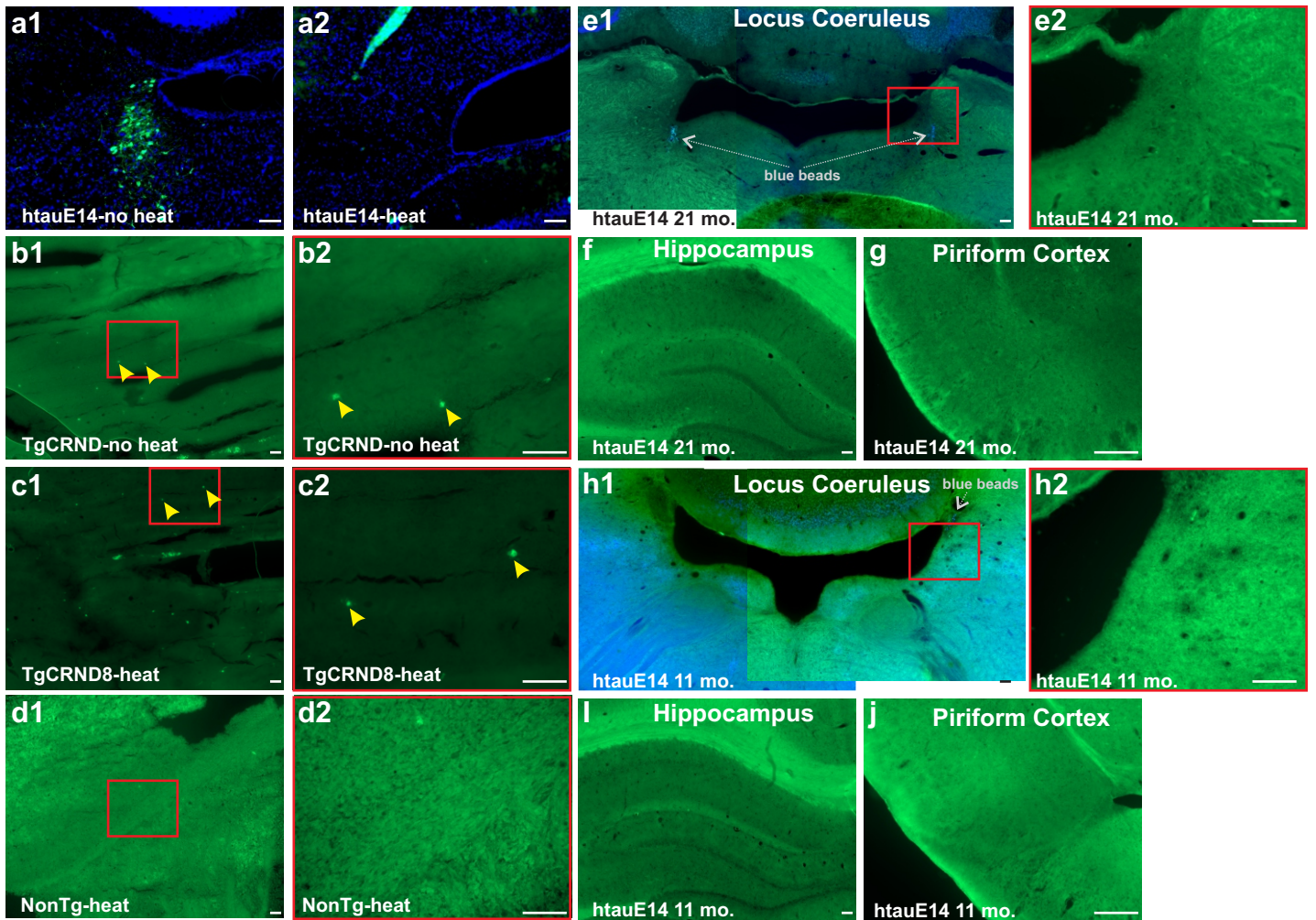


Additional File 5



No tangle formation is apparent in htauE14 brains

a1-a2. Ten min 90°C heat treatment quenches GFP signal in a htauE14-EGFP brain. **a1** shows GFP⁺ locus coeruleus cells without heat treatment and **a2** shows GFP quenching with heat in another section of the same brain. **b-c.** Thioflavin staining of neurofibrillary tangles in a TgCRND8¹ mouse (gift from Dr Bennett at University of Ottawa) section without heat treatment (**b1-b2**) and with heat treatment (**c1-c2**). Heat treatment does not prevent the detection of thioflavin positive tangles. Arrows indicate stained tangles. **b2** and **c2** are enlargements from the red square areas in **b1** and **c1** correspondingly. **d.** Thioflavin staining in a nonTg control mouse tissue showing no tangle formation. **e-g.** No tangle formation in a 21 month-old htauE14 rat 7 months post-infusion. **e1-e2**, Locus coeruleus; **f**, hippocampus; **g**, piriform cortex. **h-j.** No tangle formation in a 11 month-old htauE14 rat 8 months post-infusion. **h1-h2**, Locus coeruleus; **i**, hippocampus; **j**, piriform cortex. All tissue in panel **e-j** were treated with heat before thioflavin staining. Scale bars, 100 μm.

¹Granger et al. A TgCRND8 mouse model of Alzheimer's disease exhibits sexual dimorphisms in behavioral indices of cognitive reserve. *J Alzheimers Dis.* 2016, 53(1), 757-73.