Midbrain projection to the basolateral amygdala encodes anxiety-like behaviors

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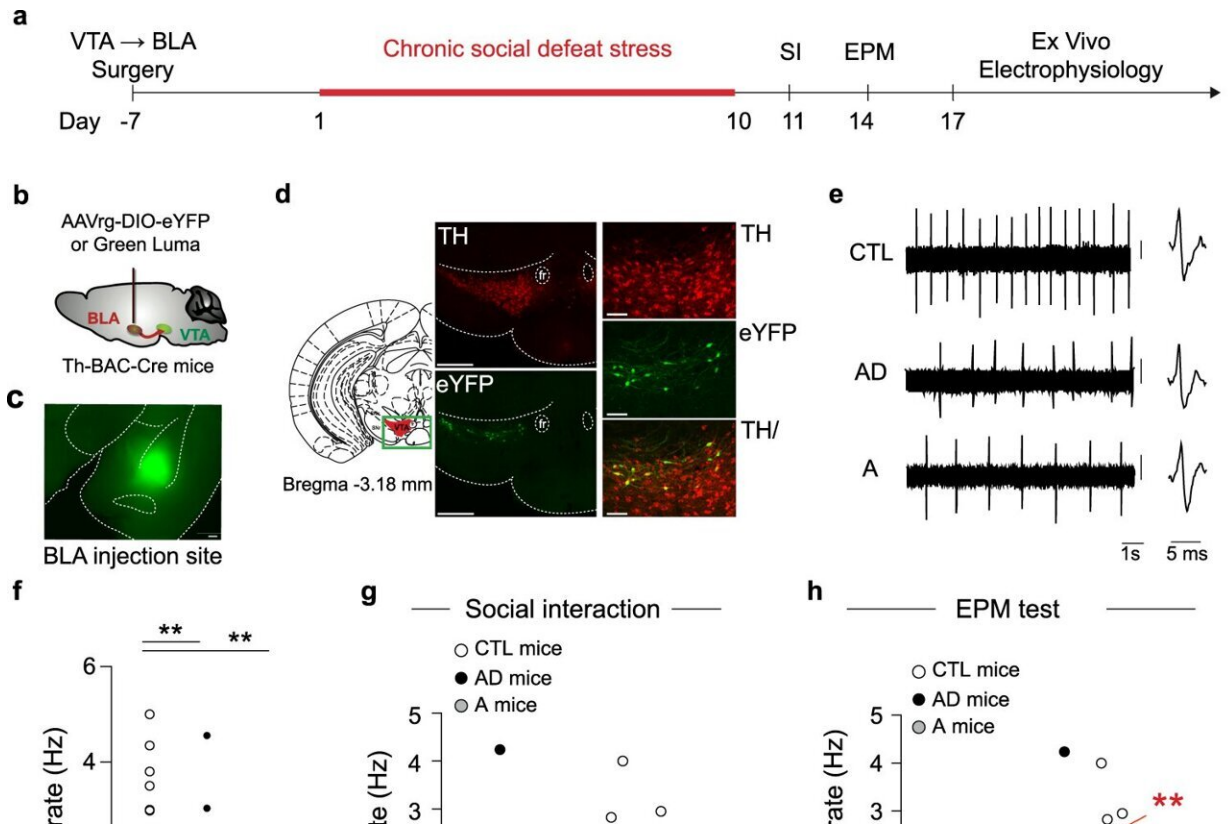

Anxiety-like behavior correlates with the hypoactivity of VTA → BLA dopamine neurons. a Experimental timeline. b Schematic of the brain surgery to dissect VTA → BLA circuit. c BLA surgery injection site (scale bar=500 μm). d Morphological validation showing the targeted VTA → BLA dopamine neurons in TH-BAC-Cre mice injected with AAVrg-DIO-eYFP (scale bar = 500 and 100 μm, representative images of the 23 recorded mice). e Sample traces of ex vivo cell-attached recordings from CTL, AD, and A mice (scale bar = 0.2 mV). f Spontaneous firing activity of VTA → BLA dopamine neurons in AD and A

mice compared to control mice (mean ± s.e.m., ANOVA, $F(_{2, 104}) = 6.750$ p = 0.0018; post hoc test, t = 3.48 p = 0.002; t = 3.50 p = 0.003, n = 30, 31, 45 neurons, n = 23 combined C57BL6/J and TH-BAC-Cre mice injected with AAVrg-DIO-eYFP and Green Luma, respectively). g Pearson correlation analyses of VTA → BLA dopamine neuron firing with the social interaction behavior after CSDS (p = 0.59, 3–7 neurons per mouse, n = 23 combined C57BL6/J and TH-BAC-Cre mice). h Pearson correlation analyses of VTA → BLA dopamine neuron firing activity with the time in EPM open arms (p = 0.0015, 3–7 neurons per mouse, n = 23 combined C57BL6/J and TH-BAC-Cre mice). i Sample traces of ex vivo whole-cell recordings from CTL, AD, and A mice at a 40 pA step current injection. j VTA → BLA dopamine neurons excitability in AD and A mice compared to CTL mice following incremental steps in currents injections (20–280 pA; mean ± s.e.m., RM two-way ANOVA: group effect: $F(_{2, 33}) = 3.818$ p = 0.021; Interaction $F(_{28, 434}) = 3.164$ p = 1.08e−07; post hoc tests: t = 2.41 p = 0.04; t = 2.53 p = 0.04; t = 1.95 p = 0.04; t = 2.63 p = 0.04; t = 1.64 p = 0.04; t = 2.52 p = 0.04; t = 1.72 p = 0.04; t = 2.25 p = 0.04; n = 11, 12, 14 neurons/4, 5, 6 TH-BAC-Cre mice). k VTA → BLA dopamine neurons rheobase in AD and A mice compared to CTL mice (mean ± s.e.m., ANOVA: Group effect: $F(_{2, 33}) = 4.016$ p = 0.013; post hoc tests t = 2.43 p = 0.04; t = 2.85 p = 0.02; n = 11, 13, 14 neurons/4, 5, 6 TH-BAC-Cre mice). l VTA → BLA dopamine neurons hyperpolarization-activated current, i.e., I_h current in AD and A mice compared to CTL mice following incremental voltage steps (mean ± s.e.m., RM two-way ANOVA: group effect: $F(_{2, 33}) = 4.194$ p = 0.017; interaction $F(_{10, 175}) = 3.393$ p = 9.7e−06; post hoc tests t = 2.22 p = 0.04; t = 2.71 p = 0.025; n = 11, 13, 14 neurons/4, 5, 6 TH-BAC-Cre mice). m VTA → BLA dopamine neurons sag ratio in AD and A mice compared to CTL mice (mean ± s.e.m., ANOVA: group effect: $F(_{2, 32}) = 7.225$ p = 0.001; t = 3.04 p = 0.009; t = 3.79 p = 0.002, n = 11, 13, 14 neurons/4–6 TH-BAC-Cre mice). In all panels, two-sided statistical analyses post hoc corrected tests were performed, *p