Axonal conduction velocity in CA1 area of hippocampus is reduced in a mouse model of Alzheimer’s disease, rTg4510

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Background

We previously reported that conduction velocity of Schaffer collaterals in CA1 area of hippocampus is reduced in an age-dependent manner in two amyloid precursor protein transgenic mouse models, line 41 (APP Swe/Lon) and APP/PS1 (cross between tg-2576 (APPSwe) and a mutant PS1 (m146l) mouse). Here we asked whether similar deficit in Vc is also present in a mouse model of tauopathy, rTg4510, which over-expresses microtubule-associated protein tau carrying a P301L mutation. Hyper-phosphorylated tau disrupts axonal cytoskeleton and transport, potentially resulting in abnormal levels of Na+ and/or K+ channels and Na+/K+ - ATPases, which may contribute to changes in Vc.

Methods

We measured Vc in axons of Schaffer collaterals in CA1 area of hippocampus. We used a transverse hippocampal slice preparation with two extracellular recording electrodes to capture propagation of compound action potentials (CAPs) elicited by a stimulating electrode in the presence of synaptic transmission blockers (CNQX, APV, and picrotoxin). Vc (in µm/ms) was calculated as d/t, where d is the linear distance between recording electrodes (200µm-600µm) and t is the time of CAP propagation. The distance between recording electrodes and the width of a stimulating electrode were determined using two separate deep learning neural networks trained to detect the width of calibration probe (stim electrode) and tips of recording probes.

Our results demonstrate that conduction velocity is reduced in two separate deep amyloid precursor protein transgenic mouse models, line 41 (APP Swe/Lon) and APP/PS1 (cross between tg-2576 (APPSwe) and a mutant PS1 (m146l) mouse), and in a mouse model of tauopathy, rTg4510, which over-expresses microtubule-associated protein tau carrying a P301L mutation. Therefore, our findings suggest that both tauopathy and Alzheimer’s disease may contribute to changes in axonal conduction velocity.

Summary

We find that conduction velocity in three AD mouse models is reduced compared with age-matched WT controls. Reduction in conduction velocity is greatest in rTg4510, a mouse model of tauopathy. Reducing conduction velocity may result in temporal dysregulation of hippocampal networks, affecting memory and cognition.

References

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