Using brain scans of people on mind-altering drugs to learn more about neurotransmitter systems

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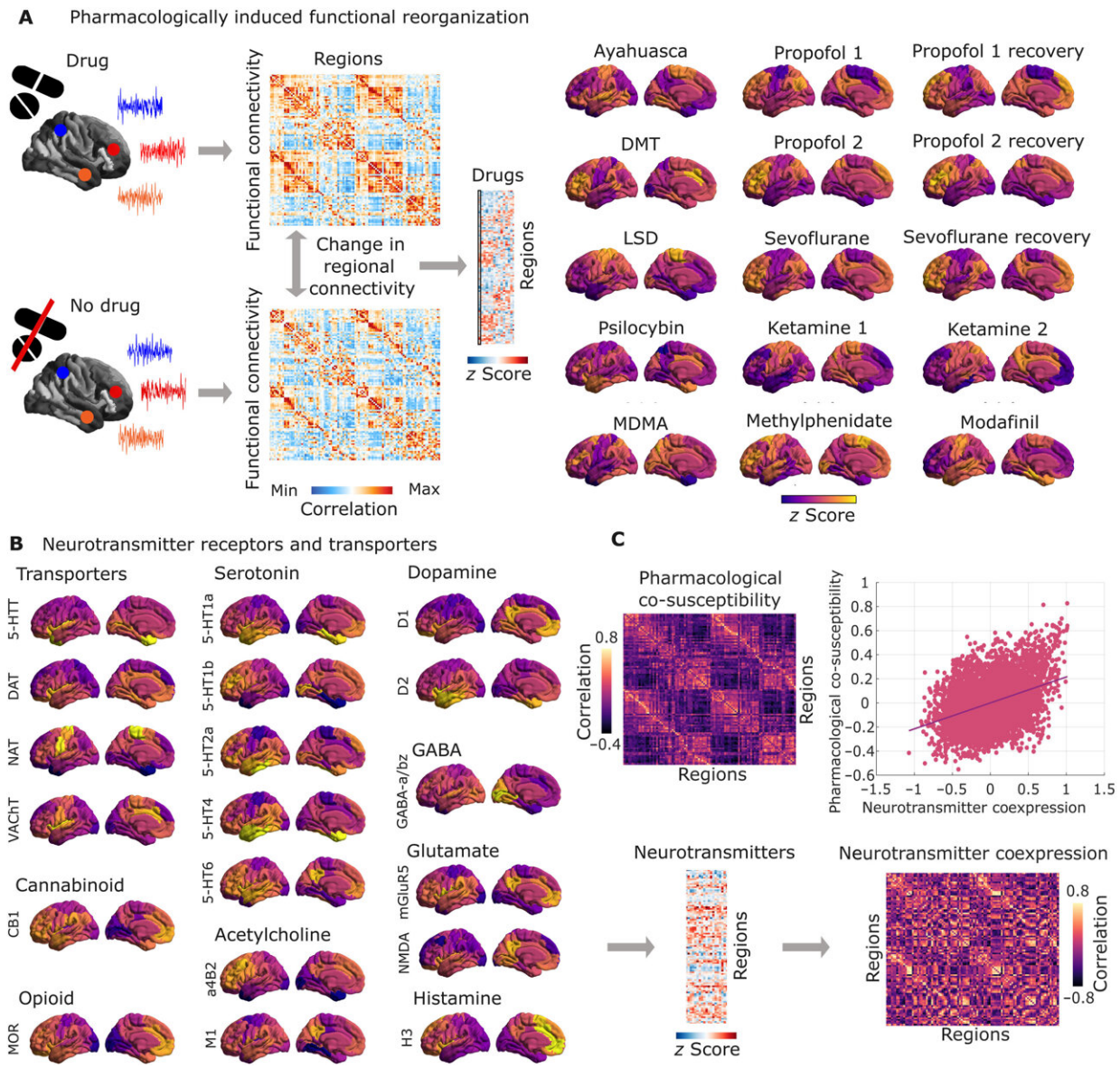

Overview of receptors and pharmacological rs-fMRI data. (A) For each psychoactive drug, its pattern of pharmacologically induced functional reorganization is quantified as the average (across subjects) of the within-subject difference in regional FC weighted degree (sum of each region's positive connections) between task-free fMRI scans at baseline and under the drug's effects. The result is a map of 100 cortical regions with 15 drug-related contrasts. (B) Neurotransmitter systems are mapped with PET with radioligands for 15 receptors and 4 transporters, resulting in a map of 100 cortical regions with 19 neurotransmitters. (C) A region-by-region matrix of pharmacological co-susceptibility is obtained by pairwise correlation of the regional patterns of drug-induced FC changes across all concatenated subject-wise delta maps. A region-by-region matrix of neurotransmitter coexpression is obtained by pairwise correlation of the regional patterns of neurotransmitter expression, concatenated across all 19 receptor and transporter PET maps. These two matrices are significantly correlated (Spearman's correlation across N = 4950 edges) even after removing the exponential relationship with Euclidean distance between regions. Credit: *Science Advances* (2023). DOI: 10.1126/sciadv.adf8332

An international team of neuroscientists, anesthesiologists and other medical researchers has learned more about the changes that occur in brain neurotransmitter systems under the influence of psychedelics, anesthetics and cognitive enhancers by studying PET and fMRI scans of brains of people administered such drugs. The study is published in *Science Advances*.

Prior research has led to the use of a variety of mind-altering drugs by medical practitioners in medical contexts to achieve beneficial medical results—anesthetics allow for conducting pain-free surgery, for example, and psychedelics have proven to be useful tools for treating mental disorders such as PTSD. What is not known, however, is the additional impact such drugs have on the brain. In this new effort, the researchers sought to learn more about the effects on a neural system level.

The researchers obtained and analyzed 1,200 PET scans of human brains under the influence of mind-altering drugs, either as part of medical treatment or as part of work in other research efforts. The scans were divided by category; psychedelics, anesthetics and cognitive enhancers. They also analyzed a second dataset of fMRI brain scans taken after administration of mind-altering drugs.

The research team found that the drugs had impacts on multiple neurotransmitter systems—not just those being targeted. In addition to expected relationships, such as links between MDMA and serotonin receptors, they found that many of the mind-altering drugs could impact neurotransmitters distant from intended targets. They also found that such unintended consequences could differ depending on the dosage of the drug administered.

The researchers suggest their work provides a new starting point for studying the far-reaching impact of mind-altering drugs on patients, and also for learning more about how neurotransmitter systems are related. They also suggest that what they learned in their work could be useful in vetting new drugs.

More information: Andrea I. Luppi et al, In vivo mapping of pharmacologically induced functional reorganization onto the human brain's neurotransmitter landscape, *Science Advances* (2023). DOI: 10.1126/sciadv.adf8332