Correlation of Aβ-pE(3) and ptau in human and mouse brain

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BACKGROUND

Senile plaques frequently contain pyroglutamate amyloid β [Aβ-pE(3)], a N-terminally truncated Aβ species that is more closely linked to Alzheimer's Disease (AD) compared to other Aβ species. Tau protein is highly phosphorylated at several residues in AD, specifically tau protein phosphorylated (ptau) at Ser202/Thr205 is known to be increased in AD. First studies suggest that the two pathologies of Aβ plaque formation and tau phosphorylation might be linked.

MATERIALS and METHODS

Human cortical brain tissue of different Braak stages and brain tissue of two transgenic mouse models, APP_{SL} and 5xFAD, were histologically investigated for levels of Aβ-pE(3) and ptau Ser202/Thr205. Statistical analysis determined whether Aβ-pE(3) and ptau Ser202/Thr205 levels correlate in human brains or in brains of transgenic AD mouse models.

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SUMMARY and CONCLUSION

Our results show that Aβ-pE(3) and ptau Ser202/Thr205 levels strongly correlate in human as well as in murine cortical tissues. Further, the data indicate that tau phosphorylation might be amplified by Aβ-pE(3). Results are published in Neddens et al., 2020 PlosOne.

RESULTS

Quantitative image analysis showed that Aβ-pE(3) formation increases already at earlier Braak stages while ptau Ser202/Thr205 increases at later stages. Further analyses revealed strong correlations between the two pathologies in the temporal, frontal, cingulate and occipital cortex. Evaluation of murine transgenic brain tissue demonstrated a slow but steady increase of Aβ-pE(3) from 6 to 12 months of age in the cortex of APP_{SL} mice and a very early and strong Aβ-pE(3) increase in 5xFAD mice. Levels of ptau Ser202/Thr205 increased at the age of 9 months in APP_{SL} mice and already at 6 months in 5xFAD mice. Correlation analyses revealed a strong correlation between the two pathologies in APP_{SL} mice.

HUMAN SAMPLES

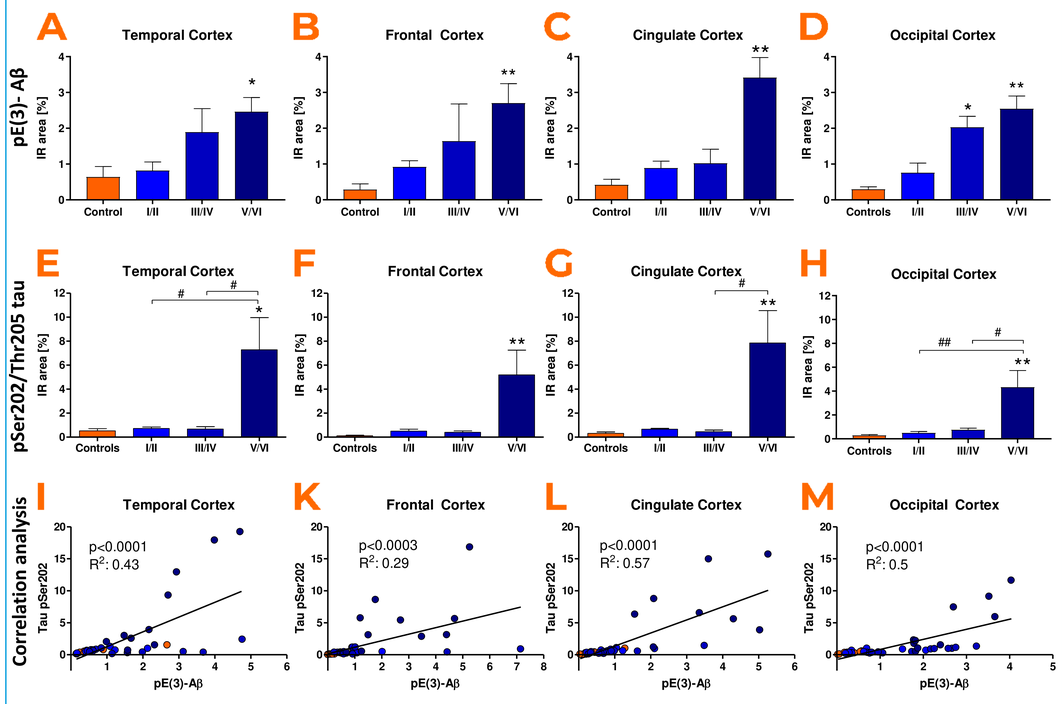

Figure 1. Pyroglutamate amyloid-β and pSer202/Thr205 tau expression in different cortical regions of AD patients' brain samples. A-D: Pyroglutamate amyloid-β (pE(3)-Aβ); E-H: pSer202/205 tau. I-M: Correlation analysis of pE(3)-Aβ and pSer202/Thr205 tau. n = 5 per group; mean + SEM; A-H: One-way ANOVA followed by Bonferroni *post hoc* test; I-M: Pearson correlation. *compared to controls; # differences between Braak stages.

MURINE SAMPLES

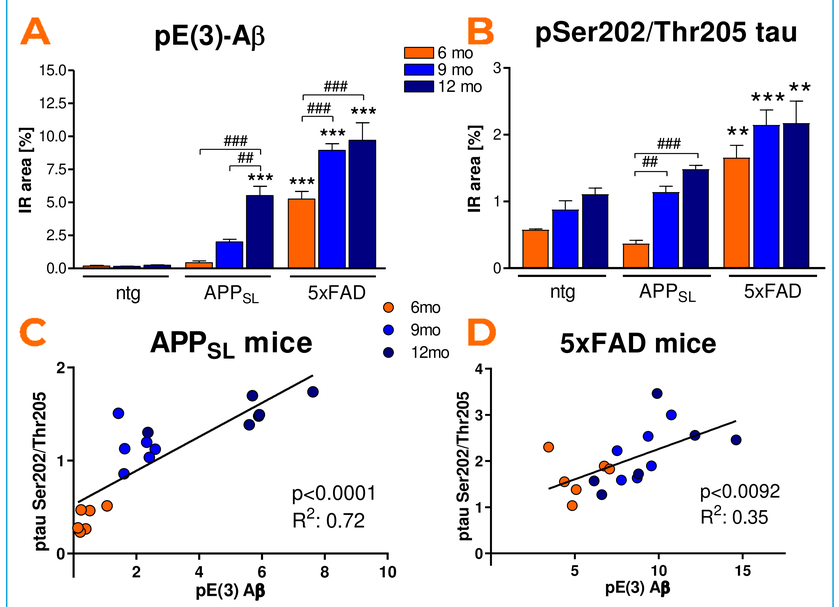

Figure 2. Pyroglutamate amyloid-β and pSer202/Thr205 tau expression in the cortex of 6, 9 and 12 months old APP_{SL} and 5xFAD mice. A,B: Percentage of immunoreactive area (IR) of pyroglutamate amyloid-β (pE(3)-Aβ) and pSer202/ Thr205 tau. Two-way-ANOVA with Bonferroni *post hoc* test. Mean + SEM. *compared to nontransgenic littermates (ntgs); # differences between age groups of one genotype. C,D: Correlation analysis of Aβ-pE(3) and pSer202/ Thr205 tau in APP_{SL} and 5xFAD mice. n = 5 per group. E: Representative images of pE(3)-Aβ and pSer202/Thr205 tau labeling in the cortex of 9 month old 5xFAD mice and non-transgenic littermates.