

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

Magdalena Temmel¹, Joerg Neddens¹, Stefanie Flunkert¹, Lauren Walker², Johannes Attems², Birgit Hutter-Paier¹

¹QPS Austria GmbH, Parkring 12, 8074 Grambach, Austria

²Translational and Clinical Research Institute and Newcastle University Institute for Ageing, Campus for Ageing and Vitality, Newcastle upon Tyne, NE4 5PL, UK

BACKGROUND

Senile plaques frequently contain pyroglutamate amyloid β [A β -pE(3)], a N-terminally truncated A β species that is more closely linked to Alzheimer's Disease (AD) compared to other A β 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 A β 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 A β -pE(3) and ptau Ser202/Thr205. Statistical analysis determined whether A β -pE(3) and ptau Ser202/Thr205 levels correlate in human brains or in brains of transgenic AD mouse models.

For more information about the model

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office-austria@qps.com

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SUMMARY and CONCLUSION

Our results show that A β -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 A β -pE(3). Results are published in Neddens et al., 2020 PlosOne.

RESULTS

Quantitative image analysis showed that A β -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 A β -pE(3) from 6 to 12 months of age in the cortex of APP_{SL} mice and a very early and strong A β -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

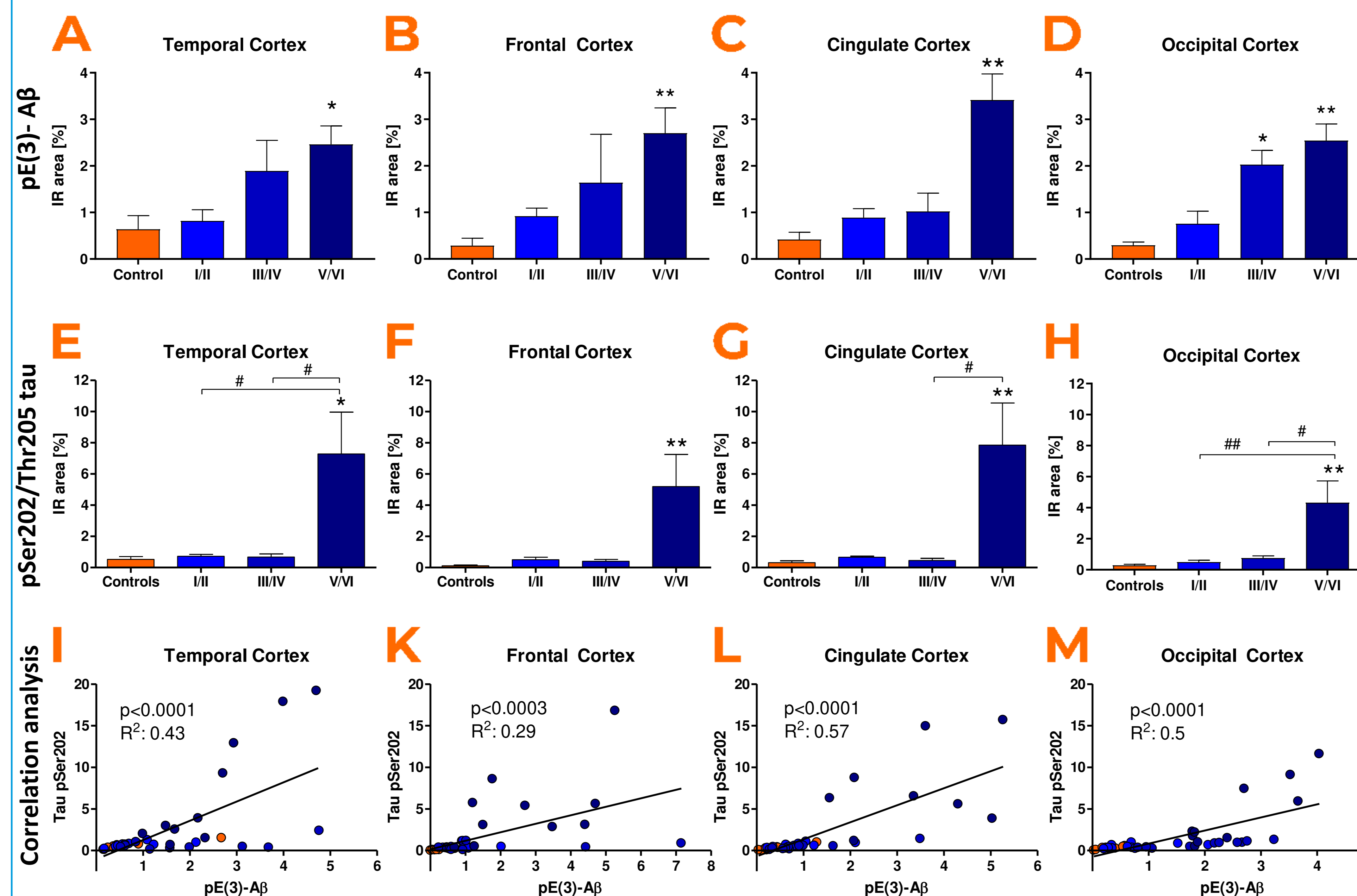


Figure 1. Pyroglutamate amyloid- β and pSer202/Thr205 tau expression in different cortical regions of AD patients' brain samples. A-D: Pyroglutamate amyloid- β (pE(3)-A β); E-H: pSer202/205 tau. I-M: Correlation analysis of pE(3)-A β and pSer202/Thr205 tau. n = 5 per group; mean + SEM; A-H: One-way ANOVA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

MURINE SAMPLES

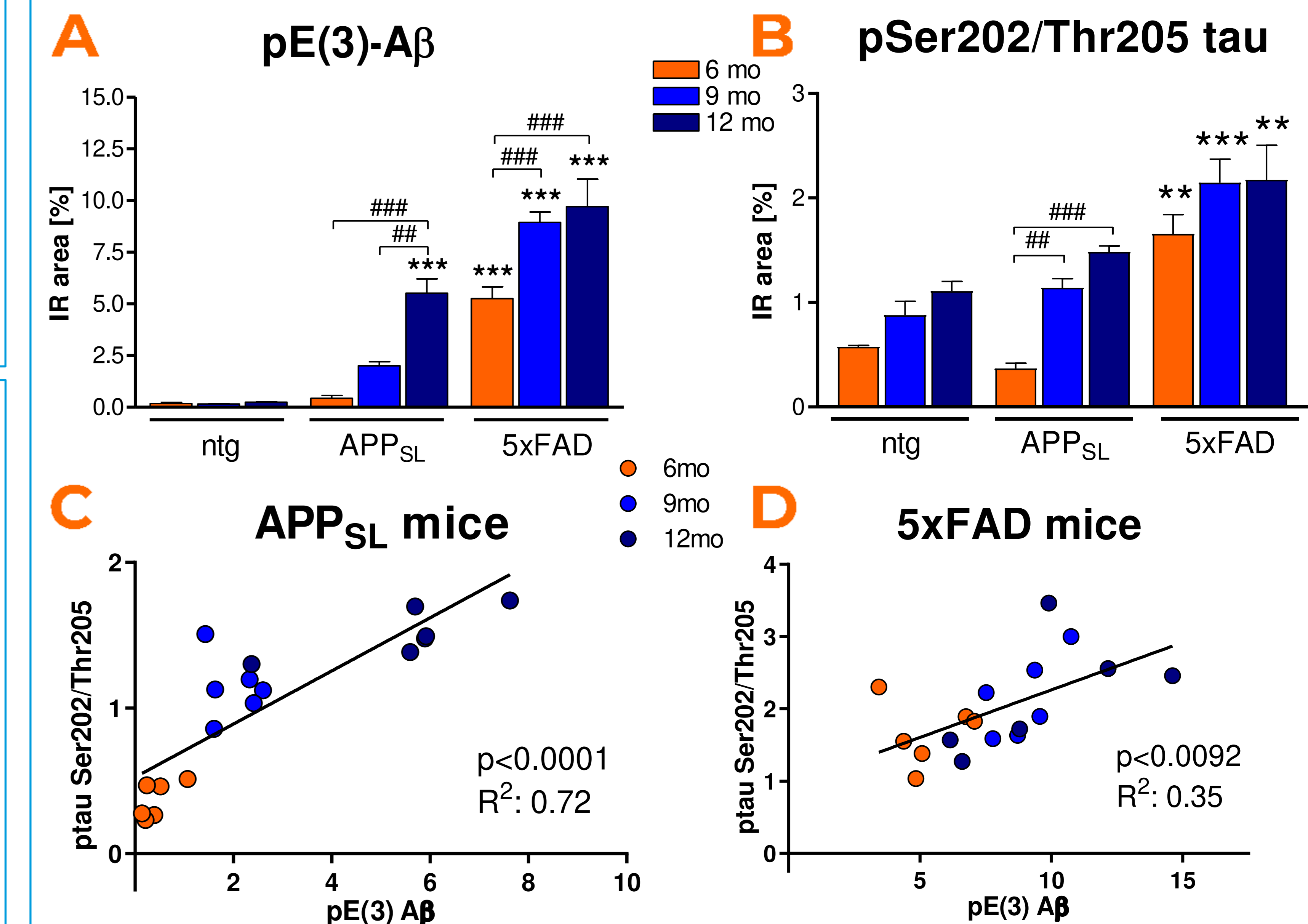


Figure 2. Pyroglutamate amyloid- β and pSer202/Thr205 tau expression in the cortex of 6, 9 and 12 months old APP_{SL} and 5xFAD mice. A,B: Percentage of immunoreactive area (IR) of pyroglutamate amyloid- β (pE(3)-A β) and pSer202/Thr205 tau. Two-way-ANOVA with Bonferroni *post hoc* test. Mean + SEM.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

