**Figure legend for supplemental figures**

**Familiar observers/Surgery mice**

|   | Ratio | P value |
|---|-------|---------|
| HIPPO | 1.24  | 0.2189  |
| ZI   | 1.06  | 0.8191  |
| VMH  | 0.98  | 0.9210  |
| Acb  | 0.87  | 0.2534  |
| PVT  | 0.86  | 0.3801  |
| PFC  | 0.73  | 0.0409  |
| Pir  | 0.59  | 0.0557  |
| DM   | 0.54  | 0.0086  |
| Xi   | 0.47  | 0.0022  |
| IMD  | 0.20  | 0.0001  |
| BMA  | 0.00  | 0.0001  |
| CM   | 0.00  | 0.0001  |

**Figure S1.** Heat map of the comparisons between familiar observers and surgery mice.
| REAGENT or RESOURCE | SOURCE | IDENTIFIER |
|---------------------|--------|------------|
| Antibodies          |        |            |
| Rabbit polyclonal to c-Fos | Abcam | Cat#ab190289 |
| Mouse monoclonal [2H2] to c-Fos | Abcam | Cat#ab208942 |
| Rabbit orexin receptor 1+2 polyclonal antibody | Bioss antibodies | Cat#bs-1095R |
| Anti-NeuN Antibody, clone A60 | Sigma-Aldrich | Cat#MAB377 |
| Rabbit polyclonal to Orexin A | Abcam | Cat#ab6214 |
| Donkey anti-Rabbit Alexa Fluor 488 | Life Technologies | Cat#A21206 |
| Donkey anti-Mouse Alexa Fluor 488 | Invitrogen | Cat#A21202 |
| Donkey anti-Rabbit Alexa Fluor 594 | Invitrogen | Cat#A21207 |
| Donkey anti-Mouse Alexa Fluor 594 | Invitrogen | Cat#A21203 |
| Hoechst              | Thermo Scientific | Cat#RC 21732420 |
| Viruses              |        |            |
| pAAV2-hSyn-hM4D(Gi)-mCherry | Addgene | Cat#50475-AAV2 |
| pAAV2-hSyn-mCherry   | Addgene | Cat#114472-AAV2 |
| pAAV2-hSyn-EGFP      | Addgene | Cat#50465-AAV2 |
| Drugs                |        |            |
| DREADD Agonist 21    | Abcam  | Cat#ab235545 |
| Ibotenic acid        | Abcam  | Cat#ab120041 |
| Critical Commercial Assays |        |            |
| Mouse IL-6 Immunoassay | R&D systems | Cat#M600B |
| Chemicals            |        |            |
| 10× RIPA Buffer      | Thermo Scientific | Cat#89901 |
| Ketamine             | Zoetis | N/A        |
### Table S2. Statistical values of ANOVAs

| Data location in the figures | F or H values                  | P values |
|------------------------------|--------------------------------|----------|
| Figure 1C (Grey + black zones) | F(2,36) = 7.609                  | 0.002    |
| Figure 1C (light zones)       | F(2,360) = 13.156                | < 0.001  |
| Figure 2E                     | H = 4.550 (df = 2) on rank       | 0.103    |
| Figure 4B                     | F(3,20) = 11.505                 | < 0.001  |
| Figure 4D                     | F(3,22) = 14.383                 | < 0.001  |
| Figure 4E                     | F(3,25) = 5.962                  | 0.003    |
| Figure 4G                     | F(2,12) = 19.517                 | < 0.001  |
| Figure 4I                     | F(4,24) = 6.188                  | 0.001    |
| Figure 5A at 2 h after interaction | F(4,21) = 68.619                | < 0.001  |
| Figure 5A at 6 h after interaction | F(4,21) = 41.494                | < 0.001  |
| Figure 5A at 24 h after interaction | F(4, 21) = 6.065               | 0.002    |
| Figure 5B at 2 h after interaction | F(4,21) = 1.166                 | 0.354    |
| Figure 5B at 6 h after interaction | F(4,21) = 5.688                 | 0.003    |
| Figure 5B at 24 h after interaction | F(4,21) = 4.501                 | 0.009    |
| Figure 5C at 2 h after interaction | F(4,21) = 2.642                 | 0.062    |
| Figure 5C at 6 h after interaction | F(4,21) = 13.857                | < 0.001  |
| Figure 5C at 24 h after interaction | F(4,21) = 17.475                | < 0.001  |
| Figure 5D Serum               | F(2,15) = 2.516                  | 0.114    |
| Figure 5D Hippocampus         | F(2,21) = 3.577                  | 0.046    |
| Figure 5D Cerebral cortex     | F(2,19) = 6.515                  | 0.007    |
| Figure 6D Allo-grooming       | F(2,34) = 28.913                 | < 0.001  |
| Figure 6D Allo-licking        | F(2,34) = 6.123                  | 0.005    |
| Figure 6D Allo-grooming + all-licking | F(2, 34) = 32.045         | < 0.001  |
| Figure 6E Grey + black zone   | F(3,45) = 4.267                  | 0.010    |
| Figure 6E Light zone          | F(3,45) = 4.267                  | 0.010    |
| Figure 7B Allo-grooming       | H = 11.901 (df = 3) on rank      | 0.008    |
| Figure 7B Allo-licking        | H = 9.275 (df = 3) on rank       | 0.026    |
| Figure 7B Allo-grooming + all-licking | H = 12.711 (df = 3) on rank    | 0.005    |
| Figure 7C Grey + black zone   | F(4,56) = 2.942                  | 0.028    |
| Figure 7C Light zone          | F(4,56) = 3.425                  | 0.014    |
| Figure 8B Allo-grooming       | F(2,36) = 5.847                  | 0.006    |
| Figure 8B Allo-licking        | F(2,36) = 4.197                  | 0.023    |
| Figure 8B Allo-grooming + all-licking | F(2,36) = 8.771                | < 0.001  |
| Figure 8C Grey + black zone   | F(3,50) = 4.283                  | 0.009    |
| Figure 8C Light zone          | F(3,50) = 5.435                  | 0.003    |