

# PNAS

[www.pnas.org](http://www.pnas.org)

Supplementary Information for

Brain-wide functional architecture remodeling by alcohol dependence and abstinence

Adam Kimbrough, Daniel J. Lurie, Andres Collazo, Max Kreifeldt, Harpreet Sidhu, Giovana  
Camila Macedo, Mark D'Esposito, Candice Contet, Olivier George

Olivier George

Email: [olgeorge@ucsd.edu](mailto:olgeorge@ucsd.edu)

**This PDF file includes:**

Figures S1 to S8  
Tables S1 to S1

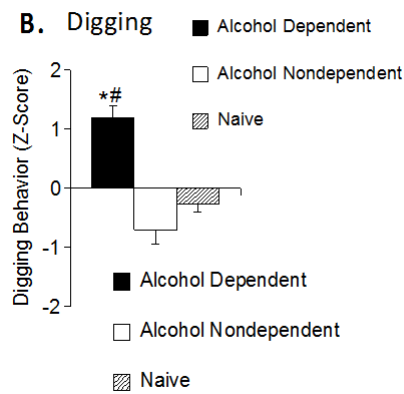
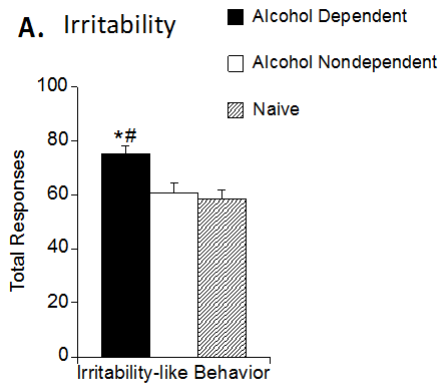


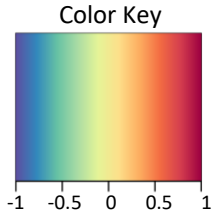
Fig. S1. Withdrawal behaviors for separate control groups (alcohol-nondependent and naive mice) compared with alcohol-dependent mice. **A.** The number of irritable-like responses was significantly higher in alcohol-dependent mice (black bar) compared with both alcohol-nondependent mice (white bar) and naive mice (hashed bar). **B.** Alcohol-dependent mice (black bar) exhibited a significant increase in digging behavior compared with both alcohol-nondependent mice (white bar) and naive mice (hashed bar). \* $p < 0.05$ , vs. naive; # $p < 0.05$ , vs. alcohol-nondependent.



**Fig. S2.** Saccharin intake in alcohol-dependent, nondependent, and naive (water) mice, expressed at mg/kg/24 h. Average saccharin intake over 7 days of testing was not different between alcohol-dependent (black bar), alcohol-nondependent (white bar), and naive (hashed bar) mice.







Alcohol Dependent

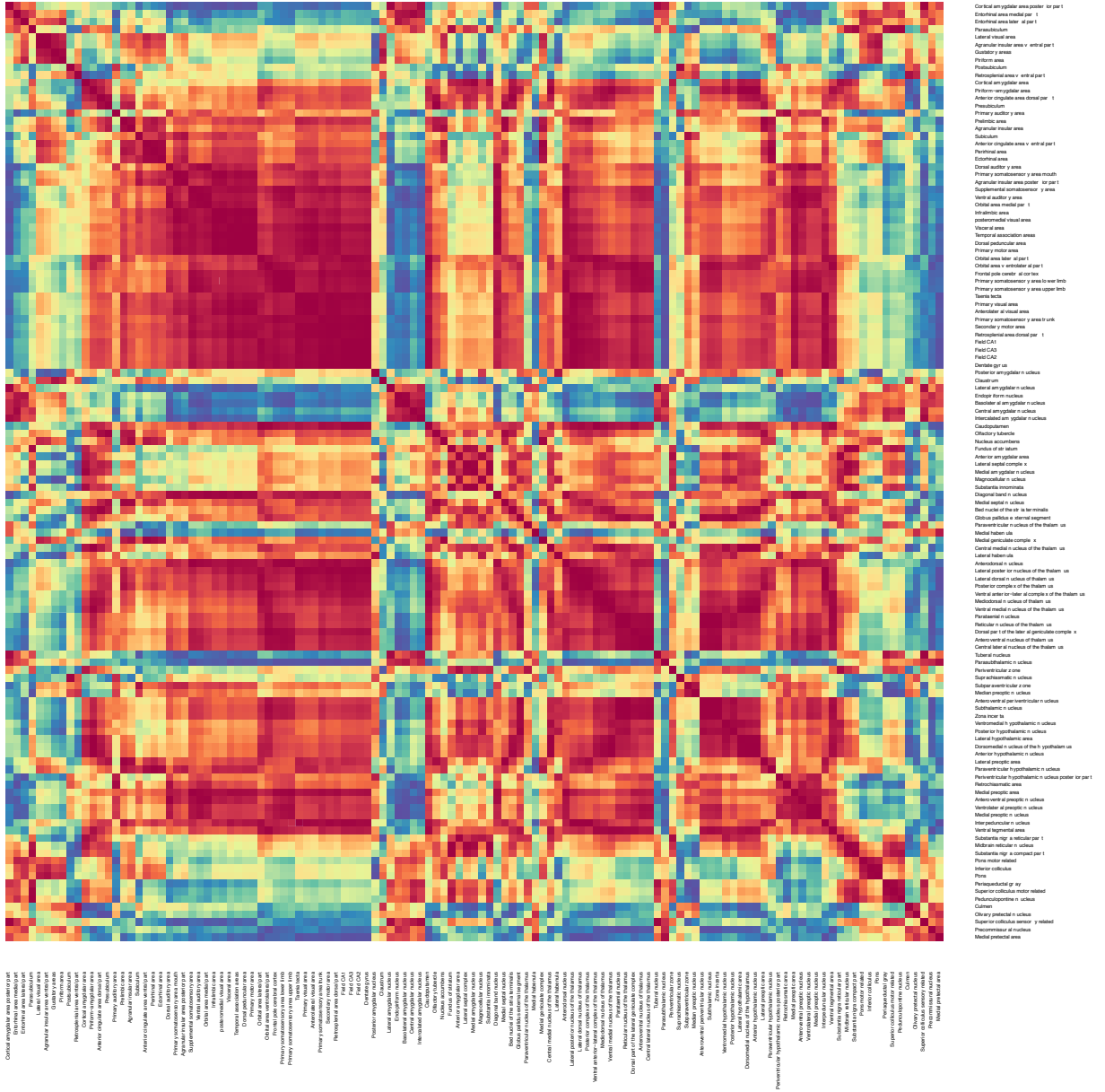


Fig. S5. Interbrain region Pearson correlations for alcohol dependent mice with region labels.



Naive

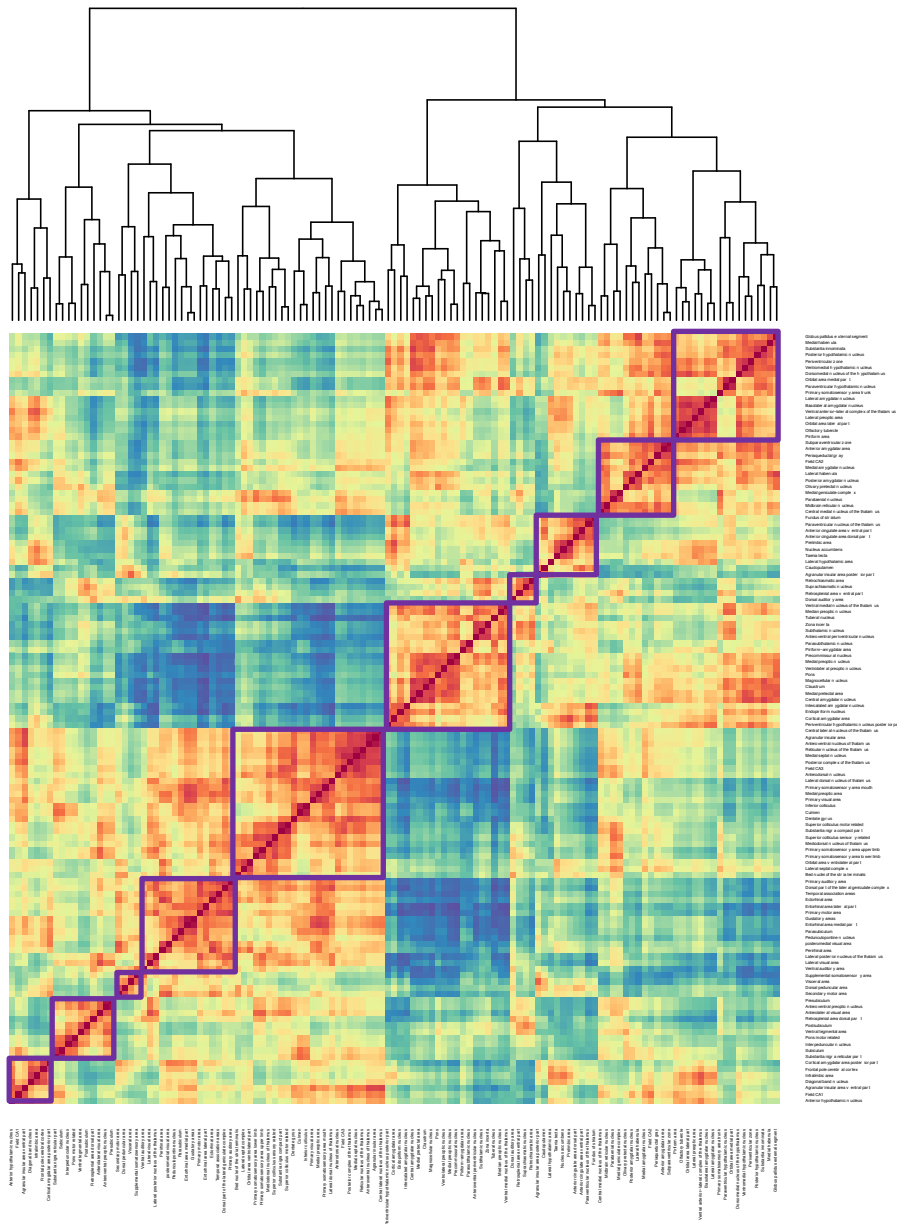


Fig. S6. Hierarchical clustering and modules for naive mice with region labels.







**Table S1.** Brain region names, abbreviations, Allen Brain atlas grouping, abstinence module, participation coefficient, and within-module degree Z score values for abstinence network.

| <b>Brain Region</b>                     | <b>Abbreviation</b> | <b>Allen Group Name</b> | <b>Abstinence Module</b> | <b>PC</b> | <b>WMDz</b> |
|---|---------------------|-------------------------|--------------------------|-----------|-------------|
| Agranular insular area                  | AI                  | Cortical Plate          | C                        | 0         | -1.46       |
| Agranular insular area, posterior part  | AIp                 | Cortical Plate          | C                        | 0         | -0.51       |
| Agranular insular area, ventral part    | AIv                 | Cortical Plate          | B                        | 0.67      | -1.02       |
| Anterior cingulate area, dorsal part    | ACAd                | Cortical Plate          | C                        | 0.26      | -0.77       |
| Anterior cingulate area, ventral part   | ACAv                | Cortical Plate          | C                        | 0.25      | -1.83       |
| Anterolateral visual area               | VISal               | Cortical Plate          | C                        | 0         | 0.73        |
| Cortical amygdalar area                 | COA                 | Cortical Plate          | B                        | 0.49      | 0.74        |
| Cortical amygdalar area, posterior part | COAp                | Cortical Plate          | A                        | 0.16      | 1.61        |
| Dentate gyrus                           | DG                  | Cortical Plate          | C                        | 0         | 1.13        |
| Dorsal auditory area                    | AUDd                | Cortical Plate          | C                        | 0         | -0.37       |
| Dorsal peduncular area                  | DP                  | Cortical Plate          | C                        | 0         | 0.58        |
| Ectorhinal area                         | ECT                 | Cortical Plate          | C                        | 0.08      | -0.12       |
| Entorhinal area, lateral part           | ENTl                | Cortical Plate          | A                        | 0.44      | -0.12       |
| Entorhinal area, medial part            | ENTm                | Cortical Plate          | A                        | 0.45      | 0.41        |
| Field CA1                               | CA1                 | Cortical Plate          | C                        | 0         | 1.33        |
| Field CA2                               | CA2                 | Cortical Plate          | C                        | 0         | 1.41        |
| Field CA3                               | CA3                 | Cortical Plate          | C                        | 0         | 1.39        |
| Frontal pole, cerebral cortex           | FRP                 | Cortical Plate          | C                        | 0         | 0.96        |
| Gustatory areas                         | GU                  | Cortical Plate          | A                        | 0.49      | -1.26       |
| Infralimbic area                        | ILA                 | Cortical Plate          | C                        | 0         | 0.35        |
| Lateral visual area                     | VISl                | Cortical Plate          | B                        | 0.65      | -1.04       |
| Orbital area, lateral part              | ORBl                | Cortical Plate          | C                        | 0         | 1.13        |
| Orbital area, medial part               | ORBm                | Cortical Plate          | C                        | 0         | -0.03       |
| Orbital area, ventrolateral part        | ORBvl               | Cortical Plate          | C                        | 0         | 1.10        |
| Parasubiculum                           | PAR                 | Cortical Plate          | B                        | 0.27      | 0.52        |
| Perirhinal area                         | PERI                | Cortical Plate          | C                        | 0.06      | -0.85       |
| Piriform area                           | PIR                 | Cortical Plate          | A                        | 0.50      | -0.88       |
| Piriform-amygdalar area                 | PAA                 | Cortical Plate          | C                        | 0.30      | -0.60       |
| Posteromedial visual area               | VISpm               | Cortical Plate          | C                        | 0         | 0.21        |
| Postsubiculum                           | POST                | Cortical Plate          | B                        | 0.64      | -1.55       |
| Prelimbic area                          | PL                  | Cortical Plate          | C                        | 0         | -0.32       |
| Presubiculum                            | PRE                 | Cortical Plate          | C                        | 0.31      | -1.31       |
| Primary auditory area                   | AUDp                | Cortical Plate          | C                        | 0.44      | -2.18       |
| Primary motor area                      | Mop                 | Cortical Plate          | C                        | 0         | 0.57        |
| Primary somatosensory area, lower limb  | SSp-l               | Cortical Plate          | C                        | 0         | 0.93        |
| Primary somatosensory area, mouth       | SSp-m               | Cortical Plate          | C                        | 0         | -0.15       |

|   |        |                   |   |      |       |
|---|--------|-------------------|---|------|-------|
| Primary somatosensory area, trunk       | SSp-tr | Cortical Plate    | C | 0    | 1.09  |
| Primary somatosensory area, upper limb  | SSp-ul | Cortical Plate    | C | 0    | 0/86  |
| Primary visual area                     | VISp   | Cortical Plate    | C | 0    | 0.73  |
| Retrosplenial area, dorsal part         | RSPd   | Cortical Plate    | C | 0    | 1.06  |
| Retrosplenial area, ventral part        | RSPv   | Cortical Plate    | A | 0.50 | -1.66 |
| Secondary motor area                    | MOs    | Cortical Plate    | C | 0    | 1.11  |
| Subiculum                               | SUB    | Cortical Plate    | C | 0.13 | -1.75 |
| Supplemental somatosensory area         | SSs    | Cortical Plate    | C | 0    | 0.68  |
| Taenia tecta                            | TT     | Cortical Plate    | C | 0    | 0.89  |
| Temporal association areas              | Tea    | Cortical Plate    | C | 0    | 0.51  |
| Ventral auditory area                   | AUDv   | Cortical Plate    | C | 0    | 0.46  |
| Visceral area                           | VISC   | Cortical Plate    | C | 0    | 0.61  |
| Basolateral amygdalar nucleus           | BLA    | Cortical Subplate | A | 0    | 1.25  |
| Clastrum                                | CLA    | Cortical Subplate | A | 0.47 | -1.28 |
| Endopiriform nucleus                    | EP     | Cortical Subplate | A | 0.17 | 0.79  |
| Lateral amygdalar nucleus               | LA     | Cortical Subplate | A | 0.32 | 0.36  |
| Posterior amygdalar nucleus             | PA     | Cortical Subplate | C | 0.42 | -2.43 |
| Anterior amygdalar area                 | AAA    | Striatum          | B | 0.48 | -0.04 |
| Caudoputamen                            | CP     | Striatum          | C | 0    | 1.26  |
| Central amygdalar nucleus               | CEA    | Striatum          | A | 0.47 | 0.81  |
| Fundus of striatum                      | FS     | Striatum          | B | 0.12 | 1.29  |
| Intercalated amygdalar nucleus          | IA     | Striatum          | A | 0.35 | 1.37  |
| Lateral septal complex                  | LSX    | Striatum          | B | 0.50 | 0.96  |
| Medial amygdalar nucleus                | MEA    | Striatum          | B | 0.50 | 1.01  |
| Nucleus accumbens                       | ACB    | Striatum          | C | 0.38 | -1.85 |
| Olfactory tubercle                      | OT     | Striatum          | C | 0.07 | -0.99 |
| Bed nuclei of the stria terminalis      | BST    | Pallidum          | C | 0.33 | -0.84 |
| Diagonal band nucleus                   | NDB    | Pallidum          | C | 0    | 0.34  |
| Globus pallidus external segment        | GPe    | Pallidum          | C | 0.21 | -0.66 |
| Magnocellular nucleus                   | MA     | Pallidum          | B | 0.41 | -0.60 |
| Medial septal nucleus                   | MS     | Pallidum          | C | 0    | -0.71 |
| Substantia innominata                   | SI     | Pallidum          | B | 0.47 | 1.26  |
| Anterodorsal nucleus                    | AD     | Thalamus          | C | 0    | 0.77  |
| Anteroventral nucleus of the thalamus   | AV     | Thalamus          | C | 0    | 0.94  |
| Central lateral nucleus of the thalamus | CL     | Thalamus          | C | 0    | 0.92  |
| Central medial nucleus of the thalamus  | CM     | Thalamus          | C | 0.32 | -0.60 |

|  |      |              |   |      |       |
|--|------|--------------|---|------|-------|
| Lateral geniculate complex, dorsal part              | LGd  | Thalamus     | C | 0    | 1.10  |
| Lateral dorsal nucleus of the thalamus               | LD   | Thalamus     | C | 0    | 1.14  |
| Lateral habenula                                     | LH   | Thalamus     | C | 0.22 | -1.68 |
| Lateral posterior nucleus of the thalamus            | LP   | Thalamus     | C | 0    | 1.07  |
| Medial geniculate complex                            | MG   | Thalamus     | C | 0.32 | -1.83 |
| Medial habenula                                      | MH   | Thalamus     | A | 0    | -1.33 |
| Mediodorsal nucleus of the thalamus                  | MD   | Thalamus     | C | 0.10 | 0.58  |
| Parataenial nucleus                                  | PT   | Thalamus     | C | 0.04 | 0.34  |
| Paraventricular nucleus of the thalamus              | PVT  | Thalamus     | B | 0.40 | -0.64 |
| Posterior complex of the thalamus                    | PO   | Thalamus     | C | 0    | 0.59  |
| Reticular nucleus of the thalamus                    | RT   | Thalamus     | C | 0.04 | 0.26  |
| Ventral anterior-lateral complex of the thalamus     | VAL  | Thalamus     | C | 0    | 1.00  |
| Ventral medial nucleus of the thalamus               | VM   | Thalamus     | C | 0.18 | 0.13  |
| Anterior hypothalamic nucleus                        | AHN  | Hypothalamus | C | 0.24 | -0.22 |
| Anteroventral periventricular nucleus                | AVPV | Hypothalamus | C | 0.08 | 0.05  |
| Anteroventral preoptic nucleus                       | AVP  | Hypothalamus | C | 0    | -0.05 |
| Dorsomedial nucleus of the hypothalamus              | DMH  | Hypothalamus | C | 0.23 | -0.15 |
| Lateral hypothalamic area                            | LHA  | Hypothalamus | C | 0.31 | -0.71 |
| Lateral preoptic area                                | LPO  | Hypothalamus | C | 0    | -0.37 |
| Medial preoptic area                                 | MPO  | Hypothalamus | C | 0    | 0.75  |
| Medial preoptic nucleus                              | MPN  | Hypothalamus | C | 0    | 0.23  |
| Median preoptic nucleus                              | MEPO | Hypothalamus | B | 0.32 | -1.82 |
| Parasubthalamic nucleus                              | PSTN | Hypothalamus | A | 0    | 1.12  |
| Paraventricular hypothalamic nucleus                 | PVH  | Hypothalamus | C | 0    | -0.45 |
| Periventricular hypothalamic nucleus, posterior part | PVp  | Hypothalamus | C | 0    | -1.41 |
| Periventricular zone                                 | PVZ  | Hypothalamus | B | 0.13 | 1.12  |
| Posterior hypothalamic nucleus                       | PH   | Hypothalamus | C | 0.22 | -0.82 |
| Retrochiasmatic area                                 | RCH  | Hypothalamus | C | 0.11 | -1.56 |
| Subparaventricular zone                              | SBPV | Hypothalamus | C | 0.18 | -1.95 |
| Subthalamic nucleus                                  | STN  | Hypothalamus | C | 0.04 | 0.28  |
| Suprachiasmatic nucleus                              | SCH  | Hypothalamus | B | 0.50 | -1.55 |
| Tuberal nucleus                                      | TU   | Hypothalamus | A | 0.49 | -0.31 |
| Ventrolateral preoptic nucleus                       | VLPO | Hypothalamus | C | 0    | 0.32  |

|                                      |       |              |   |      |       |
|--------------------------------------|-------|--------------|---|------|-------|
| Ventromedial hypothalamic nucleus    | VMH   | Hypothalamus | C | 0.31 | -0.92 |
| Zona incerta                         | ZI    | Hypothalamus | C | 0.04 | 0.19  |
| Inferior colliculus                  | IC    | Midbrain     | B | 0.58 | -0.78 |
| Interpeduncular nucleus              | IPN   | Midbrain     | C | 0    | 0.91  |
| Medial pretectal area                | MPT   | Midbrain     | A | 0    | -0.15 |
| Midbrain reticular nucleus           | MRN   | Midbrain     | B | 0.35 | 1.27  |
| Olivary pretectal nucleus            | OP    | Midbrain     | A | 0.30 | -0.91 |
| Pedunculo pontine nucleus            | PPN   | Midbrain     | B | 0.45 | 0.43  |
| Periaqueductal gray                  | PAG   | Midbrain     | B | 0.50 | 0.12  |
| Precommissural nucleus               | PRC   | Midbrain     | A | 0    | 0.17  |
| Substantia nigra, compact part       | SNC   | Midbrain     | B | 0.14 | 0.78  |
| Substantia nigra, reticular part     | SNr   | Midbrain     | B | 0.50 | 0.67  |
| Superior colliculus, motor related   | SCm   | Midbrain     | B | 0.39 | 0.70  |
| Superior colliculus, sensory related | SCs   | Midbrain     | A | 0.38 | 0.90  |
| Ventral tegmental area               | VTA   | Midbrain     | C | 0.03 | 0.57  |
| Pons                                 | P     | Hindbrain    | B | 0.63 | -0.76 |
| Pons, motor related                  | P-mot | Hindbrain    | B | 0.49 | -1.07 |
| Culmen                               | CUL   | Cerebellum   | A | 0    | -0.90 |