Supplementary Material:

1. Supplementary Methods:

**Genotyping**

Offspring was genotyped by PCR analysis of tail DNA at P6 or after weaning. For the GR<sup>lox/lox</sup> phenotype, we used the following primers:

Primer A (GR<sub>flox</sub>-1): 5’-GGCATGCACATTACGGCCTTCT-3’
Primer B (GR<sub>flox</sub>-8): 5’-CCTTCTCATCCATGTCAGCATGT-3’
Primer C (GR<sub>flox</sub>-4): 5’-GTGTAGCAGCCAGCTTACAGGA-3’

The genotype-dependent sizes of the different PCR products are 390 base pairs (GR<sup>null</sup>), 275 base pairs (GR<sup>lox</sup>) or 225 base pairs (GR<sup>wt</sup>).

For the Cre genotype, we used the following primer pair:

Primer A (Cre-F): 5’-GATGCGTGCCAGGATTATGC-3’
Primer B (Cre-R): 5’-AATCGCCATCTTCCAGCAG-3’

PCR product size: 574 base pairs.

To confirm a functioning PCR reaction in the absence of a Cre PCR product, we included a second primer pair as control:

Primer A (CTSQ-up): 5’-ACAAGGTCTGTGAATCATGC-3’
Primer B (CTSQ-dn): 5’-TTACAATGTGGATTTTGTGGG-3’

PCR product size: 1098 base pairs.

**GR immunohistochemistry**

Pituitary cryosections of GR<sup>POMC</sup>Cre and control animals (18 μm thick) were treated with antibodies recognizing the GR (1:100, Abcam, UK). Nonspecific binding for GR was blocked with 5% serum in 1 x PBS. Sections were incubated with primary antibody overnight at 4°C, washed with PBS, incubated with secondary antibody for 60 minutes at room temperature (1:250 biotinylated sheep anti-rabbit IgG, Vector Laboratories, Burlingame, CA), incubated in an avodin/avidin complex reagent (Vector Laboratories) for 60 minutes, washed with 1 x PBS, and incubated in 0.05% 3’3-Diaminobenzidine (DAB, Sigma D-0426).

**Behavioral analysis**

All behavioral tests (n=10 per genotype, age 10-14 weeks) were performed between 8 am and 12 am in the same room where the animals were housed.

**Open Field**

Open field arenas were made of gray PVC (50 x 50 x 50 cm) and evenly illuminated during testing (50 lux). General locomotor activity was recorded for 5 minutes (distance travelled) using a video-tracking system (Anymaze 4.20, Stoelting, Illinois, USA).
Elevated Plus Maze
The elevated plus maze consisted of two opposed open arms (30 x 5 x 0.5 cm) and two opposed enclosed arms (30 x 5 x 15 cm) out of gray PVC which were connected by a central platform (5 x 5 cm) shaping a plus sign. Animals were placed into the centre of the plus maze and were allowed to explore the maze for 5 minutes. Percent of time spent in the open arms and percent entries to the open arms were recorded.

Dark-Light Box
The dark-light box consisted of two plexiglas compartments, a dark one (15 x 20 x 25 cm) and a lit one (30 x 20 x 25 cm; 650 lux), connected by a 4 cm long tunnel. For the assessment of anxiety-related behavior the animals were placed in the dark compartment and the time spent in each compartment and the number of entries to each compartment were recorded.

Forced Swim Test
Mice were put into a glass beaker (diameter 10 cm, height 30 cm) filled with warm water (25°C, height 20 cm) for 5 minutes. The number, duration and latency of swimming, struggling and floating behavior were recorded.

Y-maze test
The Y-maze was made of grey PVC and consisted of three walled arms with an angle of 120° between each of the two arms differentially marked by tape symbols. The arms were 30 x 10 x 15 cm (l x w x h) each and evenly illuminated during testing (40 lux). The Y-maze test comprises two trials separated by an intertrial interval (ITI) to assess spatial recognition memory. During the first trial the mouse was allowed to explore two of the three arms for 10 minutes while the third arm was blocked. After an ITI of 30 minutes the second trial was conducted during which all three arms were accessible for 5 minutes. The percentage time spent in the novel arm compared to the known arms was scored.
2. Supplementary Tables:

Supplementary table 1: Genotype distribution of the offspring

<table>
<thead>
<tr>
<th>genotype</th>
<th>distribution (%)</th>
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<tbody>
<tr>
<td></td>
<td>-Cre</td>
</tr>
<tr>
<td>+/+</td>
<td>27.7</td>
</tr>
<tr>
<td>lox/+</td>
<td>46.2</td>
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<tr>
<td>lox/lox</td>
<td>26.2</td>
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</tbody>
</table>

Supplementary table 2: Gene expression in adult GR\textsuperscript{POMCCre} and control animals. Controls: N=15; GR\textsuperscript{POMCCre}: N=8.

<table>
<thead>
<tr>
<th>measure</th>
<th>genotype</th>
<th>statistics</th>
</tr>
</thead>
<tbody>
<tr>
<td>CRH mRNA in PVN</td>
<td>16.22 ± 0.8</td>
<td>14.91 ± 0.8</td>
</tr>
<tr>
<td>AVP mRNA in PVN</td>
<td>63.81 ± 4.8</td>
<td>70.90 ± 11.7</td>
</tr>
<tr>
<td>GR mRNA in CA1</td>
<td>17.87 ± 0.8</td>
<td>19.83 ± 0.6</td>
</tr>
<tr>
<td>MR mRNA in CA1</td>
<td>6.29 ± 0.7</td>
<td>7.76 ± 0.9</td>
</tr>
<tr>
<td>MR mRNA in CA3</td>
<td>8.11 ± 0.7</td>
<td>8.52 ± 1.1</td>
</tr>
<tr>
<td>MR mRNA in DG</td>
<td>8.32 ± 0.7</td>
<td>8.60 ± 0.7</td>
</tr>
</tbody>
</table>