

Anti-tau conformational scFv MC1 antibody efficiently reduces pathological tau species in adult JNPL3 mice

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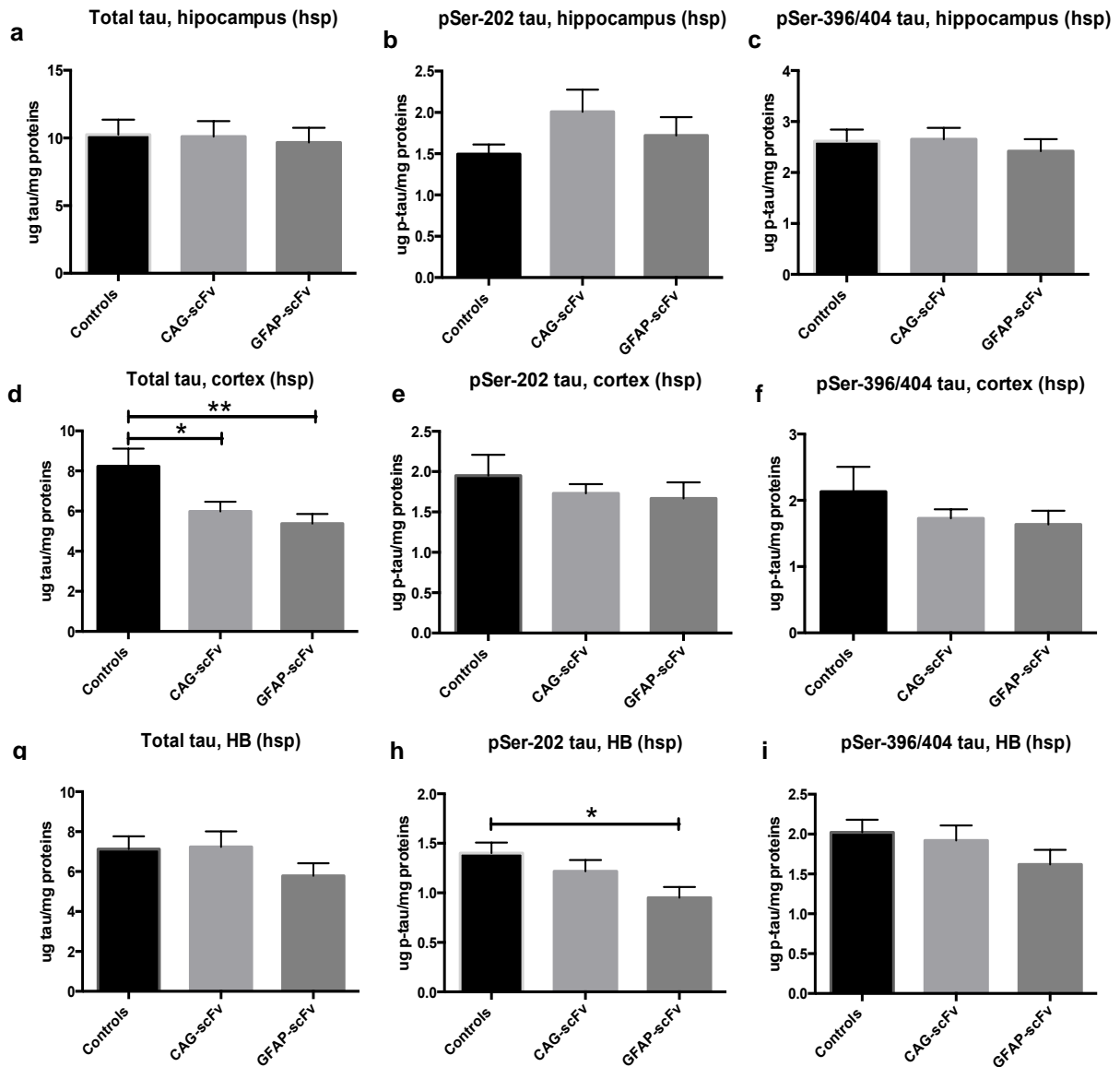


Fig. S1 Total and phosphorylated soluble tau in hippocampus, cortex and HB. **(a, b, c)** In the hippocampus, total tau was not modulated, as well as the pSer202 and pSer396-404 phospho-epitopes. **(d, e, f)** In the cortex, a significant reduction of total soluble tau was reached with both the CAG (* $P=0.0325$ by one-way ANOVA) and the GFAP promoter (** $P=0.006$ by one-way ANOVA). **(g, h, i)** In the HB, phosphorylation at Ser202 was significantly decreased in the GFAP-scFMC1 treatment group (* $P=0.0112$ by one-way ANOVA). Error bars indicate means \pm SEM

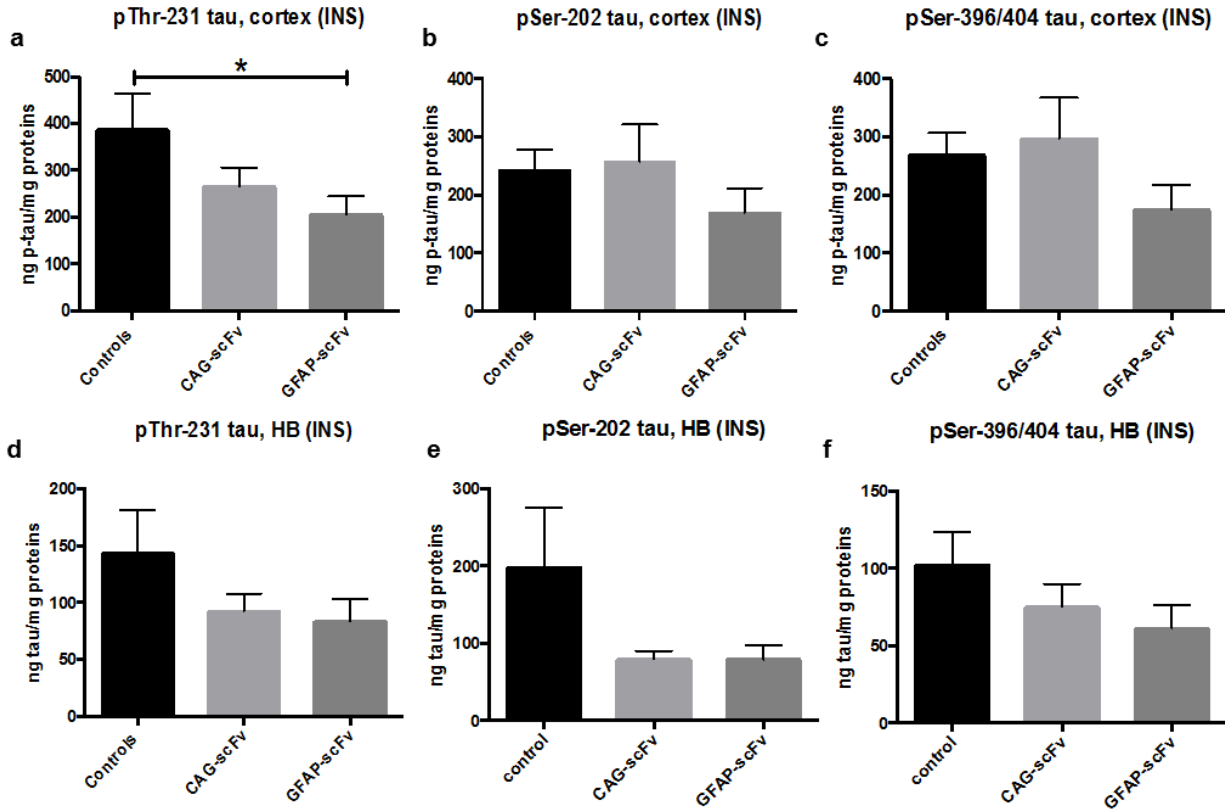


Fig. S2 Phosphorylated insoluble tau (INS) in cortex and HB. **(a, b, c)** Phosphorylation levels of insoluble tau in the cortex: the pThr231 residues showed a significant reduction (* $P=0.0398$ by non-parametric Kruskal-Wallis test) in the GFAP expressed group, while pSer202 ($P=0.0685$) and pSer396-404 ($P=0.0649$) showed a non-significant trend towards reduction in the same treatment cohort. **(d, e, f)** In the HB, no significant decrease in phosphorylated insoluble tau was detected, with a trend to reduction on pSer396-404 in the GFAP-scFv treated group ($P=0.0768$). Error bars indicate means \pm SEM

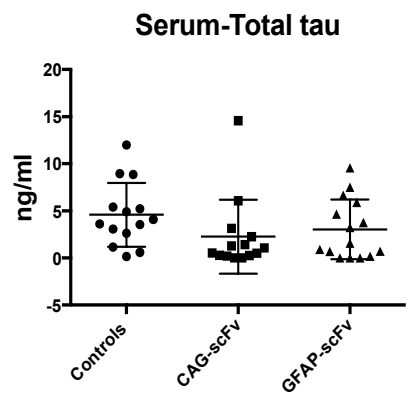


Fig. S3 Tau levels in serum. At sacrifice, total tau was analyzed in serum (ng/ml), showing no significant difference between groups

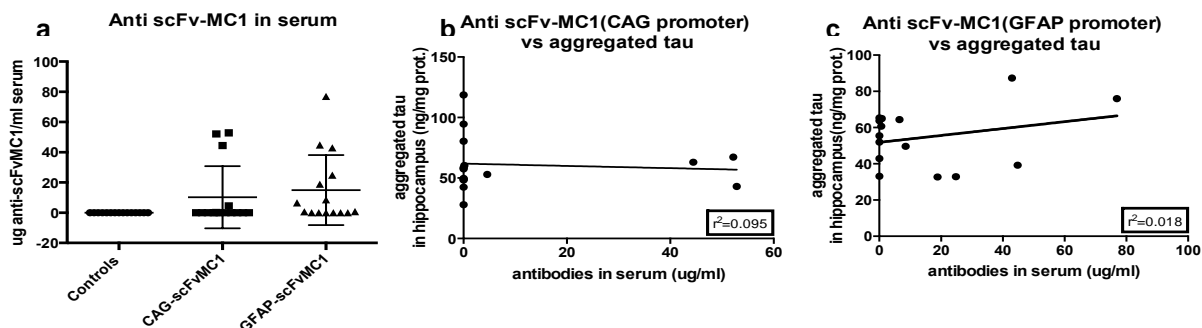


Fig. S4 Antibodies directed to the scFv-MC1, in serum. **(a)** At sacrifice, few animals in both groups of treatment were positive for the presence of anti-scFv-MC1. **(b)** Linear regression analysis: in the neuronal expression group (CAG promoter) no significant correlation was detected between the concentration of anti-scFvMC1 antibodies in the serum (ug/ml) and the concentrations of the oligomeric/aggregated tau in hippocampus ($r^2= 0.095$). **(c)** In the astrocytic expression group (GFAP promoter) the same analysis was performed, again with no significant correlation between anti-scFvMC1 antibodies and oligomeric/aggregated tau in hippocampus ($r^2= 0.018$)