In Vivo Functional Brain Mapping in a Conditional Mouse Model of Human Tauopathy (*tau*$_{P301L}$) Reveals Reduced Neural Activity in Memory Formation Structures

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Introduction

Tauopathies are characterized by intracellular deposition of the microtubule-associated protein tau as filamentous aggregates. The rTg4510 mouse conditionally expresses mutant human tau protein in various forebrain areas under the Tet-off expression system. Mice develop neurofibrillary tangles, with significant neuronal loss and cognitive deficits by 6 months of age. Previous behavioral and biochemical work has linked the expression and aggregates of mutant tau to functional impairments.

Experimental

The present work used manganese-enhanced magnetic resonance imaging (MEMRI) to investigate basal levels of brain activity in the rTg4510 and control mice.

Results and Discussion

Our results show an unmistakable curtailment of neural activity in the amygdala and hippocampus, two regions known for their role in memory formation, but not the cortex, cerebellum, striatum and hypothalamus in tau expressing mice.

Conclusions

Behavioral impairments associated with changes in activity in these areas may correspond to age progressive mutant tau$_{P301L}$-induced neurodegeneration.

Acknowledgements

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References

[1] Perez, P. D., *et al.* Molecular Neurodegeneration in revision (2013).

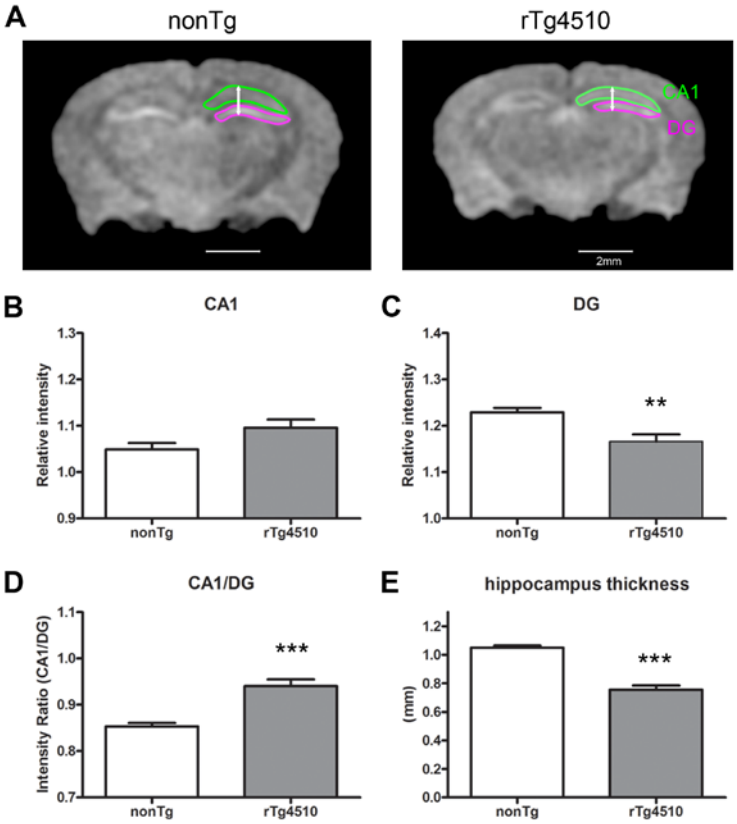

Figure Caption: Manganese enhanced intensity and thickness of hippocampus. **A)** Representative coronal sections of non Tg and rtg4510 mouse brains. The coronal slices were at the level Bregma -2 mm. Sub-regions of hippocampus were drawn as CA1 (green) and DG (purple). Arrows showed the analyzed position of hippocampus thickness. The position was set at 1.5 mm from center. Scale bar=2 mm. **B)** Relative intensity of CA1 region was normalized by averaged intensity of whole brain. **C)** Relative intensity of DG region was normalized by averaged intensity of whole brain. **D)** Ratio of intensity between CA1 and DG. E. Comparison of hippocampus thickness between non Tg (n=5) and rTg4510 (n=5) mice. **p<0.01, ***p<0.001.