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Advancing the Cognitive Neuroscience of Psychedelics

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Center for the Neuroscience of Psychedelics

Disclosures

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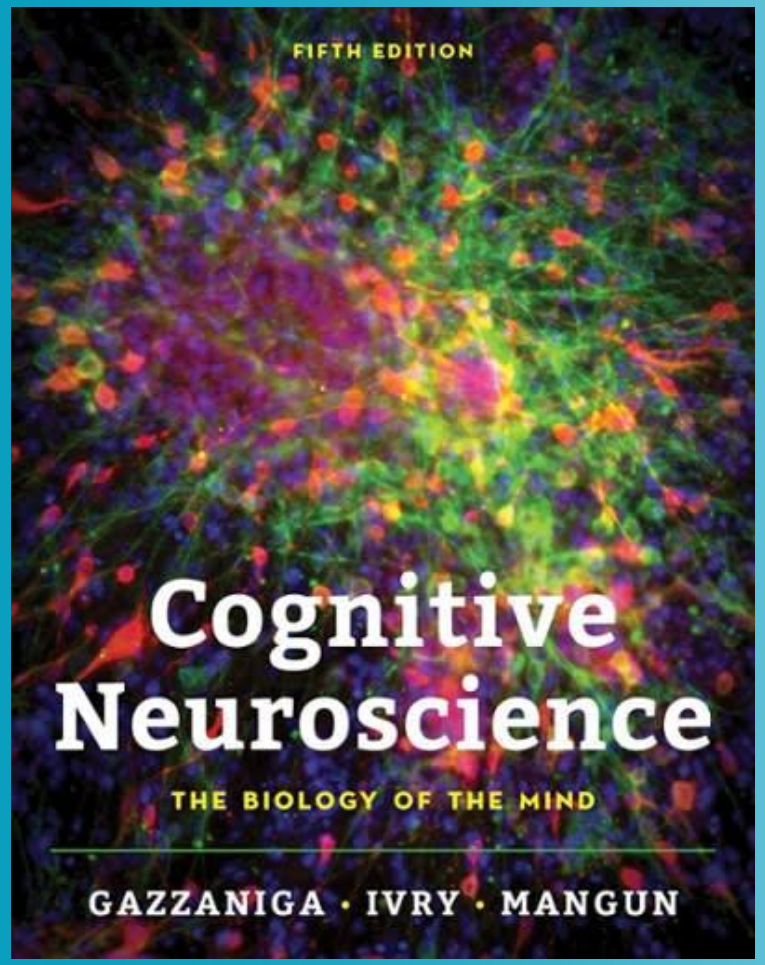
I have the following relevant financial relationship with a commercial interest to disclose:

atai stock

SAB for SAMA Therapeutics, Consultant for Seaport Therapeutics and Lightstone Ventures

What is Cognitive Neuroscience?



Cognitive neuroscience is the study of the neural basis of human thought, emotion and behavior.

What is Cognitive Neuroscience?

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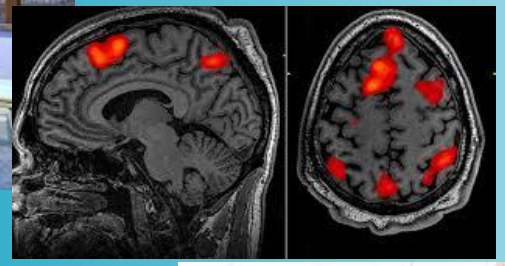
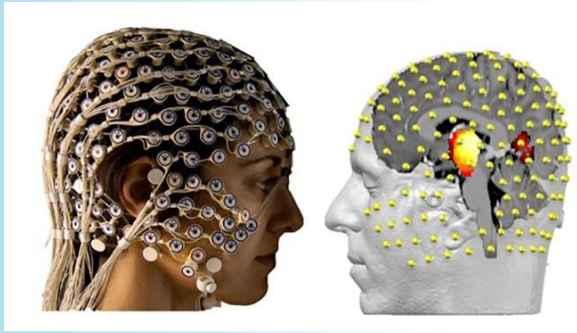
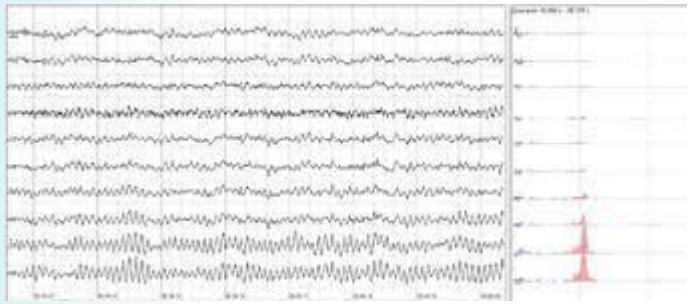
To accomplish their research, cognitive neuroscientists use neuroimaging, neurophysiology, and neuromodulation coupled with various cognitive and emotional processing tasks.







How is cognitive neuroscience relevant for psychiatry?

Identify biomarkers for risk stratification, diagnosis, and prognosis.

Provide a better understanding of processes underlying mental illness.

Identify biomarkers for treatment response.

How is cognitive neuroscience relevant for psychiatry?

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Provide a mechanistic understanding of how treatments work.

Identify either brain regions or brain networks, that can be treated with neuromodulation.

Allow for neurofeedback as an intervention.

Towards a Cognitive Neuroscience of Psychedelics

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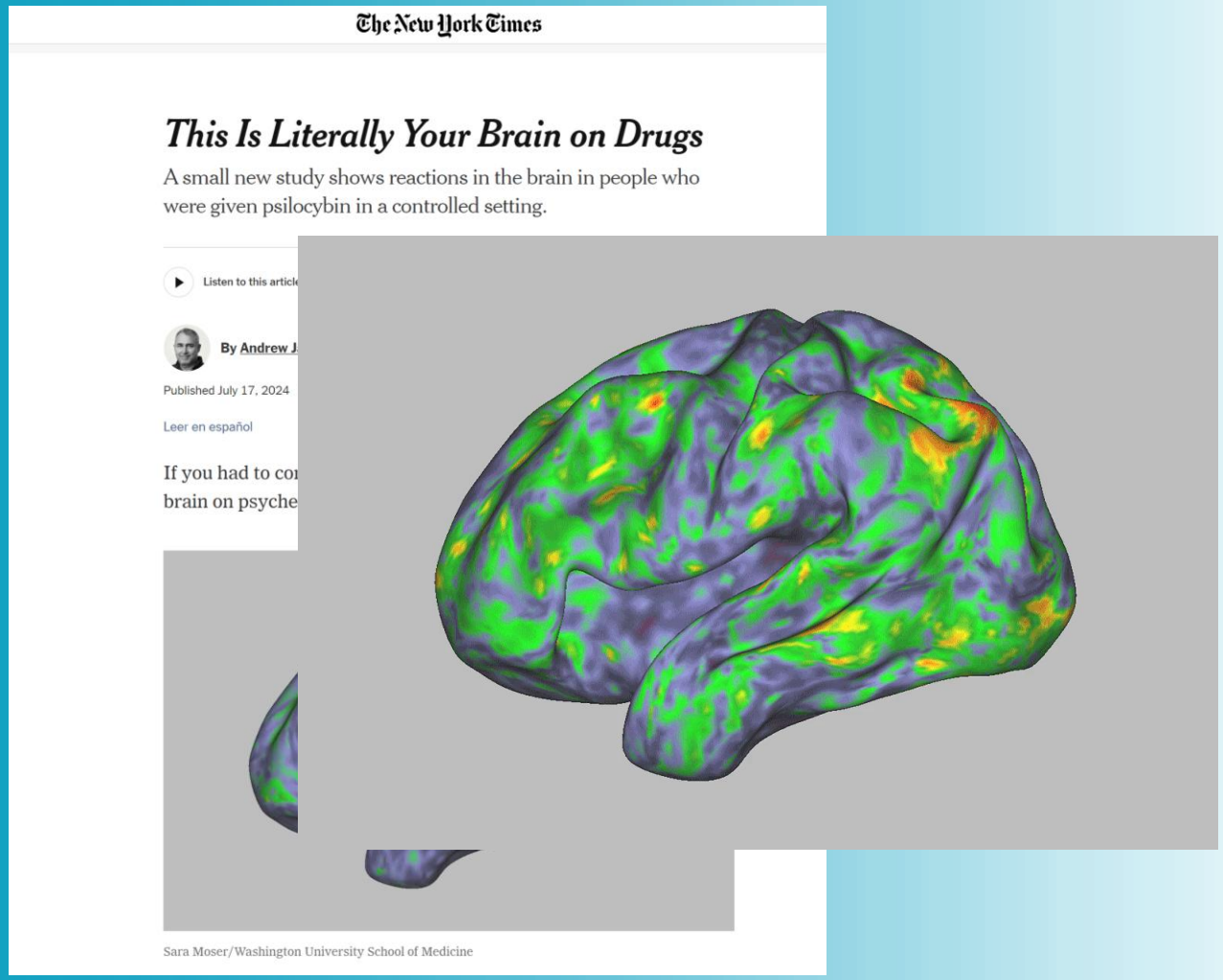


The New York Times

Psilocybin Spurs Brain Activity in Patients With Depression, Small Study Shows

The chemical derived from psychedelic mushrooms l
alleviate symptoms of depression and generated dete
neural responses that lasted weeks.

Share full article 101

A mushroom of the genus Psilocybe, which contains the psychoactive ch
psilocybin. Alana Paterson for The New York Times

By Andrew Jacobs
April 11, 2022

Research • April 11, 2022

Psilocybin Rewires the Brain for People with Depression

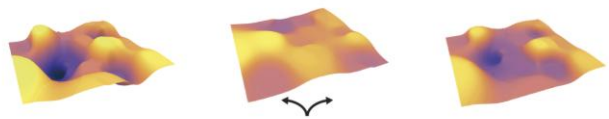
Study Suggests New Mechanism for How Psychedelics Affect the Brain

By Laura Kurtzman

Psilocybin fosters greater connections between different regions of the brain in depressed people, freeing them up from long-held patterns of rumination and excessive self-focus, according to a new study by scientists at UC San Francisco and Imperial College London.

The discovery points toward a general mechanism through which psychedelics may be acting therapeutically on the brain to alleviate depression and possibly other psychiatric conditions that are marked by fixed patterns of thinking.

Depression | **Psilocybin** | **Post-treatment**



The depressed brain encourages rigid thought patterns that impact well-being. This can be viewed as a "landscape" with deep wells that make it difficult for patients to "move between" different thoughts and perspectives. *Image by Richard Daws, Kings College London*

Psilocybin therapy "flattens" the brain's landscape and "opens up" the rigidity of the depressed to allow new thoughts, insight, and perspectives to emerge. *Image by Richard Daws, Kings College London*

Post-treatment, a flatter landscape makes it easier for patients to experience healthier flexibility and diversity in their thought patterns. *Image by Richard Daws, Kings College London*

The research on neural correlates of psychedelics is nascent.

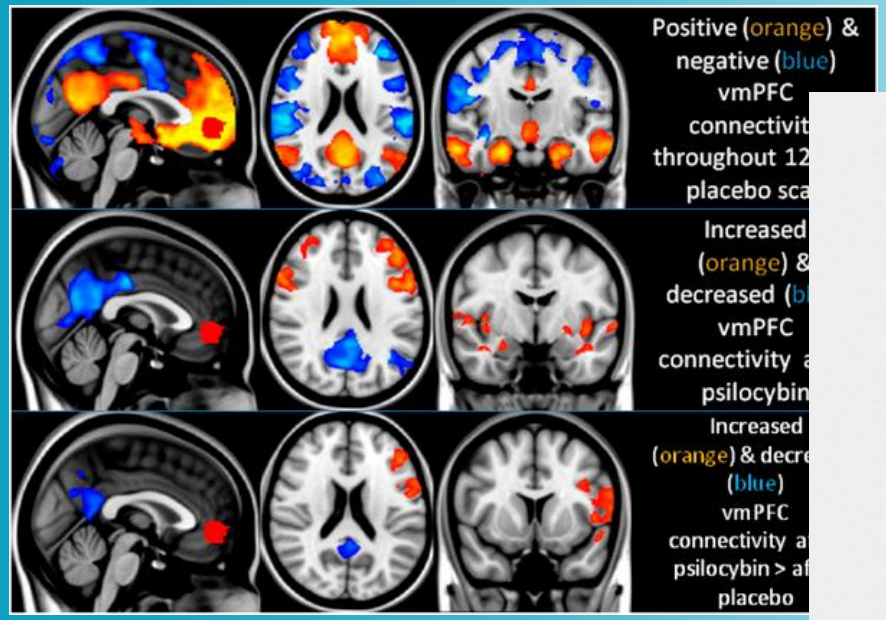
There have been a total of 51 papers on fMRI findings related to seretonergic psychedelics, of which 42 are of resting state, derived from 17 data sets, and of those 22/42 are derived from two original data sets, and those were with IV administration in individuals with previous experience. (McCulloch et al., 2021)

The majority of neuroimaging studies to date are during resting state/"task-free" conditions.

Resting state networks differ in important ways from networks underlying cognitive function; regions activated during rest are not always activated during cognitive tasks, and the converse is also true.

The same brain region can be involved in multiple cognitive functions and its pattern of functional connectivity can differ across cognitive functions.

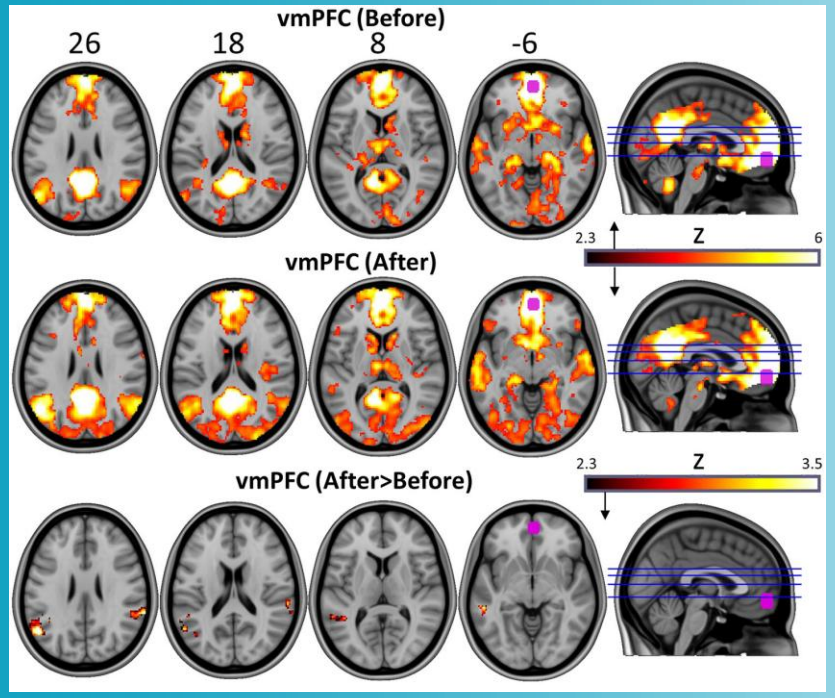
The Default Mode Network and Snow Globe Effect



There was a significant decrease in resting state functional connectivity between the medial prefrontal cortex (mPFC) and posterior cingulate cortex (PCC) following psilocybin administration.

Carhart-Harris, R. L., Erritzoe, D., Williams, T., Stone, J. M., Reed, L. J., Colasanti, A., ... & Nutt, D. J. (2012). Neural correlates of the psychedelic state as determined by fMRI studies with psilocybin. Proceedings of the National Academy of Sciences, 109(6), 2138-2143.

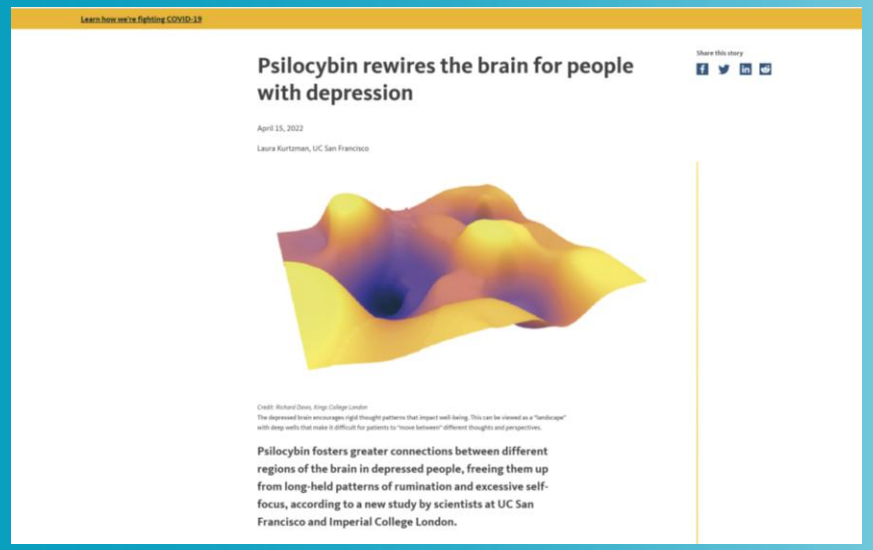
The Default Mode Network and Snow Globe Effect



Increased RSFC within the default-mode network (DMN) post-treatment.

Carhart-Harris, R. L., Roseman, L., Bolstridge, M., Demetriou, L., Pannekoek, J. N., Wall, M. B., ... & Nutt, D. J. (2017). Psilocybin for treatment-resistant depression: fMRI-measured brain mechanisms. Scientific reports, 7(1), 1-11.

Rewiring the Brain



Learn how we're fighting COVID-19

Psilocybin rewires the brain for people with depression

April 15, 2022

Laura Kurtzman, UC San Francisco

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Credit: Richard Daws, Kings College London

The depressed brain encourages rigid thought patterns that impact well-being. This can be viewed as a "landscape" with deep wells that make it difficult for patients to "move between" different thoughts and perspectives.

Psilocybin fosters greater connections between different regions of the brain in depressed people, freeing them up from long-held patterns of rumination and excessive self-focus, according to a new study by scientists at UC San Francisco and Imperial College London.

Resting state fMRI at baseline and 3 weeks after treatment with psilocybin or escitalopram in patients with MDD.

There was no significant interaction between treatment arm and scanning session on network modularity.

Daws, R. E., Timmermann, C., Giribaldi, B., Sexton, J. D., Wall, M. B., Erritzoe, D., ... & Carhart-Harris, R. (2022). Increased global integration in the brain after psilocybin therapy for depression. *Nature medicine*, *28*(4), 844-851.

Rewiring the Brain

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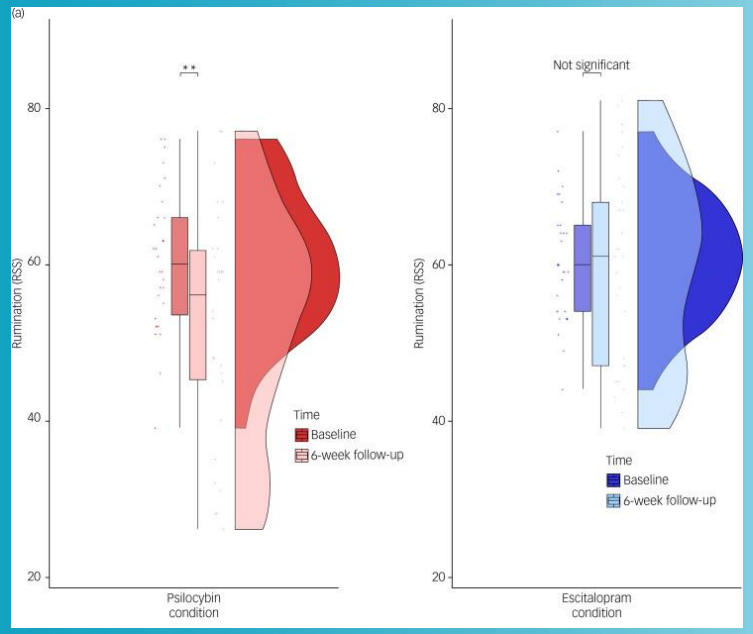
Psilocybin fosters greater connections between different regions of the brain in depressed people, freeing them up from long-held patterns of rumination and excessive self-focus, according to a new study by scientists at UC San Francisco and Imperial College London.

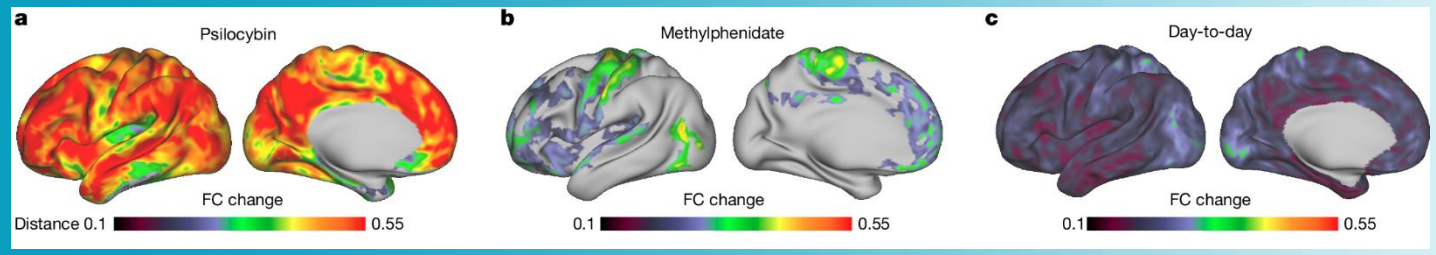


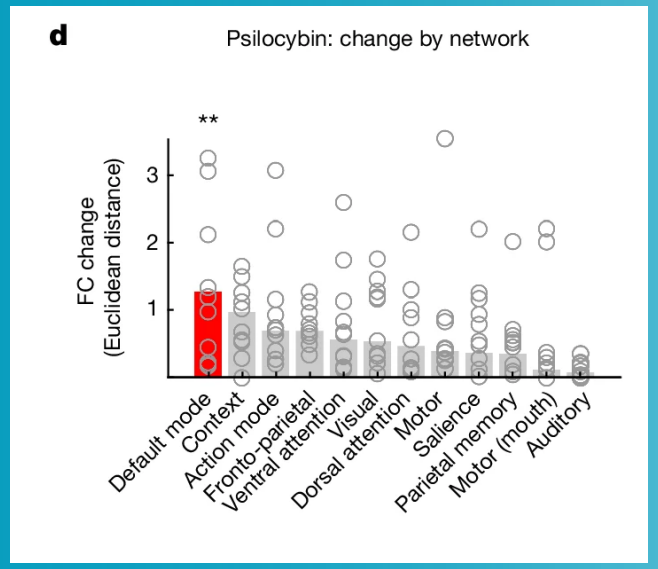
A three-way mixed ANCOVA on Trait Rumination scores revealed a significant time×response, a **nonsignificant** time×condition interaction, and a **non-significant** time×condition×response interaction.

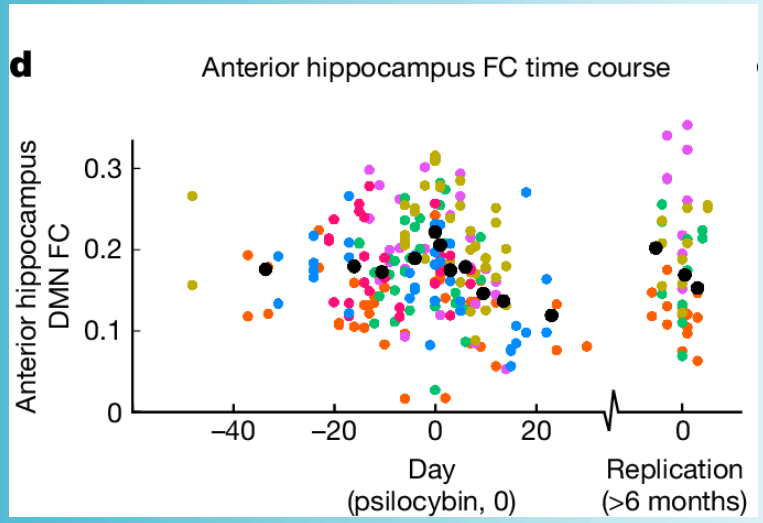
A significant decrease between Rumination scores at baseline and 6 weeks was found for **BOTH** escitalopram responders and psilocybin responders.

Barba, T., Buehler, S., Kettner, H., Radu, C., Cunha, B. G., Nutt, D. J., ... & Carhart-Harris, R. (2022). Effects of psilocybin versus escitalopram on rumination and thought suppression in depression. *BJPsych Open*, *8*(5), e163.

Rewiring the Brain







Whole-brain FC change scores were small, indicating that the brain's network structure had mostly returned to baseline.

Siegel, J. S., Subramanian, S., Perry, D., Kay, B. P., Gordon, E. M., Laumann, T. O., ... & Dosenbach, N. U. (2024). Psilocybin desynchronizes the human brain. Nature, 1-8.

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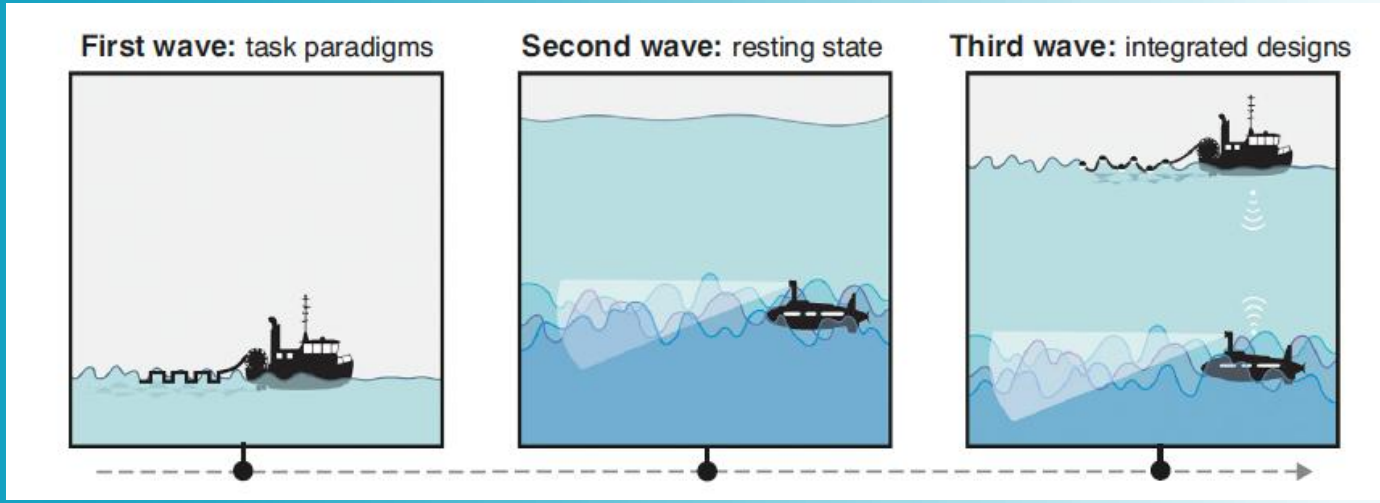

Finn, E. S. (2021). Is it time to put rest to rest?. *Trends in cognitive sciences*, *25*(12), 1021-1032.

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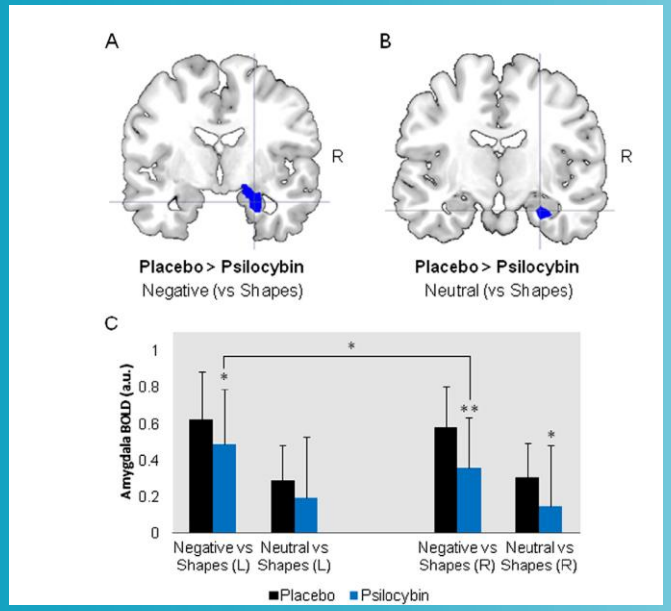
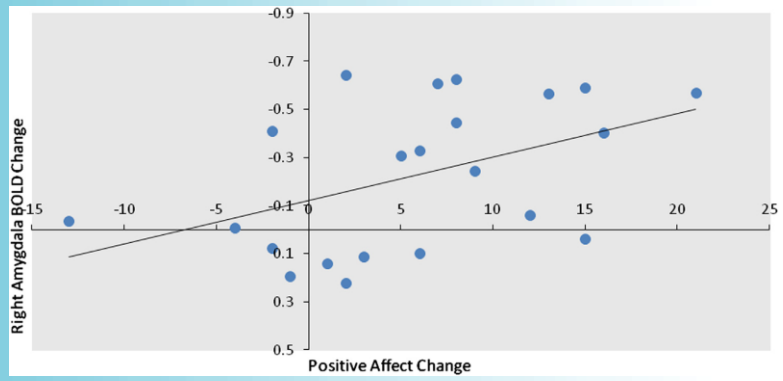
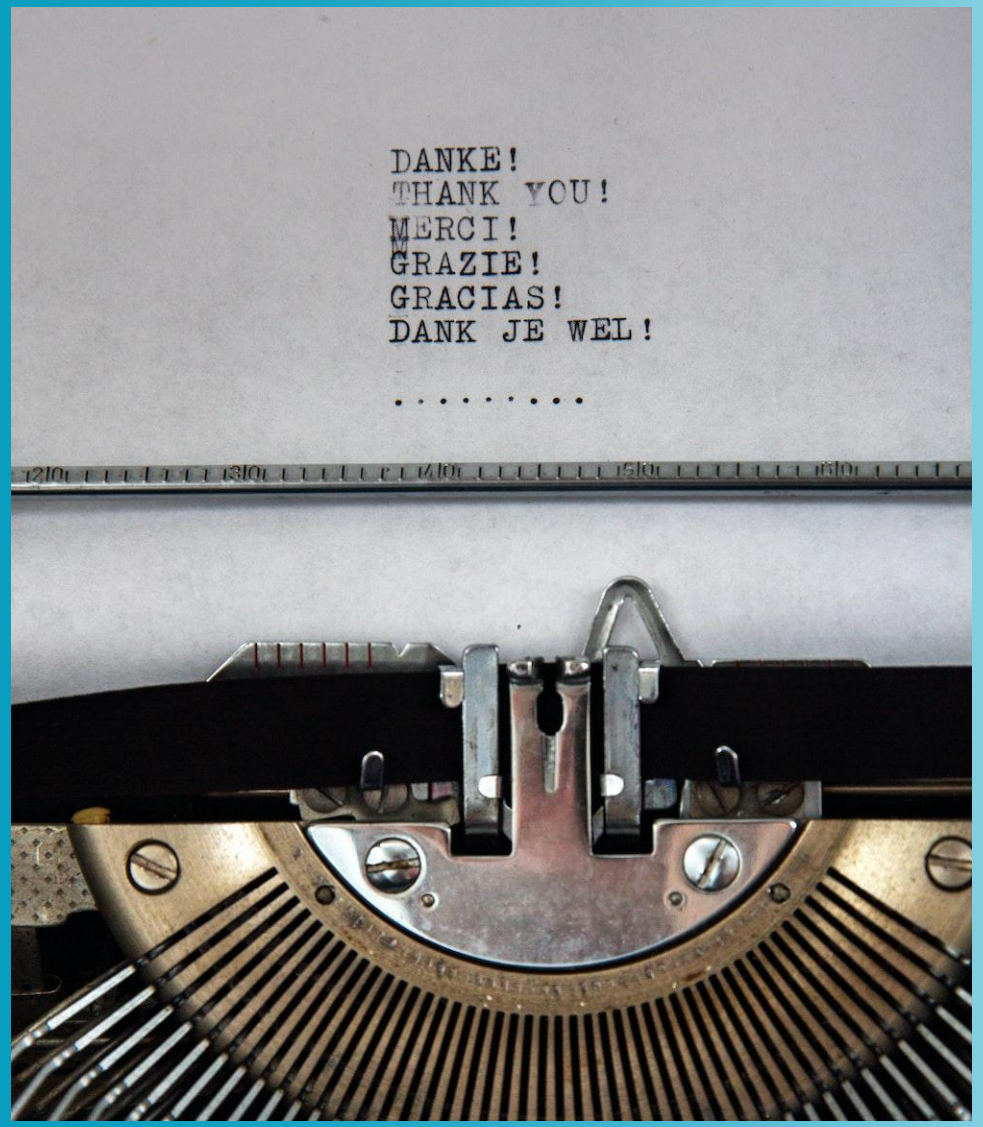
Assessed the effects of acute administration of versus placebo on amygdala reactivity to negative stimuli in 25 healthy volunteers.





Kraehenmann, R., Preller, K. H., Scheidegger, M., Pokorny, T., Bosch, O. G., Seifritz, E., & Vollenweider, F. X. (2015). Psilocybin-induced decrease in amygdala reactivity correlates with enhanced positive mood in healthy volunteers. *Biological psychiatry*, *78*(8), 572-581.



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