Amyloid Beta Causes Different Types of White Matter Damage Characterized by DTI

Hsiao-Fang Liang[1], Jennifer Mei[2], Dan Xu[1], Wei-Xing Shi[1], and Shu-Wei Sun[1,2]
[1]*Loma Linda University, Loma Linda, CA, United States,* [2]*University of California, Loma Linda, CA, United States*

Introduction Amyloid β (Aβ) is the major pathological peptide causing neural damage in the Alzheimer's disease (AD). Following the early experimental explorations in 1991 using an Aβ intracerebroventricular (icv) injection in mice (1), over 100 studies have used this animal model to produce amyloidopathy similar to human AD. In this study, we performed *in vivo* DTI to evaluate white matter degeneration in this animal AD mode.

Materials and Methods Seven 12-week-old female C57BL/6 mice were used. $A\beta_{1\text{-}42}$ (4 nmole in 3 µl) was dissolved in sterile saline and incubated at 37°C for 72 hours followed by a micro-injection into the left lateral ventricle. Two months after the injection, *in vivo* DTI was collected via spin echoes with TR 3 s, TE 29 ms, b-values of 0 and 0.85 ms/µm^2 in 6 directions by a Bruker 4.7T BioSpec to quantify axial diffusivity (λ||), radial diffusivity (λ⊥), relative anisotropy (RA), and trace of the diffusion tensor (TR). Because the abnormal visual pathway was found via DTI, Visual Evoked Potential (VEP) was also examined, followed by histology.

Results and Discussion Following an Aβ injection, ipsilateral optic tract (**Fig. 1**) and ipsilateral external capsule (**Fig. 2**) were injured detected by DTI. Both regions are adjacent to the Aβ-injected ventricle, but DTI showed different types of damage in these two regions: a decreased λ|| and an increased λ|| were found in the optic tract and external capsule, respectively. Because left optic tract contains axons extended from the right optic nerve, the damage to left optic tract possibly led to the damage in right optic nerves as shown in **Fig 1**. The injury to the visual pathway was correlated with the functional measurements using VEP (**Fig. 3**).

Conclusion Our data suggested that DTI may serve as a marker for white matter damage in AD. The changes of λ|| may characterize different types of damage, which implying different white matter pathological mechanisms induced by Aβ.

References (1) Frautschy et al, PNAS 88 (1991) 8362-8366.

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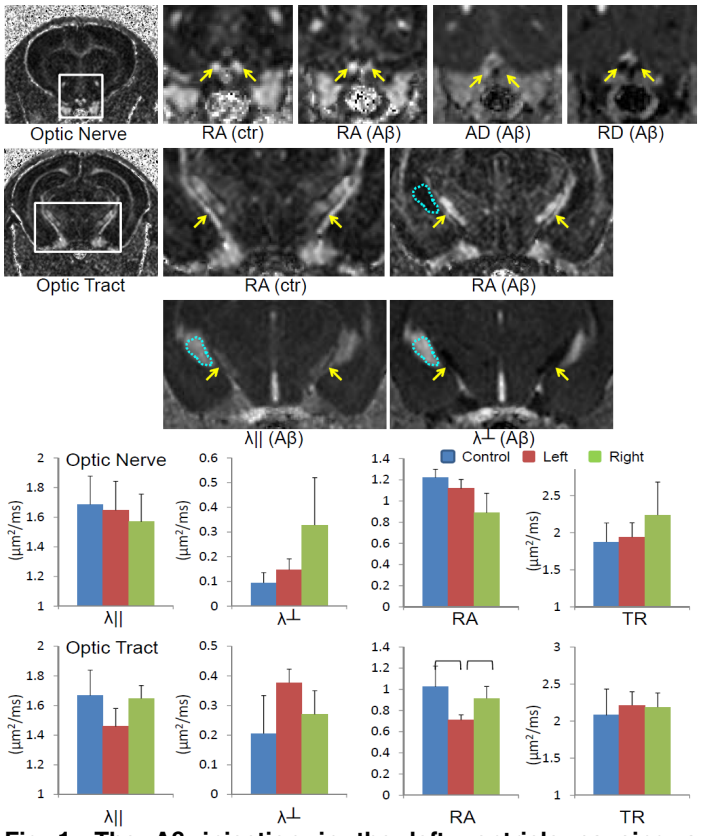

Fig 1. The Aβ injection in the left ventricle causing a decreased λ||, an increased λ⊥, and a decreased RA in left optic tract and right optic nerve.

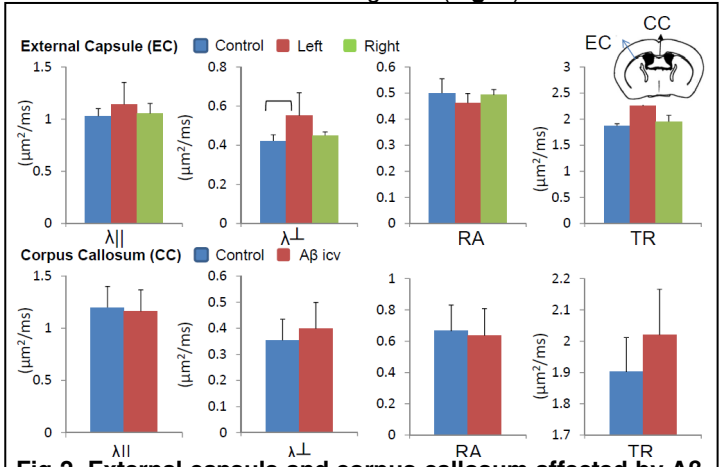

Fig 2. External capsule and corpus callosum affected by Aβ. The left (Aβ-affected side) EC produced increased λ||, λ⊥, and TR, while right EC and the whole CC did not show damage.

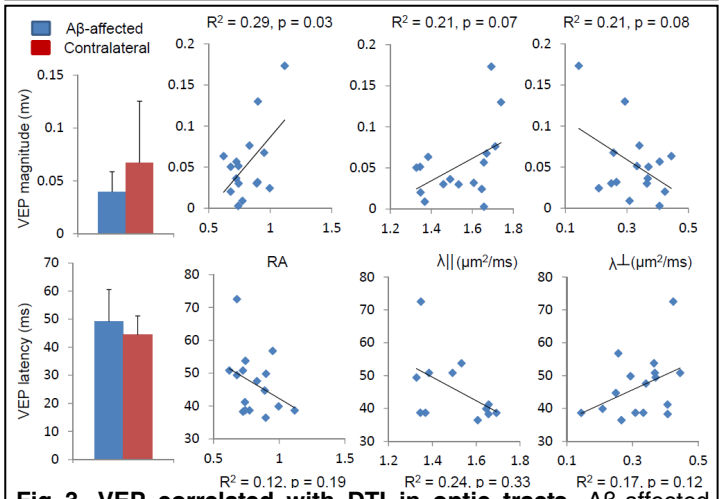

Fig 3. VEP correlated with DTI in optic tracts. Aβ-affected optic tract had reduced VEP response (reduced VEP amplitudes and elongated latency) correlated with DTI in optic tracts.