**Figure 2-1**

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **1AcKO-male** | Main Effect of Time | | | Main Effect of Genotype | | | Interaction | | |
|
| F | 3.132 | | | 7.529 | | | 4.351 | | |
| df | 5 | | | 3 | | | 15 | | |
| p value | **0.0100** | | | **<0.0006** | | | **<0.0001** | | |
|  |  |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |
| **post hoc Tukey** | 10min | 20min | 30min | 40min | 50min | 60min |  |  |  |
| WT/saline vs WT/DPAT | **0.0049** | **<0.0001** | **<0.0001** | **0.0047** | **0.008** | **0.0218** |  |  |  |
| WT/DPAT vs 1AcKO/DPAT | 0.0959 | **0.0035** | **0.0018** | **0.0035** | **0.008** | 0.3209 |  |  |  |
|  |  |  |  |  |  |  |  |  |  |
| **post hoc Tukey** |  |  |  |  |  |  |  |  |  |
| WT/saline vs WT/DPAT |  |  |  |  |  |  |  |  |  |
|  | **Mean Diff.** | **SE of diff.** | **N1** | **N2** | **q** | **DF** |  |  |  |
| **10 min** | 0.8556 | 0.2533 | 9 | 12 | 4.776 | 198 |  |  |  |
| **20 min** | 1.369 | 0.2533 | 9 | 12 | 7.645 | 198 |  |  |  |
| **30 min** | 1.128 | 0.2533 | 9 | 12 | 6.296 | 198 |  |  |  |
| **40 min** | 0.8583 | 0.2533 | 9 | 12 | 4.792 | 198 |  |  |  |
| **50 min** | 5.795E-09 | 0.2708 | 9 | 9 | 3.026E-08 | 198 |  |  |  |
| **60 min** | 0.7333 | 0.2533 | 9 | 12 | 4.094 | 198 |  |  |  |
|  |  |  |  |  |  |  |  |  |  |
|  | 20min | 30min | 40min | 50min |  |  |  |  |  |
| WT/DPAT vs 1AcKO/DPAT | **0.0035** | **0.0018** | **0.0035** | **0.008** |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |
|  | **Mean Diff.** | **SE of diff.** | **N1** | **N2** | **q** | **DF** |  |  |  |
| **20min** | -0.8806 | 0.2533 | 12 | 9 | 4.916 | 198 |  |  |  |
| **30min** | -0.9278 | 0.2533 | 12 | 9 | 5.179 | 198 |  |  |  |
| **40min** | -0.8806 | 0.2533 | 12 | 9 | 4.916 | 198 |  |  |  |
| **50min** | -0.8167 | 0.2533 | 12 | 9 | 4.559 | 198 |  |  |  |
|  |  |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

Agonist-induced hypothermia in male 1AcKO mice (Figure 2E). Statistical results of a two-way ANOVA comparing genotype and time for male WT or 1AcKO mice. Bold font indicates statistical significance.

**Figure 2-2**

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **1AcKO-female** | Main Effect of Time | | | Main Effect of Genotype | | | Interaction | | |
|
| F | 4.407 | | | 10.4 | | | 4.407 | | |
| df | 5 | | | 5 | | | 15 | | |
| p value | **<0.0001** | | | **<0.0001** | | | **<0.0001** | | |
|  |  |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |
| **post hoc Tukey** | 10min | 20min | 30min | 40min | 50min |  |  |  |  |
| WT/saline vs WT/DPAT | **<0.0001** | **<0.0001** | **<0.0001** | **0.002** | **0.003** |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |
|  | **Mean Diff.** | **SE of diff.** | **N1** | **N2** | **q** | **DF** |  |  |  |
| **10 min** | -0.07273 | 0.2749 | 7 | 11 | 0.3741 | 192 |  |  |  |
| **20 min** | 1.757 | 0.3039 | 7 | 7 | 8.176 | 192 |  |  |  |
| **30 min** | 1.429 | 0.3039 | 7 | 7 | 6.647 | 192 |  |  |  |
| **40 min** | 1.229 | 0.3039 | 7 | 7 | 5.717 | 192 |  |  |  |
| **50 min** | 1.171 | 0.3039 | 7 | 7 | 5.451 | 192 |  |  |  |
|  |  |  |  |  |  |  |  |  |  |
|  | 10min | 20min | 30min | 40min | 50min |  |  |  |  |
| WT/DPAT vs 1AcKO/DPAT | **0.001** | **0.0003** | **0.005** | **0.014** | **0.02** |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |
|  | **Mean Diff.** | **SE of diff.** | **N1** | **N2** | **q** | **DF** |  |  |  |
| **10 min** | -1.165 | 0.2749 | 7 | 11 | 5.993 | 192 |  |  |  |
| **20 min** | -1.212 | 0.2749 | 7 | 11 | 6.233 | 192 |  |  |  |
| **30 min** | -1.03 | 0.2749 | 7 | 11 | 5.298 | 192 |  |  |  |
| **40 min** | -0.939 | 0.2749 | 7 | 11 | 4.83 | 192 |  |  |  |
| **50 min** | -0.913 | 0.2749 | 7 | 11 | 4.697 | 192 |  |  |  |

Agonist-induced hypothermia in female 1AcKO mice (Figure 2E). Statistical results of a two-way ANOVA comparing genotype and time for female WT or 1AcKO mice. Bold font indicates statistical significance.

**Figure 4-1**

|  |  |  |  |
| --- | --- | --- | --- |
| Tissue | Metabolite | | |
|  | **5-HT** | **5-HIAA** | **5-HT/5-HIAA** |
| PFC | F (3, 24) = 11.43; **P <0.0001** | F (3, 24) = 1.998; P = 0.1411 | F (3, 24) = 5.546; **P = 0.0049** |
| Hippo | F (3, 24) = 17.73; **P < 0.0001** | F (3, 24) = 3.998; **P = 0.0193** | F (3, 24) = 4.470; **P = 0.0125** |
| DR | F (3, 24) = 5.496; **P = 0.0051** | F (3, 23) = 1.791; P = 0.1770 | F (3, 23) = 6.030; **P = 0.0035** |

Statistical analysis of tissue 5-HT metabolite data following fluoxetine (FLX) treatment (Figure 4). Data were analyzed by 2-way ANOVA for treatment × genotype interaction; post hoc Tukey was done comparing Vehicle vs. FLX treatment. Bold, statistically significant results; PFC, prefrontal cortex; Hippo, hippocampus; DR, dorsal raphe.

**Figure 5-1**

|  |  |  |  |
| --- | --- | --- | --- |
| Region | Immunopositive cells | | |
|  | **TPH+** | **FosB+** | **FosB/TPH+** |
| DR | F (1, 36) = 0.08796 P = 0.7685 | F (1, 37) = 0.7555 P = 0.3903 | F (1, 56) = 16.22 P = **0.0002** |
| MR | F (1, 37) = 0.03252 P = 0.8579 | F (1, 37) = 0.8385 P = 0.3658 | F (1, 35) = 5.454 P = **0.0254** |

Statistical analysis of TPH+, FosB+, and FosB/TPH+ cells in raphe of cells in 1AcKO vs. W.T. mice following fluoxetine (FLX) treatment (Figure 5B, C). Data were analyzed by 2-way ANOVA for treatment × genotype interaction; post hoc Tukey test was done comparing Vehicle vs. FLX treatment. Bold, statistically significant results; DR, dorsal raphe; MR, median raphe.

**Figure 6-1**

|  |  |
| --- | --- |
| Region | FosB+ cells |
| EC | F (1, 22) = 15.43; **P = 0.0007** |
| NAc | F (1, 21) = 1.866; P = 0.1864 |
| LSN | F (1, 24) = 3.999; **P = 0.0570** |
| MSN | F (1, 24) = 5.521; **P = 0.0273** |
| CA1 | F (1, 54) = 0.0280; P = 0.8678 |
| CA2/3 | F (1, 36) = 10.16; **P = 0.0030** |
| DG | F (1, 46) = 0.6985; P = 0.4076 |
| Amygdala | F (1, 23) = 0.4218; P = 0.5225 |
| LHb | F (1, 24) = 0.07375; P = 0.7883 |

Statistical analysis of FosB+ cells in brain regions in 1AcKO vs. W.T. mice following fluoxetine (FLX) treatment. Data from Fig. 6 were analyzed by 2-way ANOVA for treatment × genotype interaction; post hoc Tukey was done comparing Vehicle vs. FLX treatment. Bold, statistically significant results; bold italic indicates a non-significant trend. EC, entorhinal cortex; NAc, nucleus accumbens; LSN, lateral septal nucleus; MSN, medial septal nucleus; hippocampal CA1, CA2/3, and dentate gyrus (DG); Amy, amygdala; LHb, lateral habenula.