

Supporting Information

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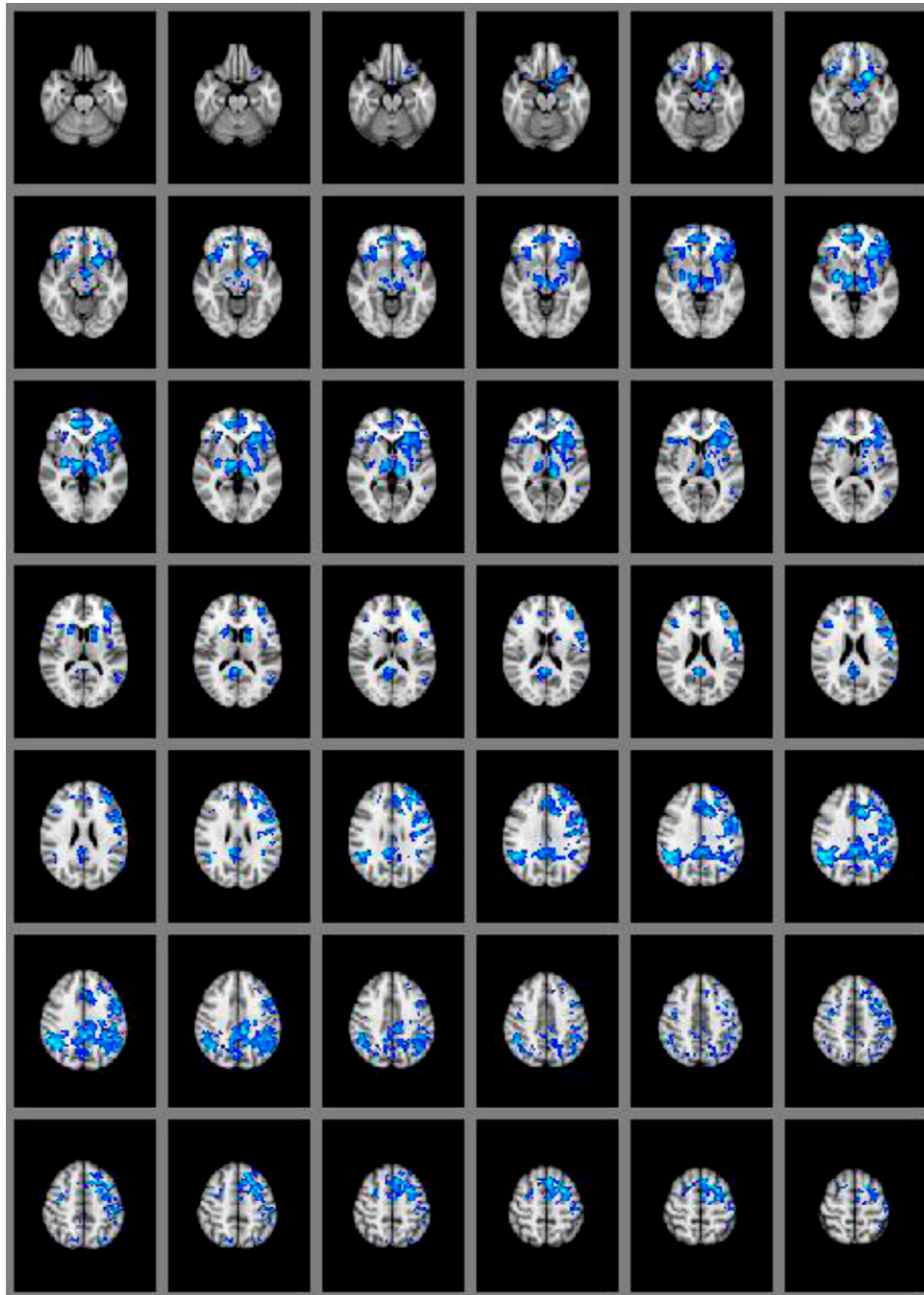


Fig. S1. Slices for arterial spin labeling (ASL) result. Lightbox display of slices showing regions where there were significant decreases in cerebral blood flow (CBF) after psilocybin versus placebo. Mixed-effects analysis, cluster threshold = 2.3, $P = 0.05$ whole-brain corrected, $n = 15$. The right hemisphere is shown on the left.

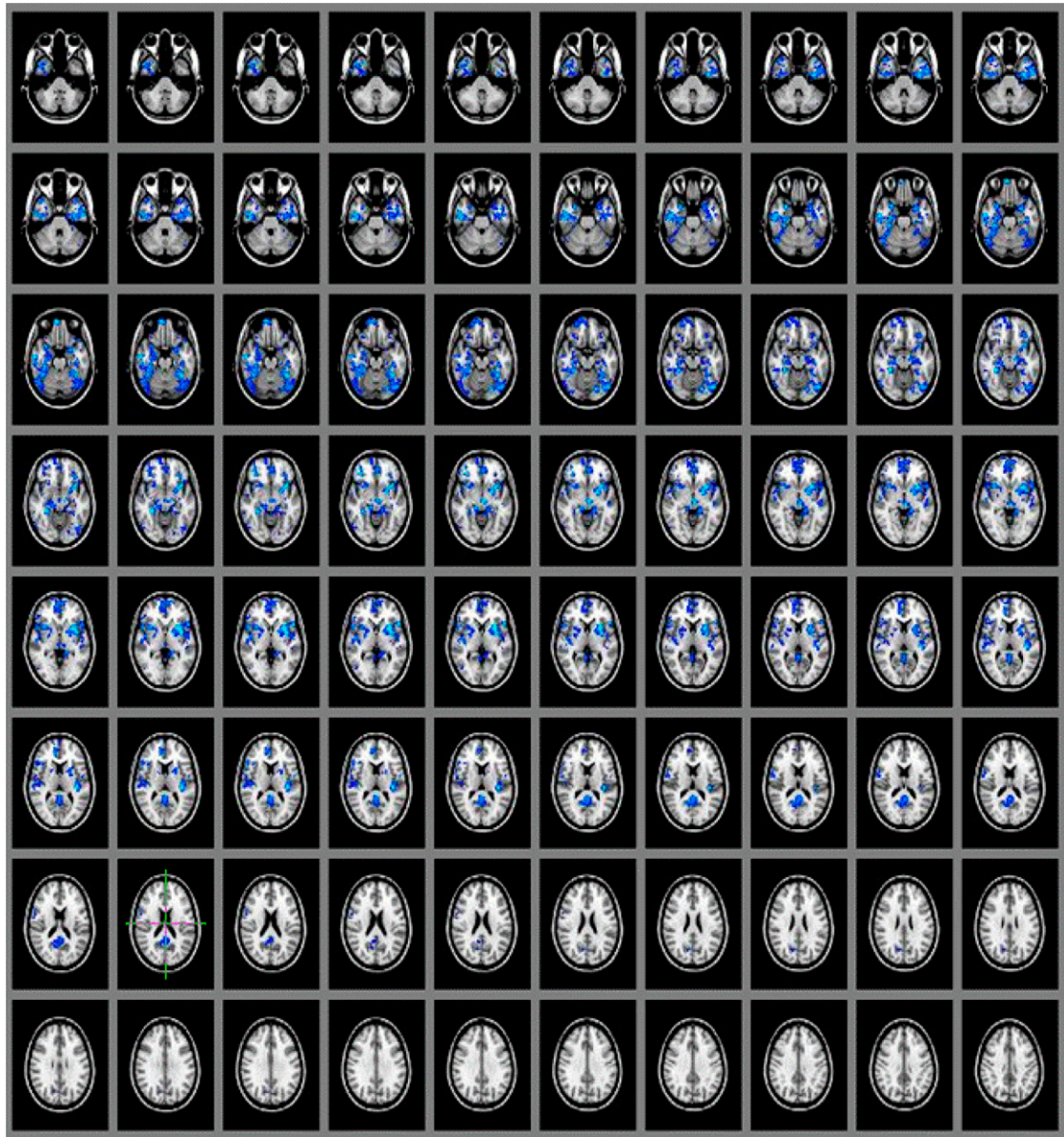


Fig. S2. Slices for blood-oxygen level-dependent (BOLD) result: Lightbox display of slices showing regions where there were significant decreases in BOLD after psilocybin vs. placebo. Mixed-effects analysis, cluster threshold = 1.8, $P < 0.05$ whole-brain corrected, $n = 15$. The right hemisphere is shown on the left.

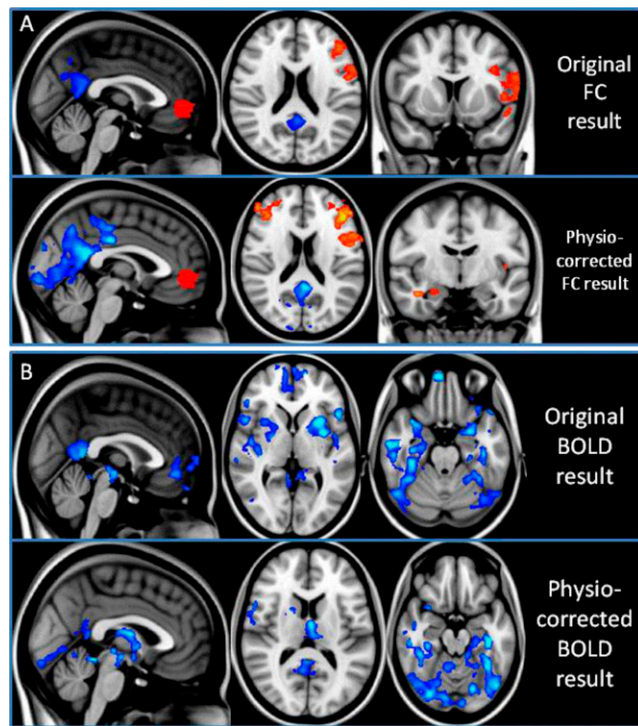


Fig. 53. Physiologically corrected results. (A) Corrected functional connectivity result. The original image used a cluster threshold of 2.3, mixed effects, $P < 0.05$, whole-brain corrected and the corrected image used a cluster threshold of 1.8, mixed effects, $P < 0.05$ whole-brain corrected. Both results show connectivity changes under psilocybin that were greater than connectivity changes under placebo (orange, increases in connectivity with the vmPFC; blue, decreases). (B) Corrected BOLD results. Both BOLD maps were based on mixed effects analyses, cluster-threshold 1.8, $P < 0.05$, whole-brain corrected. Both maps show greater decreases in BOLD after psilocybin vs. after placebo.

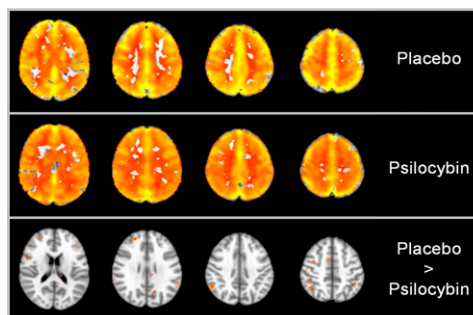


Fig. 54. Cerebrovascular reactivity (CVR) maps. The across-subject mean CVR maps are shown for both the placebo and psilocybin conditions (*Top and Middle*). Each map is thresholded at a very liberal $P < 0.01$ uncorrected threshold (t tests vs. 0). These maps demonstrate the high CVR values are located in gray matter as is expected. (*Bottom*) The results from a paired t test between placebo and drug conditions, again thresholded at $P < 0.01$ uncorrected. The paucity of differences at such a liberal threshold demonstrates that CVR remains unchanged by psilocybin.

Table S1. All items rated after each scan

Item	ASL plac	ASL psilo	BOLD plac	BOLD psilo	Combine: psilo – plac (SD)
I saw geometric patterns			0.3	73.5	73.2 (16.9)
I saw my surroundings change in unusual ways	7.1	75.3			68.2 (21.3)
I felt unusual bodily sensations			6.5	67.3	60.9 (23.1)
Things looked strange	8.1	69.9	2.2	59.3	59.5 (22)
My sense of size or space was altered	3.9	64.1	0.9	53.0	56.2 (23.2)
Sounds influenced things I saw			2.4	57.5	55.1 (21.7)
My imagination was extremely vivid	3.5	54.7	6.5	64.7	54.7 (23.9)
My perception of time was distorted			5.2	58.2	53 (20.2)
My sense of size or space was distorted			0.9	53.0	52.1 (16.3)
My sense of time was altered	6.3	55.4	5.2	58.2	51 (24.3)
The experience had a dreamlike quality	8.9	53.3	6.2	57.5	47.8 (24.2)
It felt like I was floating			3.7	51.1	47.5 (23.9)
My thoughts wandered freely	11.0	57.7	10.5	56.7	46.4 (23.2)
Everything seemed 'alive'	1.5	47.1			45.5 (21.6)
It felt like I was merging with my environment			2.2	47.3	45.1 (21.9)
I felt a sense of awe	3.1	48.0			44.9 (21.5)
The experience had a supernatural quality			0.7	44.5	43.7 (20.2)
I experienced a loss of separation from my surroundings			2.1	45.3	43.2 (18.7)
I felt a sense of joy	5.1	45.9			40.8 (25.4)
My sense of self was altered	2.6	43.3			40.7 (23.4)
The experience had a spiritual or mystical quality			1.8	40.3	38.5 (23.6)
My thinking was muddled	5.9	40.9	1.4	41.5	37.5 (19)
I felt a profound inner peace			7.0	41.3	34.3 (21.2)
I lost all sense of ego			3.2	34.6	31.4 (20.6)
The experience had a mystical quality	1.9	31.5			29.5 (19.6)
The experience had a magical or supernatural quality	2.4	31.7			29.2 (20.2)
The experience had a spiritual quality	2.7	28.2			25.5 (19)
I thought about myself and my past	4.8	22.9			18.1 (17)
I feared losing control of my mind	3.3	18.0	3.1	14.6	13.1 (16.7)
I felt afraid	5.8	13.7	6.5	20.4	10.9 (17.3)
I felt suspicious or paranoid	4.1	6.0	3.5	14.3	6.3 (12.8)

All of these items were rated at the end of each scan in a visual analog scale format with a bottom anchor of "no more than usually" and a top anchor of "much more than usually." Scores are expressed as a percentage, with 100% being a mark adjacent to the top anchor "much more than usually." All items were rated significantly higher after psilocybin than placebo with the exception of "I felt afraid" and "I felt suspicious or paranoid" (*t* tests, *P* = 0.05).

Table S2. Regional 5-HT_{2A} receptor binding potentials: 5-HT_{2A} binding potential was assessed with ¹⁸F-altanserin PET in 136 healthy adult human subjects

Brain region	BPp(av)	SD
Posterior cingulate cortex	1.64	0.51
Superior temporal cortex	1.59	0.53
Medial inferior temporal cortex	1.57	0.52
Dorsolateral prefrontal cortex (DLPFC)	1.51	0.52
Anterior cingulate cortex	1.49	0.54
Medial inferior frontal gyrus	1.49	0.50
Occipital cortex	1.47	0.47
Orbitofrontal cortex	1.46	0.54
Paracingulate cortex	1.45	0.48
Average frontal cortex	1.45	0.50
Average global neocortex	1.44	0.48
Ventrolateral prefrontal cortex (VLPFC)	1.44	0.50
Insula	1.44	0.49
Superior frontal gyrus	1.38	0.48
Sensorimotor cortex	1.09	0.39
Amygdala	0.64	0.28
Putamen/pallidum	0.51	0.16
Hippocampus	0.51	0.28
Entorhinal cortex	0.43	0.32
Thalamus	0.33	0.18
Caudate nucleus	0.25	0.17

For further details about the data presented in the table, please see Erritzoe, et al., (1) for study sample and imaging methods, Frokjaer, et al., (2) for delineation of VLPFC and DLPFC, and Svarer, et al. (3) for delineation of other brain regions. Please note that the VLPFC and the DLPFC are defined so that they are both overlapping with the medial and inferior frontal cortex, and in addition the DLPFC overlaps with the superior frontal cortex. Av, average; BP_p, binding potential normalized to plasma; 5-HT, 5-Hydroxytryptamine.

1. Erritzoe D, et al. (2009) Brain serotonin 2A receptor binding: Relations to body mass index, tobacco and alcohol use. *Neuroimage* 46:23–30.
2. Frokjaer VG, et al. (2009) High familial risk for mood disorder is associated with low dorsolateral prefrontal cortex serotonin transporter binding. *Neuroimage* 46:360–366.
3. Svarer C, et al. (2005) MR-based automatic delineation of volumes of interest in human brain PET images using probability maps. *Neuroimage* 24:969–979.