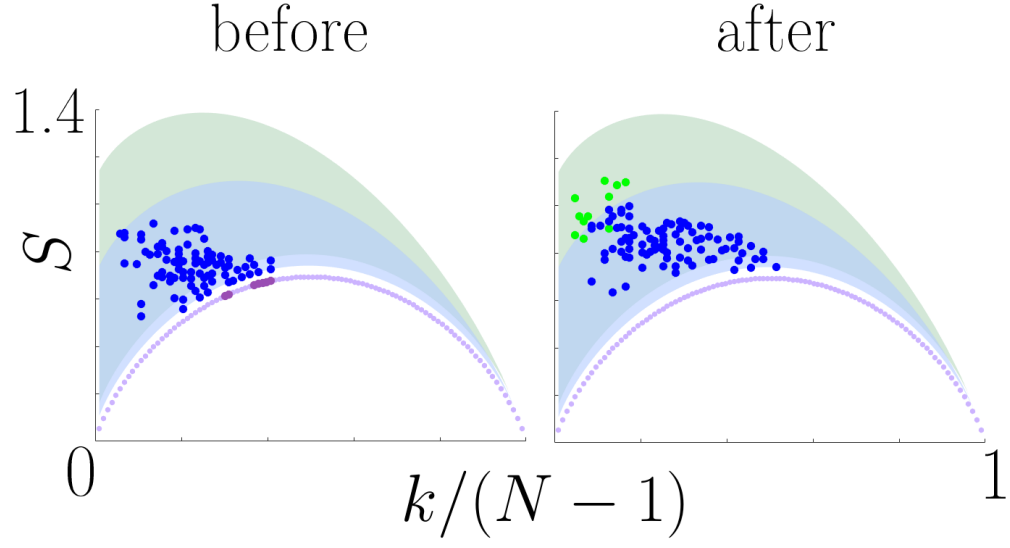
$$S[\mathcal{P}] = -\sum_{k}^{k_{max}} \mathcal{P}(k) \ln \mathcal{P}(k).$$

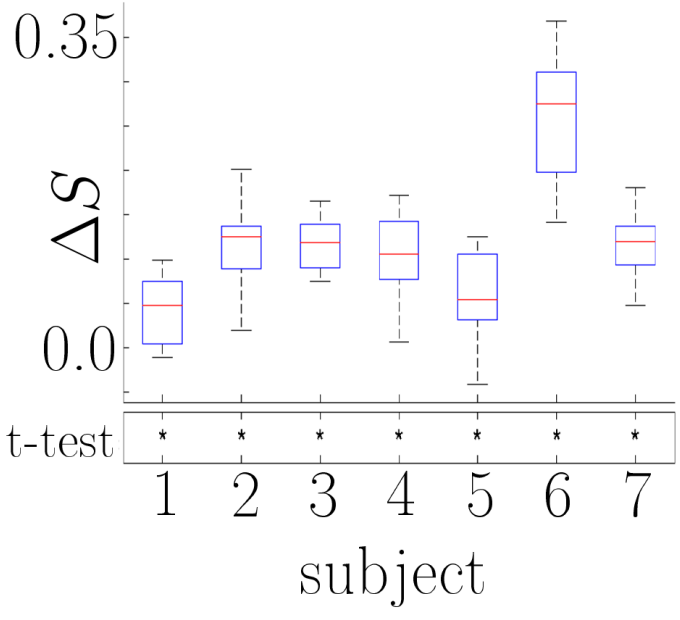
Characteristic geodesic entropy:

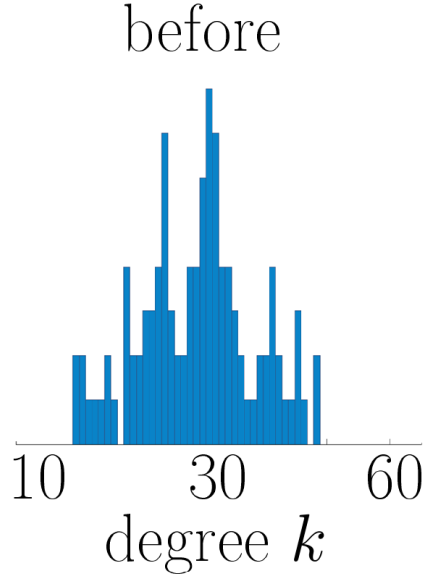
$$S[\mathcal{D}_i] = -\frac{1}{N} \sum_{i}^{N} \sum_{r}^{r_{max}} \mathcal{D}_i(r) \ln \mathcal{D}_i(r).$$

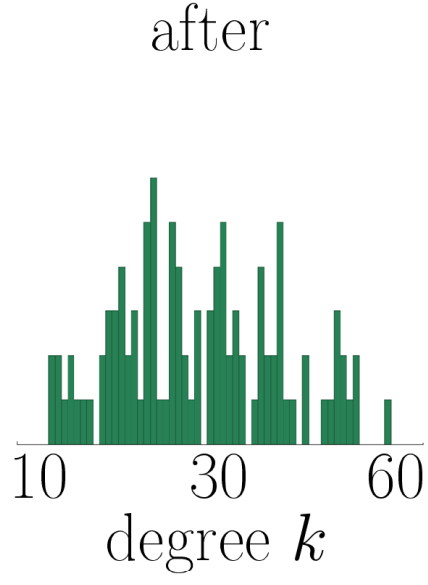
Results


0.2
ΔS
0.0
t-test
ks-test
2e-07
7e-05
1e-06
5e-10
0.0004
5e-05
3e-08
0.0003
0.0001
1 2 3 4 5 6 7


before
after
1.4
S
0
$k/(N-1)$
1


0.35
ΔS
0.0
t-test
1 2 3 4 5 6 7
subject


before
10
30
60
degree k


after
10
30
60
degree k

Entropic brain hypothesis: increased entropy in the psychedelic state.[6]

frontiers in
HUMAN NEUROSCIENCE

The entropic brain: a theory of conscious states informed by neuroimaging research with psychedelic drugs

Robin L. Carhart-Harris[1], Robert Leech[2], Peter J. Hellyer[2], Murray Shanahan[3], Amanda Feilding[4], Enzo Tagliazucchi[5], Dante R. Chialvo[6] and David Nutt[1]*

[6] R. Carhart-Harris *et al.*, *Front. Hum. Neurosci.* **8**: 20 (2014).

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A. Viol *et al.*, *Entropy* **21**: 128 (2019). DOI: 10.3390/e21020128.

C.C. Bisbee, P. Bisbee, E. Dyck, P. Farrell, *Psychedelic Prophets* (2018).

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