Tau Phosphorylation Profile of hTau Transgenic Mice

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BACKGROUND

Alzheimer's disease is characterized by phosphorylation and aggregation of the microtubule associated protein tau. Reliable *in vivo* models that mimic tau phosphorylation are needed. The hTau transgenic mouse features expression of human tau combined with a knockout of murine tau and belongs to the best animal models to test compounds directed against human tau.

MATERIALS and METHODS

To evaluate the phosphorylation profile of tau, 3-15 months old hTau mice were analyzed for total tau, pThr181, pSer202/205, pThr231 and pSer396/404 compared to non-transgenic littermates. Different brain regions were analyzed by immunofluorescent labeling. Additionally brain lysate was analyzed by MSD immunosorbent assay.

RESULTS

Our results show a progressive increase of soluble total tau, pThr231 and pThr181 while phosphorylation of the same residues does not increase in the insoluble brain fraction. Immunofluorescent labeling revealed an increase in total tau levels in the cortex and hippocampus already at the age of 3 months. Analyzing the same brain regions for pSer202/205 levels, only a slight increase at the age of 3 months but a prominent increase at the age of 12 months was observed. Analysis of pSer396/404 revealed a highly increased phosphorylation already at the age of 3 months that stabilized at this level.

SUMMARY and CONCLUSION

Our data suggest that total and ptau in hTau mice progressively increases while insoluble tau does barely change. The strongest increase in phosphorylation compared to non-transgenic littermates could be observed for pSer396/404. hTau transgenic mice are therefore a valuable model to study human phosphorylated tau and to test compounds that are directed against this target.

Contact for more information about the model:

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RESULTS

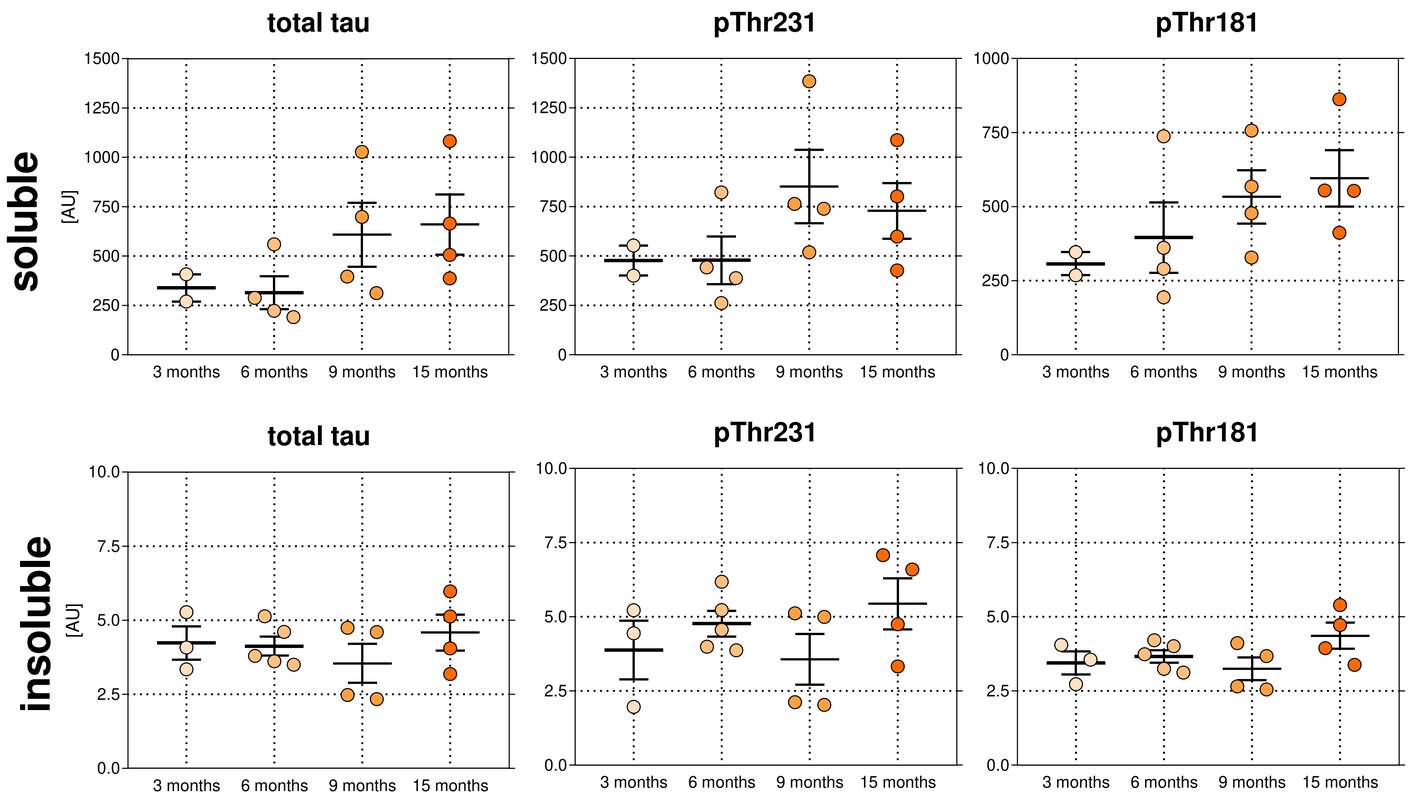

Figure 1: Soluble and insoluble total and phosphorylated tau levels in the brain of hTau mice. Soluble and insoluble tissue fractions of 3, 6, 9, and 15 months old animals were analyzed for total, pThr231 and pThr181 levels by MesoScale Discovery Immunosorbent Assay. One Way ANOVA followed by Newman's Keuls multiple comparison test. Mean±SEM; n= 2-4.

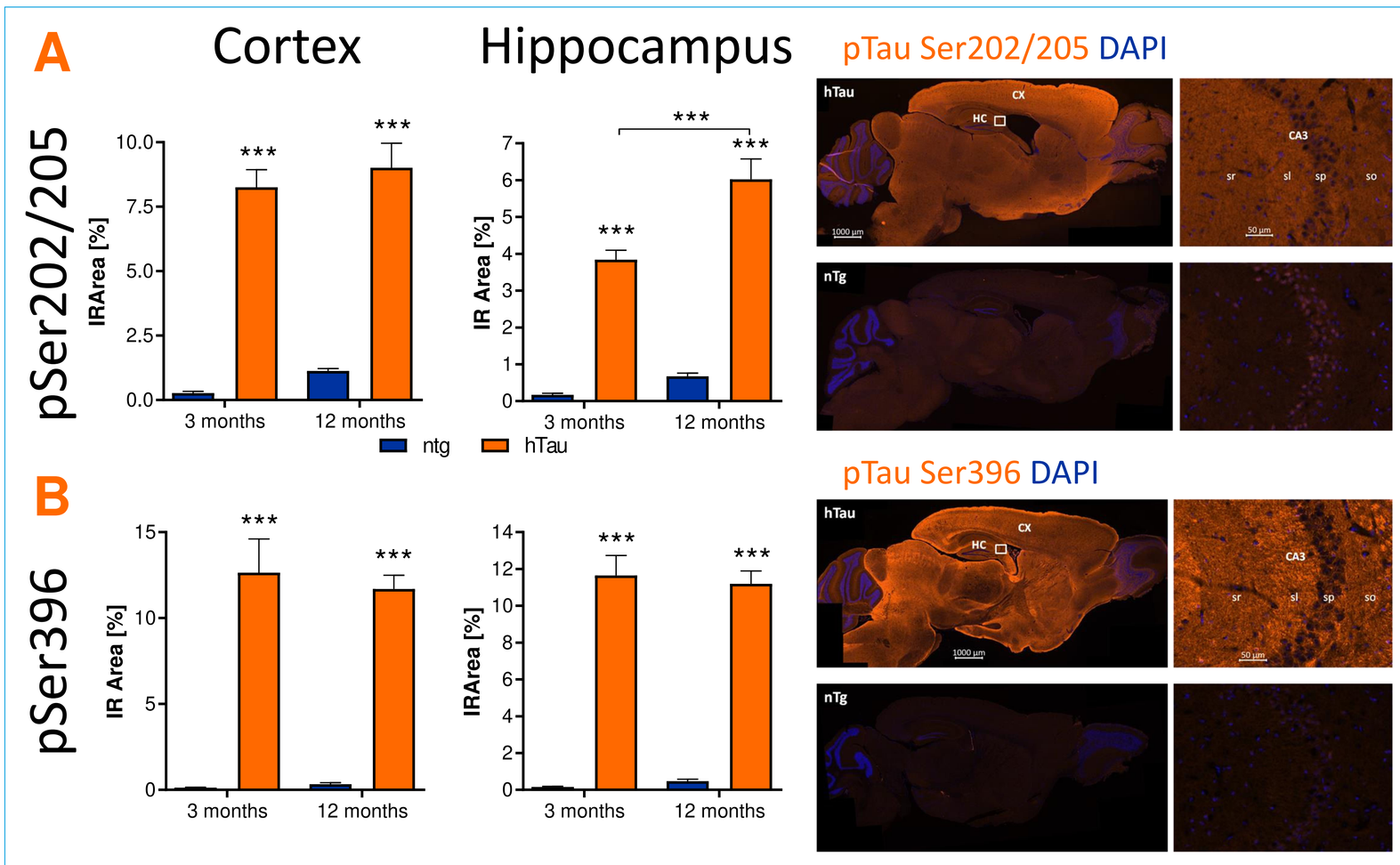

Figure 3: ptau Ser202/205 and Ser396 levels in the cortex and hippocampus of 3 and 12- months old hTau mice compared to non-transgenic littermates by EPR2402 and PHF13 antibody respectively. Immunoreactive area in percent of (A) pSer202/205 and (B) pSer396; n=8 per group. Mean + SEM; Two way ANOVA followed by Bonferroni's *posthoc* test; ***p<0.001. Representative images showing pSer202/205 and pSer396 labeling on a sagittally cut brain slice of hTau transgenic and non-transgenic littermates.

LITERATURE

Andorfer C, Kress Y, Espinoza M, de Silva R, Tucker KL, Barde YA, Duff K, Davies P. Hyperphosphorylation and aggregation of tau in mice expressing normal human tau isoforms. J Neurochem. 2003 Aug;86(3):582-90.

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