

**Title:** Shared and distinct brain regions targeted for immediate early gene expression by ketamine and psilocybin

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## **SUPPORTING INFORMATION**

### **Contents**

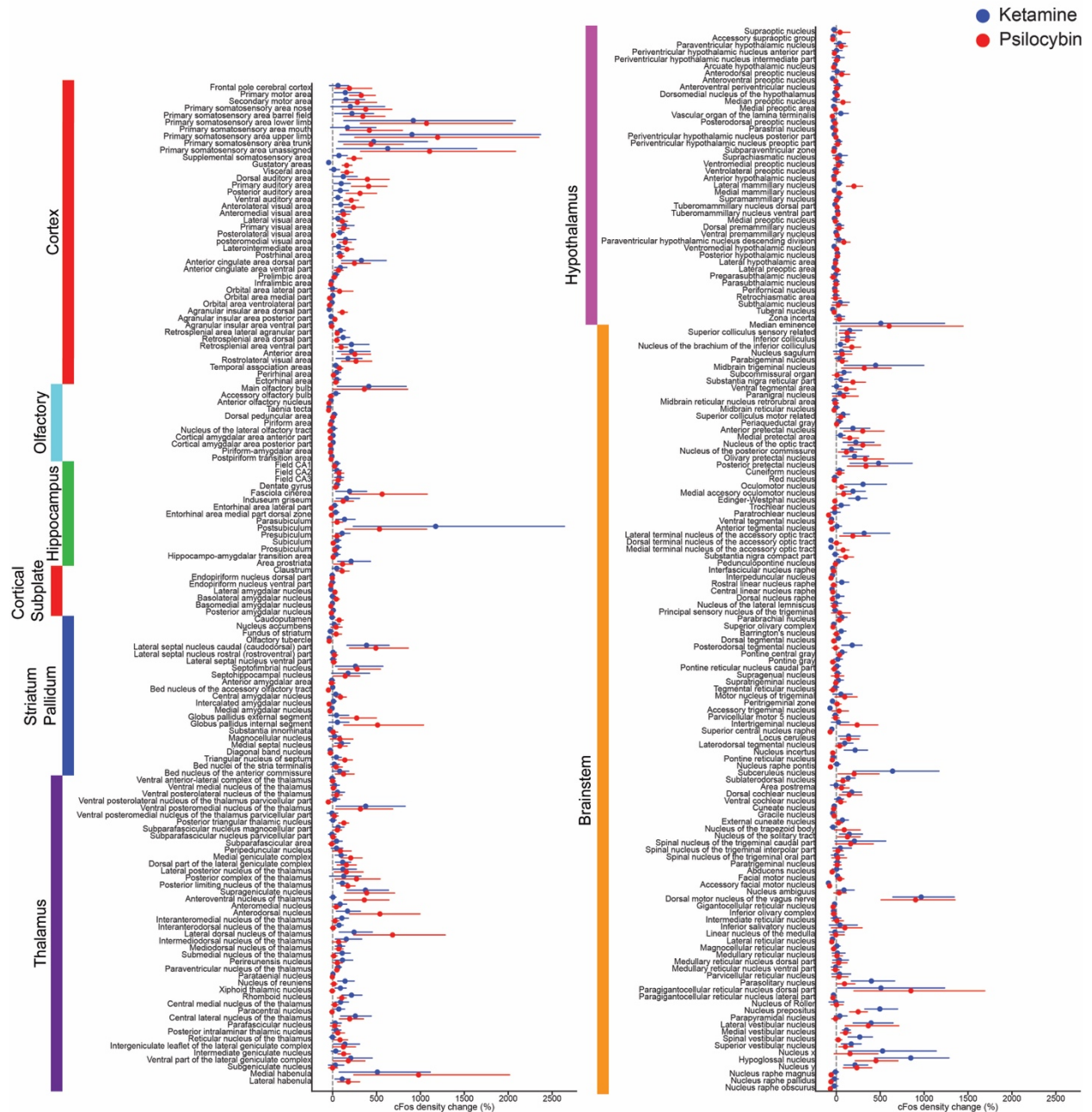
Figure S1

Figure S2

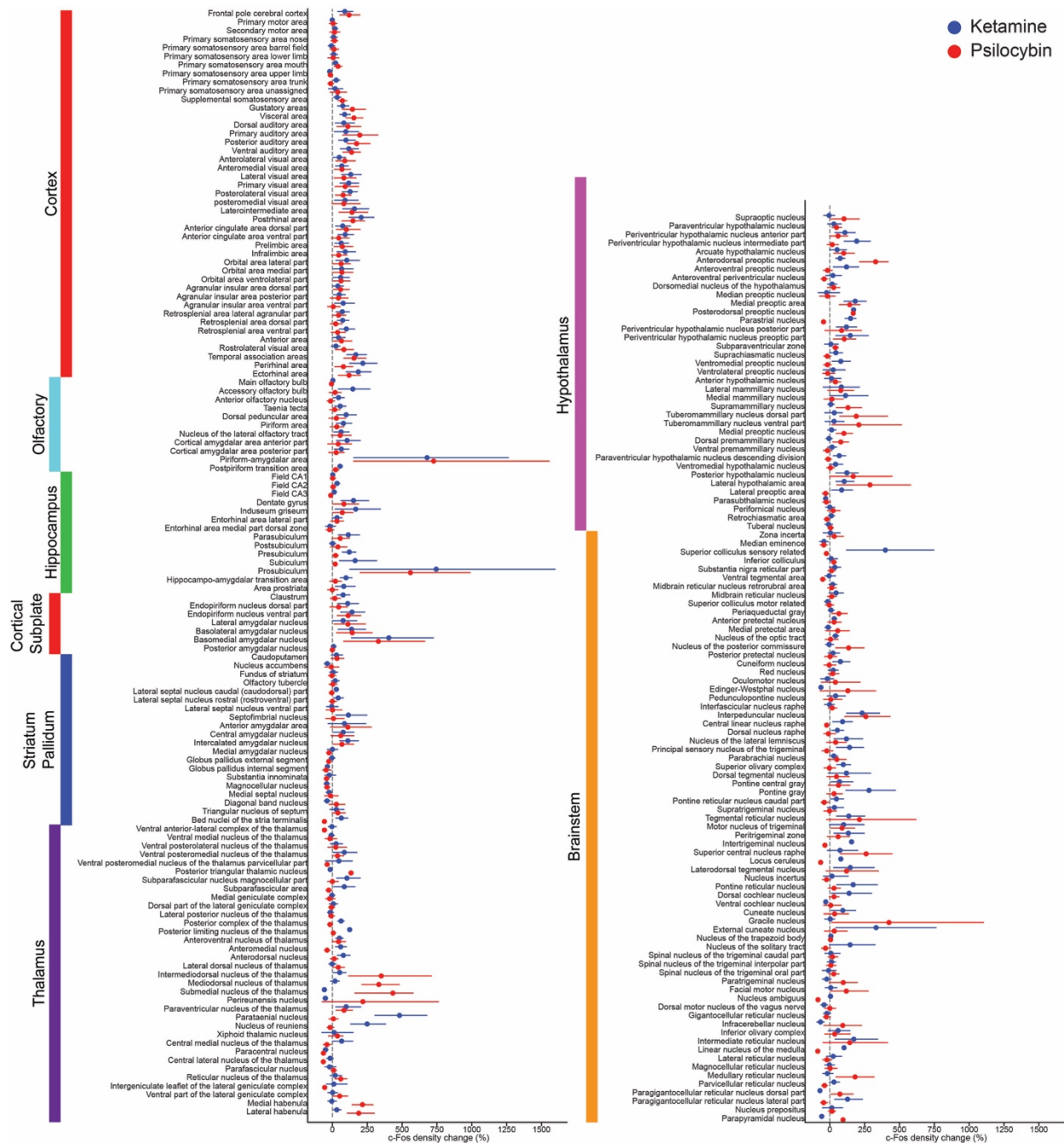
Figure S3

Figure S4

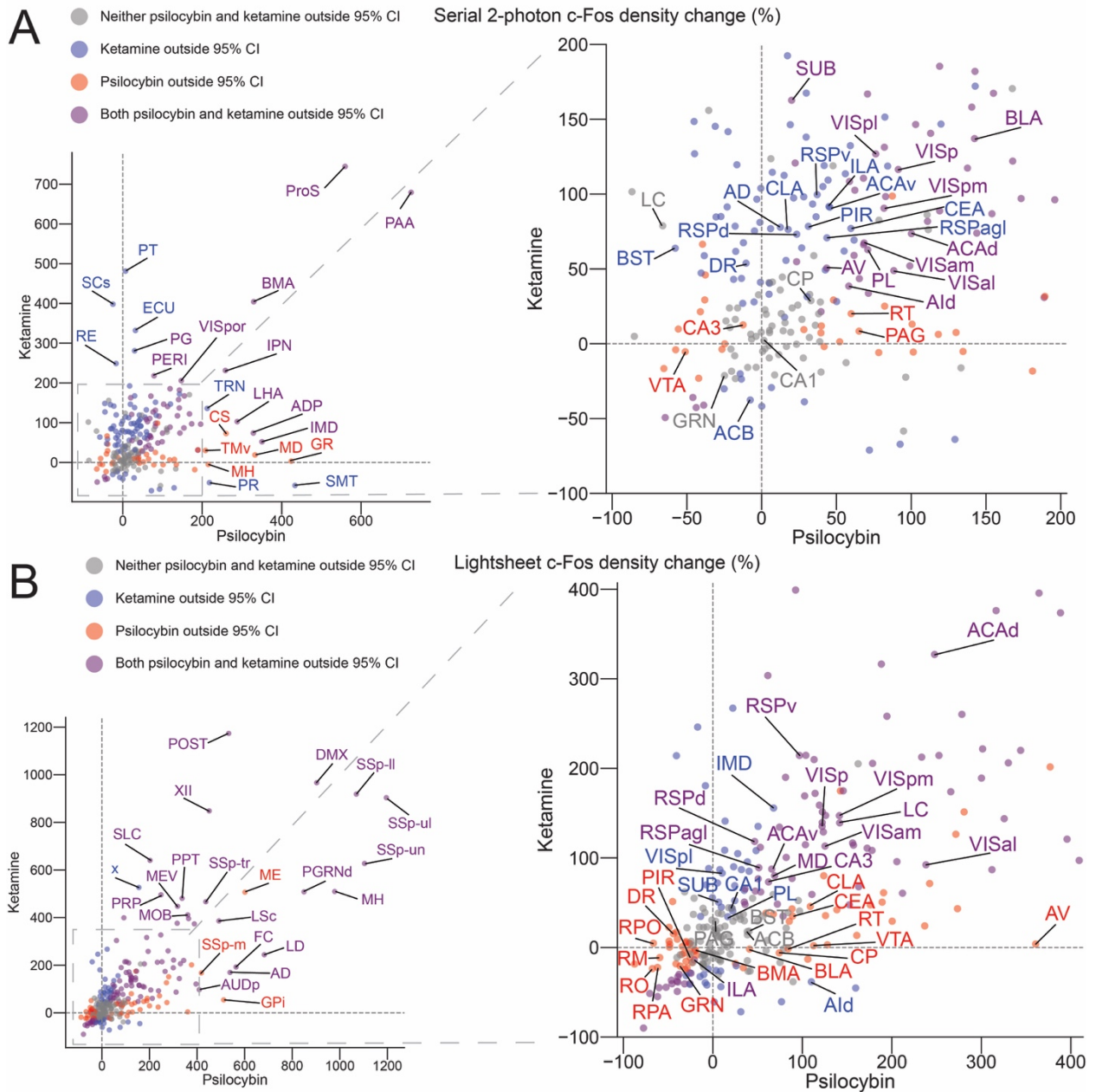
Figure S5



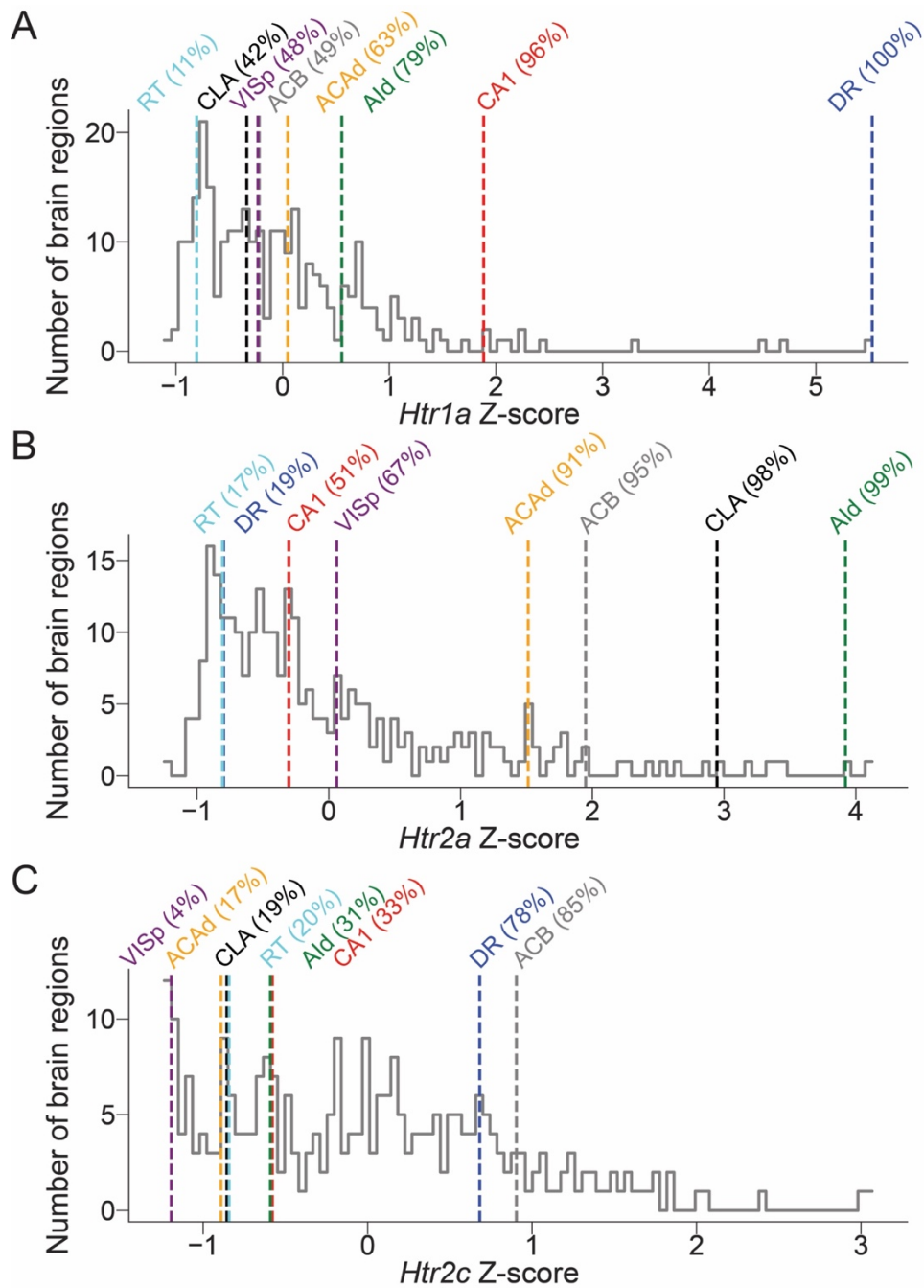
**Figure S1: Effects of psilocybin and ketamine on regional c-Fos expression as measured by serial two-photon microscopy.** Percent change in c-Fos density from saline vehicle baseline for psilocybin (red) and ketamine (blue). Circle, mean. Line, bootstrapped 95% confidence intervals assuming normal distribution.



**Figure S2: Effects of psilocybin and ketamine on regional c-Fos expression as measured by light sheet microscopy.** Percent change in c-Fos density from saline vehicle baseline for psilocybin (red) and ketamine (blue). Circle, mean. Line, bootstrapped 95% confidence intervals assuming normal distribution.

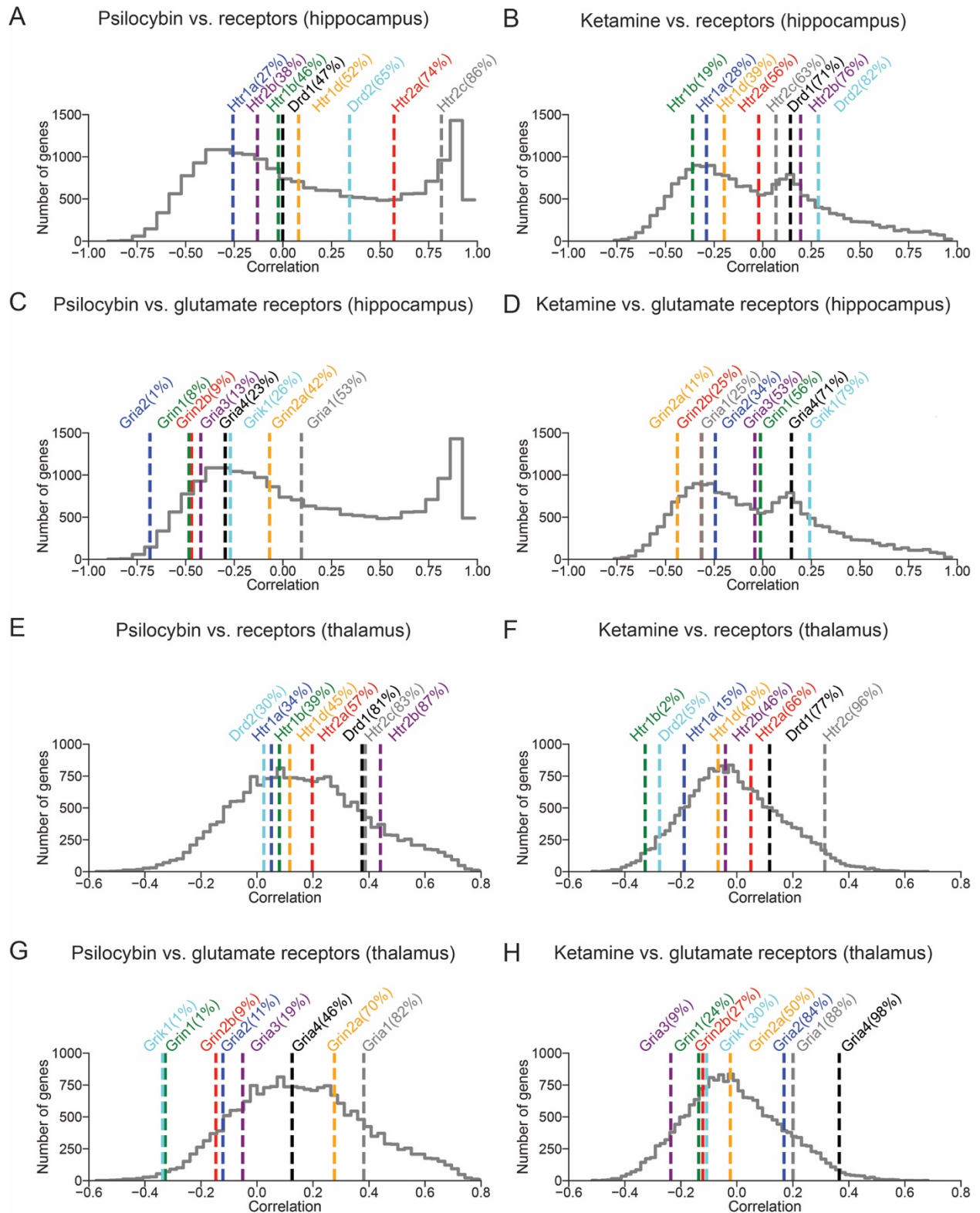


**Figure S3: Psilocybin and ketamine induce convergent and distinct differences in c-Fos expression. (A)** Scatter plot of mean percent change in c-Fos density from saline vehicle, for psilocybin (x-axis) versus ketamine (y-axis) as measured by serial two-photon microscopy. **(B)** Similar to (A) but as measured by light sheet microscopy.



**Figure S4: Differential expression of serotonin receptors across brain regions. (A)** Relative gene expression levels of *Htr1a* gene from Allen Institute in situ hybridization database across all brain regions. Grey line, histogram of Z-score for *Htr1a* gene for all brain regions. Colored lines, Z-score and percentile rank for specific brain regions. **(B)** similar to **(A)** but for *Htr2a* gene. **(C)** similar to **(A)** but for *Htr2c* gene.





**Figure S5: Potential receptors contributing to drug-evoked c-Fos expression in hippocampus and thalamus. (A)** Correlation coefficients computed for psilocybin condition in the hippocampus. Colored lines, correlation coefficients for select serotonin and dopamine

receptor genes, with percentile indicated within the parenthesis. Grey line, histogram of correlation coefficients for all 19,413 genes in the mouse genome. **(B)** Similar to (A) for ketamine. **(C)** Similar to (A) for glutamate receptors. **(D)** Similar to (C) for ketamine. **(E - H)** Similar to (A - D) except for thalamus.