Progressive Increase of Alzheimer's Disease Pathology in 5XFAD Transgenic Mice

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BACKGROUND

Today, Alzheimer's disease (AD) is one of the most devastating neurodegenerative diseases worldwide. Pathologically increased β-amyloid (Aβ) in the brain of AD patients is thought to be one of the main causes for the observed progressive cognitive decline in affected people. The development of new drugs against AD is therefore a main research focus. To be able to test these new drugs, appropriate animal models are needed. 5xFAD mice bear 5 mutations, 3 in the APP695 gene as well as 2 mutations in the presenilin 1 gene. The expression of the 5xFAD transgene is driven by the neuron-specific Thy1 promoter. The 5xFAD transgenic mouse model mimics the most crucial phenotypic pathologies of amyloidogenic neurodegeneration and is therefore among the best transgenic AD animals available.

MATERIALS and METHODS

We analyzed the soluble and insoluble fraction of whole brain lysate from 5xFAD mice over age for aggregated Aβ by A4 assay and for Aβ with MesoScale Discovery platform. Furthermore Aβ aggregates as well as neuroinflammation, as indicated by astrocytosis and activated microglia, were evaluated by quantification of immunofluorescent labeling.

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RESULTS

Our results show an early and progressive increase of Aβ 40 and 42 aggregates as well as neuroinflammation in the cortex and hippocampus of 1 to 9 months old 5xFAD mice.

Aggregated Aβ by A4 assay

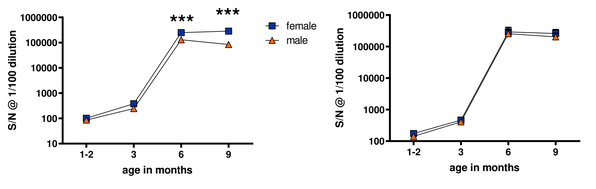

Figure 1: Aggregated Aβ species of 1 to 9 month old 5xFAD transgenic mice. A: cortex; B: hippocampus. Tissue was analyzed by A4 assay. S/N mean ± SEM of 3 - 5 female or male animals per group; S/N = signal to noise ratio. Two-way ANOVA with Bonferroni *post hoc* test; *** p<0.001. Significances show differences between sexes. Increase over age is highly significant for both sexes and brain regions (not labeled)

SUMMARY and CONCLUSION

Our results suggest that 5xFAD mice are not only a well-suited model for Aβ research but also to analyze AD-related neuroinflammation. Additionally these data give insight into the progression of the most prominent disease hallmarks in 5xFAD mice, providing a good basis for planning possible efficacy studies in those animals.

For more information about the model please visit:
www.qpsneuro.com

or send us an e-mail:
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RESULTS

Aβ and Aβ aggregates

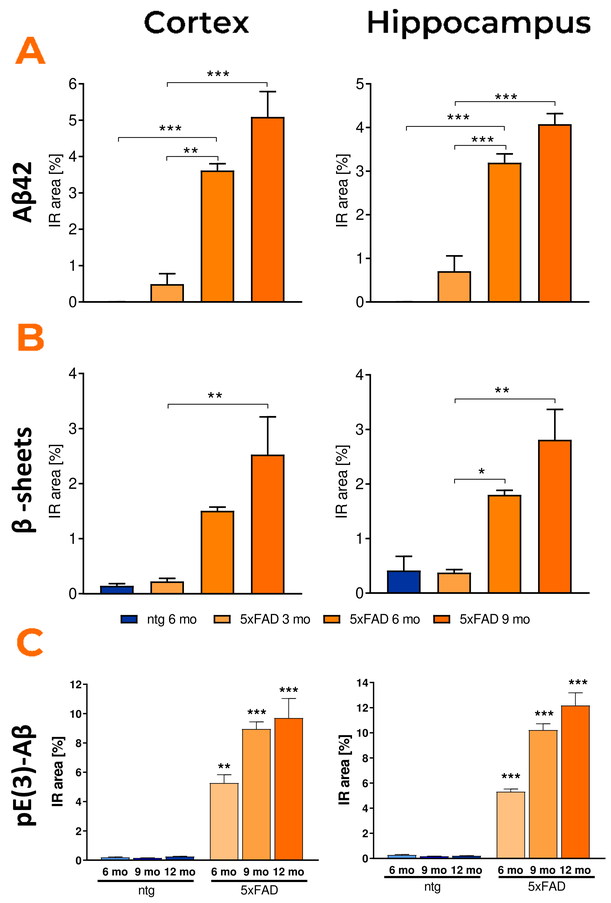

Figure 2: Quantification of Aβ42, β-sheets (Thioflavin S) and pyroglutamate amyloid-β (pE(3)-Aβ) load in the cortex and hippocampus of 6 , 9 and 12 month old 5xFAD transgenic mice. Immunoreactive (IR) area in percent in the cortex and hippocampus. Values in non-transgenic (ntg) mice represent background. n = 5. Mean + SEM. Two-way ANOVA with Bonferroni's *post hoc* test. *p<0.05; **p<0.01; ***p<0.001.

Neuroinflammation

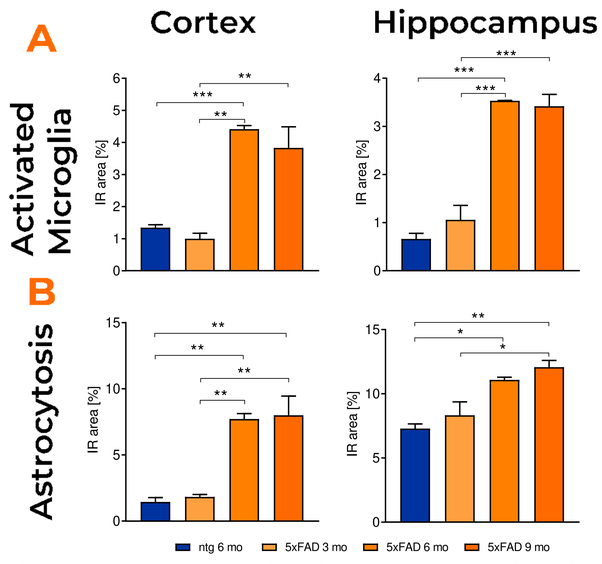

Figure 3: Neuroinflammation in 5xFAD transgenic mice. Quantification of activated microglia (**A**; CD11b labeling) and astrocytosis (**B**; GFAP labeling) in the cortex and hippocampus of 3, 6 and 9 month old 5xFAD transgenic mice. Immunoreactive area (IR) in percent. n = 5. Mean + SEM. One-Way ANOVA with Bonferroni's *post hoc* test.*p<0.05; **p<0.01; ***p<0.001.

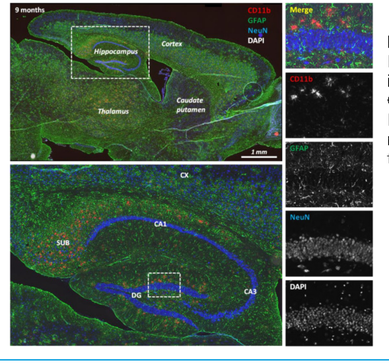

Figure 4: Representative images of CD11b, GFAP, NeuN and DAPI labeling in 9 months old 5xFAD transgenic mice.