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Program: 0293

Diffusion Bubble Model: A Novel Method For Detecting Neuroinflammation in Mouse Brain With Sanfilippo Syndrome

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Université de Montréal et du monde.

Declaration of Financial Interests or Relationships

Speaker Name: Erjun Zhang

I have no financial interests or relationships to disclose with regard to the subject matter of this presentation.

Introduction

- **Sanfilippo Syndrome**
  - **Rare genetic disease**: 1/1.5 million birth
  - **Caused by**: Lysosomal storage problem
  - **Leads to**: Neurodegeneration, progressive neuroinflammation, early death [1]
  - **Mouse model**: reproduce hallmark features: neuronal loss, neuroinflammation [2]

- **Lack of**
  - Disease progression monitor method [3]
  - Simple and efficient dMRI model to detect brain inflammation, especially in **grey matter**
- **Aim of project**
  - Create a dMRI model to detect brain microstructure changes caused by Sanfilippo Syndrome

1. Bartsocas et al., 1979 2. Martins et al. 2015 3. Daniel et al., 2022

Methods

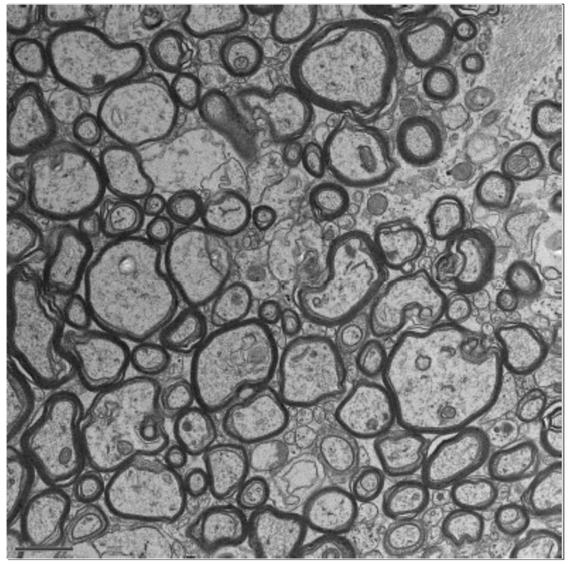
Diffusion Bubble Model (DBM) is sum of increased **isotropic** diffusion tensor

New diffusion model

Very complex

Brain microstructures

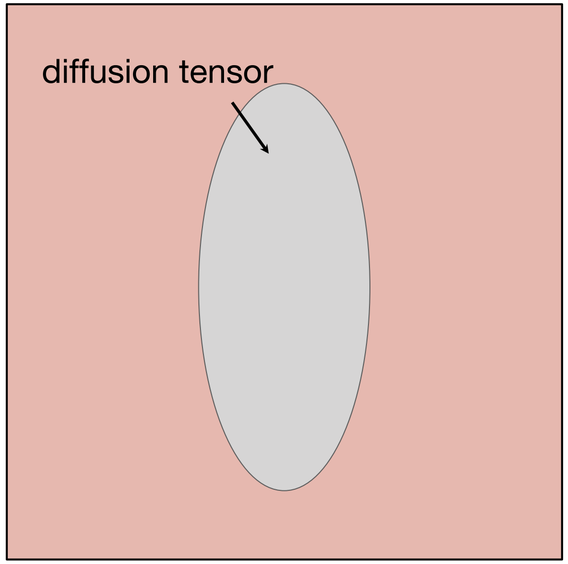
Electron Microscopy Image



Over-simplified

$$S_k = e^{-|\vec{b}_k|\mathbf{D}} + \epsilon$$

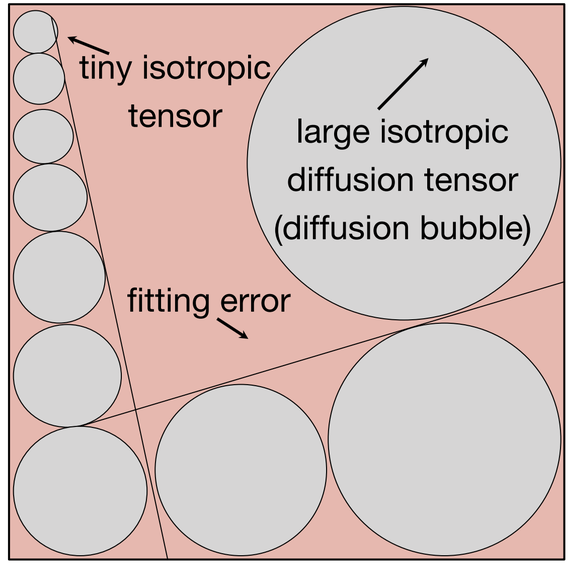
DTI



New model

$$S_k = \sum_{i=1}^{N} f_{D_i} e^{-|\vec{b}_k| D_i} + \epsilon$$

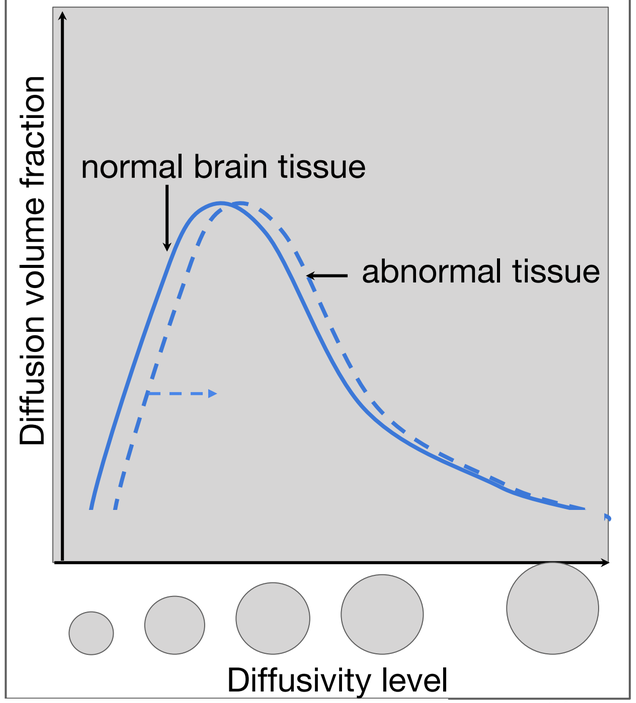
Diffusion Bubble Model



Hypothesis

Inflammation will change diffusion spectrum curve

Diffusion Spectrum Curve



When detecting brain injury (inflammation), **isotropic diffusion components matter**!

TEM image size: 1/400 mm; S_k has been normalized.

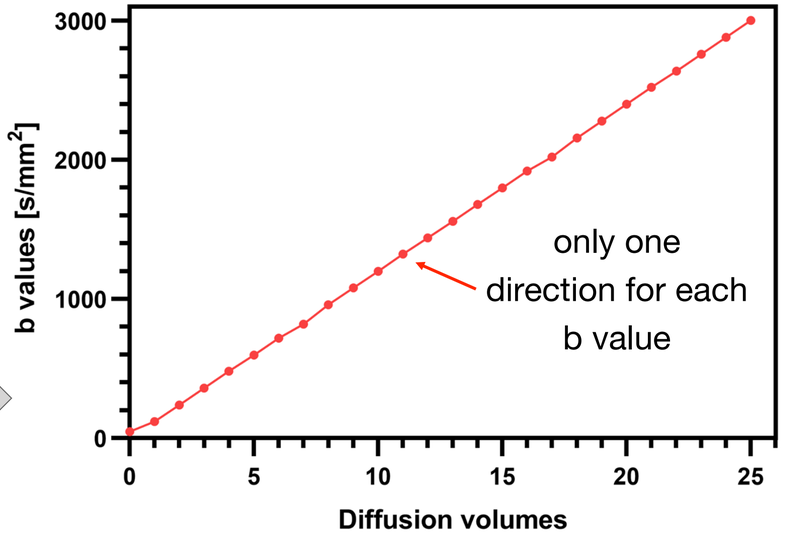
* N. S. White et al., 2013

Methods

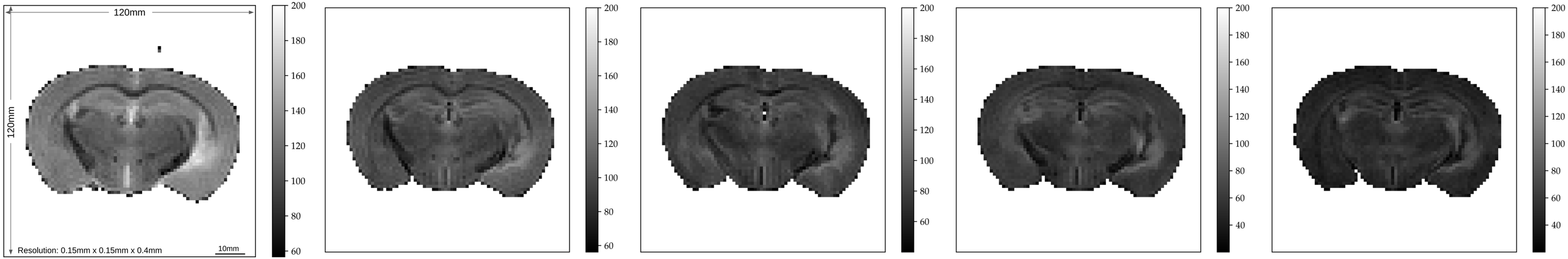
Data Acquisition

- Scanner: $7T$ Bruker
  Subjects: 10 control *vs* 8 Sanfilippo Syndrome
  Ex-vivo mice from collaborators lab [1]
- TR/TE: $3300ms/32ms$
  Resolution: $0.15 \times 0.15 \times 0.4$ mm^3
  Volumes: 1 b0 and 25 b values ($0 < b \leq 3000s/mm^2$)

Only 26 diffusion volumes were scanned for one brain
(comparable to clinical DTI diffusion volume numbers)



DWIs Acquired [2]



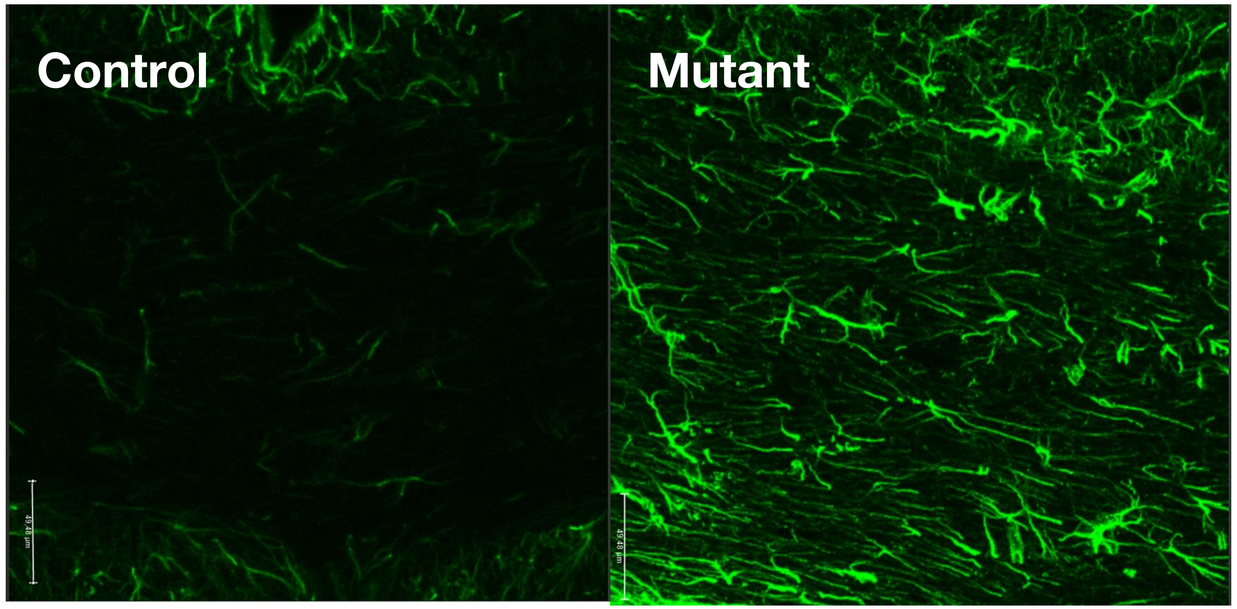
1. Martins et al 2015; 2. Mouse: sub-M2023022301, male, 7-month old, scanned on Feb. 23, 2023

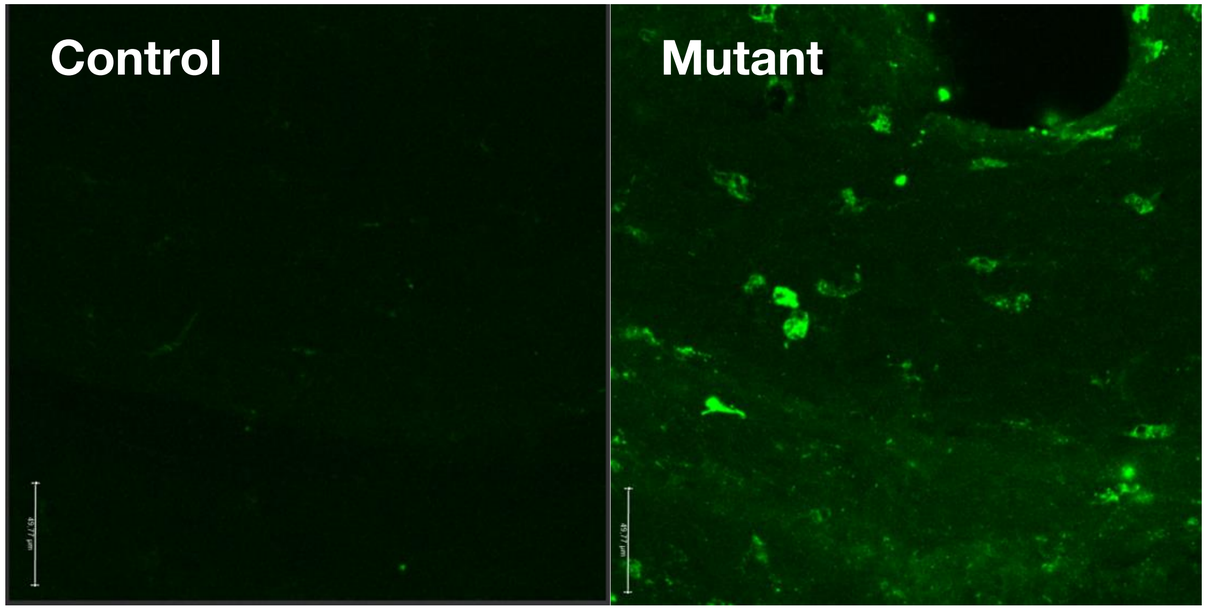
Results

Increased astrogliosis and activated microglia reveals inflammation in corpus callosum

1. Astrocyte labeling of control and mutant mice

Increased astrogliosis in the corpus callosum





2. Images of microglial activation in control and mutant

Increased activated microglia in the corpus callosum

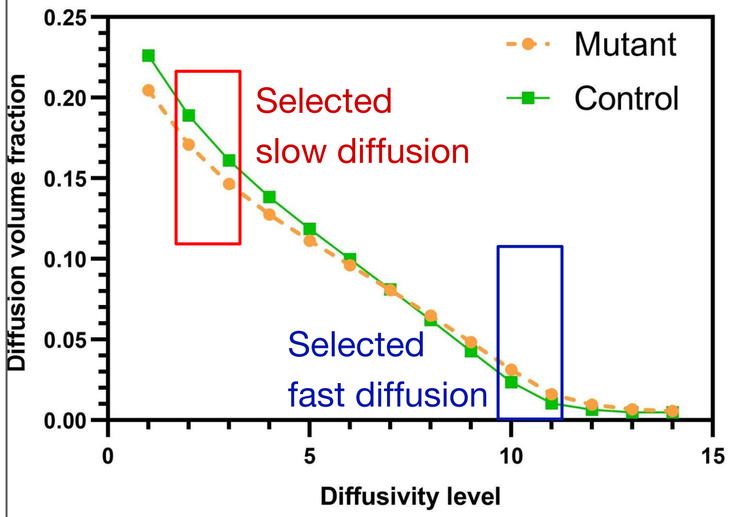
1. GFAP labeling shows astrogliosis;
2. CD68 labeling shows activated microglia

Results

In corpus callosum (white matter)

New Model Results

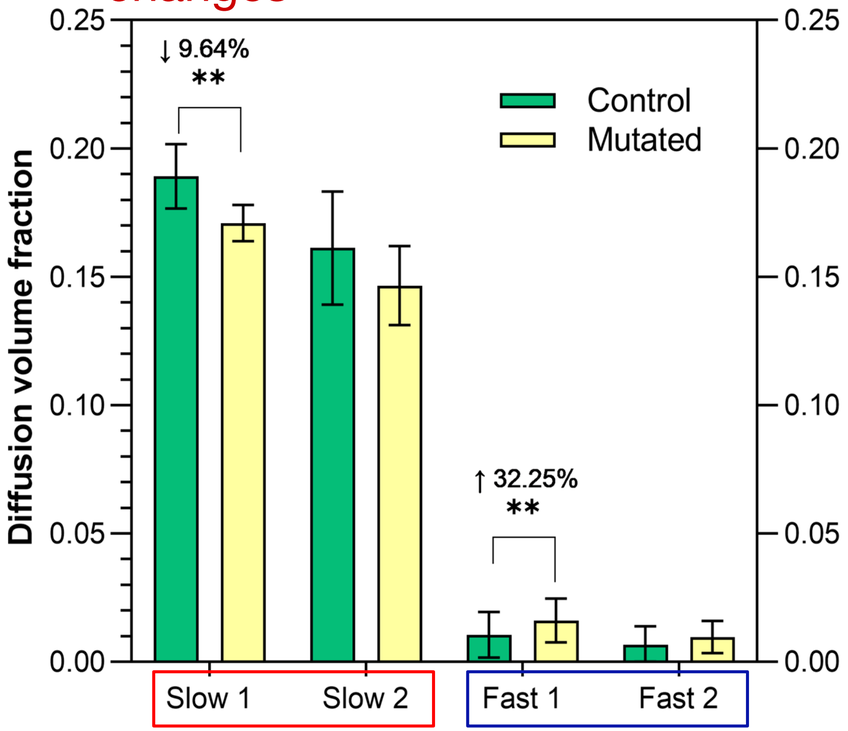
Diffusion Bubble Model



Diffusion Spectrum Curve

32.25% increase in fast diffusivity reflecting oedema

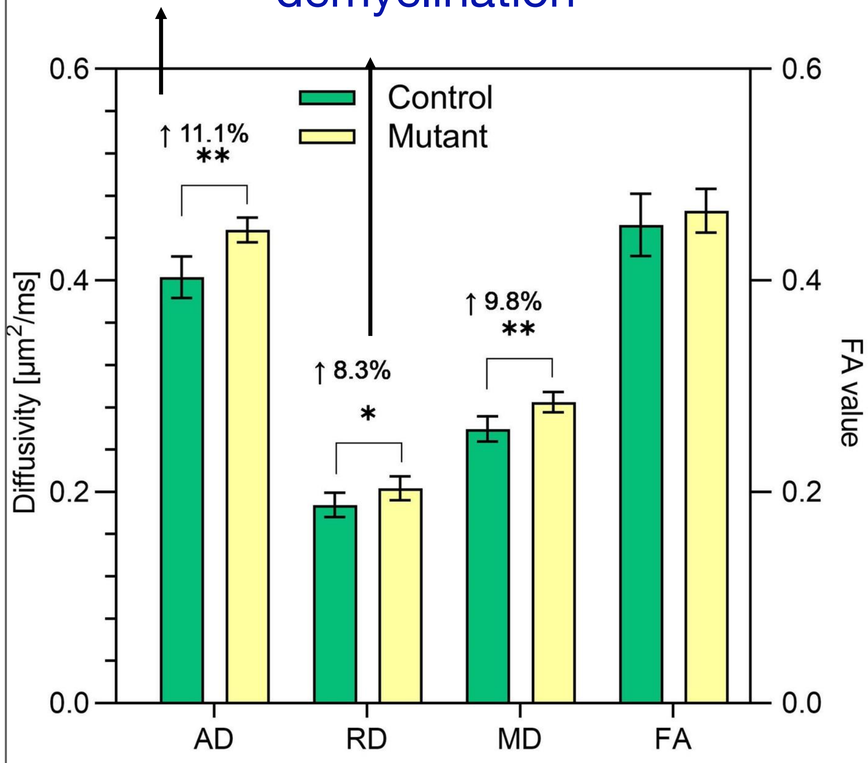
9.64% reduction in slow diffusivity reflecting complex cell related changes



DBM Slow and Fast Diffusion

Diffusion Tensor Model

Axonal impairment (swelling)
demyelination



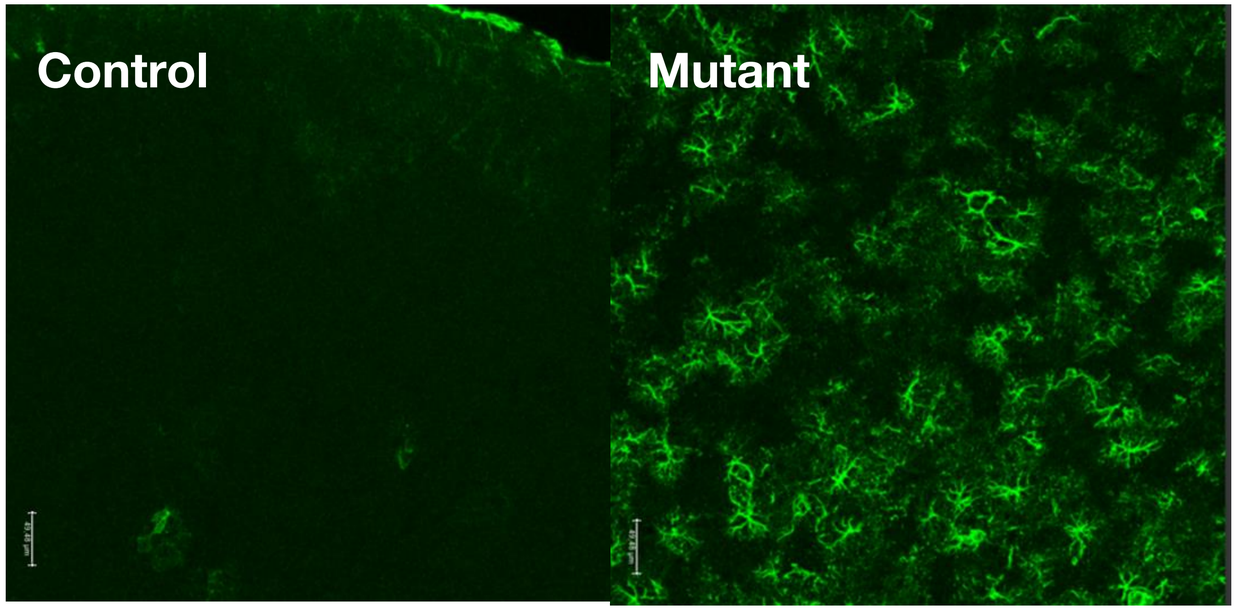
Standard DTI Result

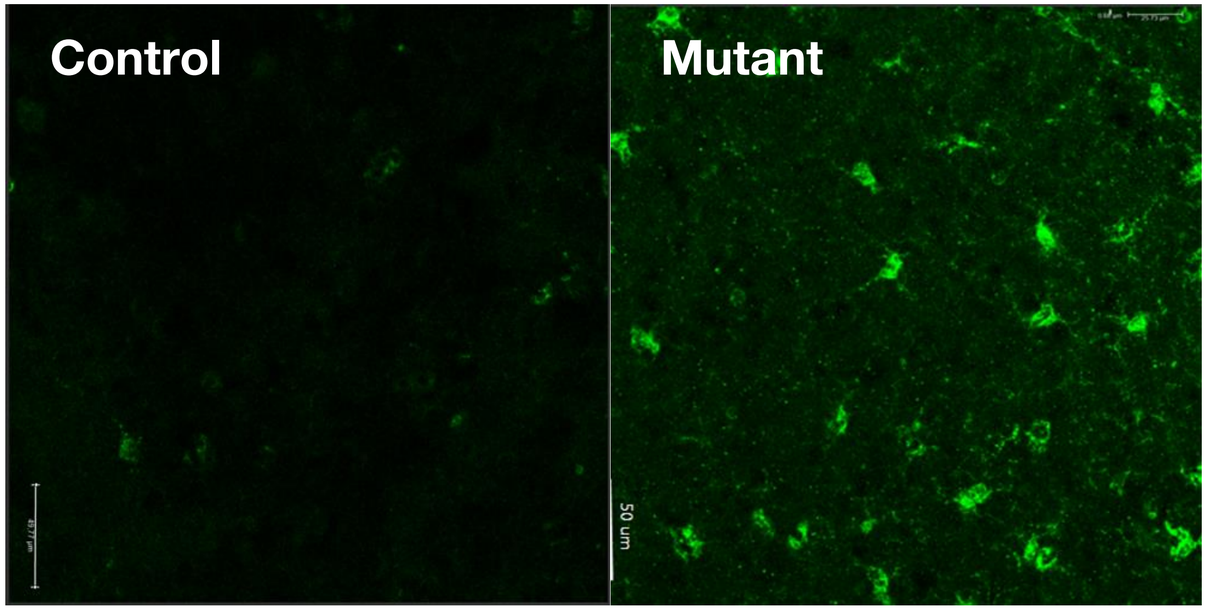
Results

Increased astrogliosis and activated microglia reveals inflammation in cortex (grey matter)

1. Astrocyte labeling of control and mutant mice

Increased astrogliosis in the cortex





2. Images of microglial activation in control and mutant

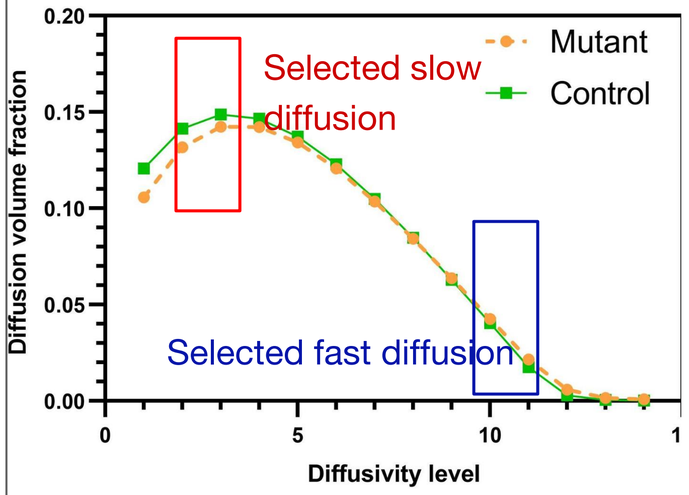
Increased activated microglia in the cortex

1. GFAP labeling shows astrogliosis; 2. CD68 labeling shows activated microglia

Results

Similar diffusion pattern in cortex (grey matter)

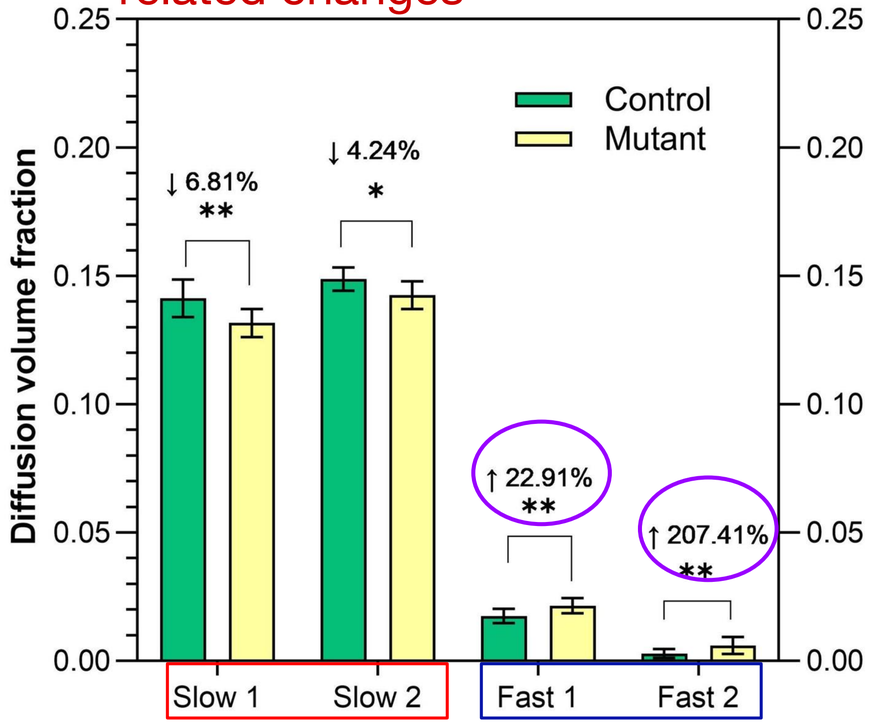
Diffusion Bubble Model



Diffusion Spectrum Curve

↑ 22.91%, 207.41% increase in Fast diffusion reflecting œdema

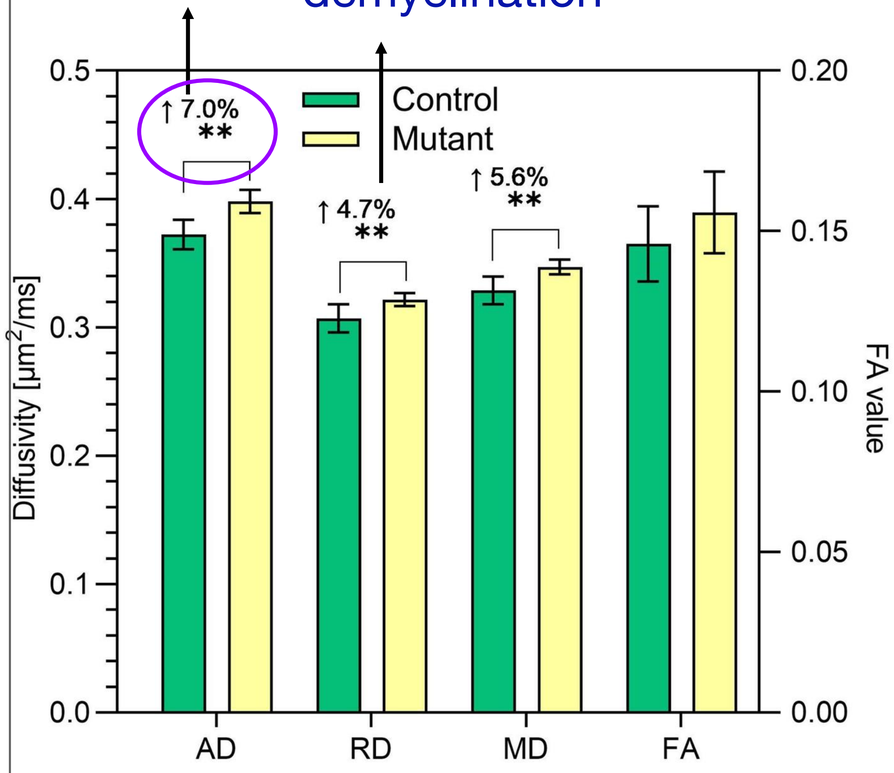
↓ 4.24%, 6.81% reduction of slow diffusion reflecting complex cell related changes



DBM Slow and Fast Diffusion

Diffusion Tensor Model

Axonal problem (swelling) demyelination



Standard DTI Result

Conclusion

- **Conclusion**
  - Diffusion bubble model, for the first time, shows the possibility of using sum of **isotropic diffusion tensors to detect brain microstructure changes and inflammation**
  - With a DTI-comparable acquisition scheme, it can take **less than 5 min for in-vivo scan and 1 minute for data processing time**, making it very attractive for clinical translation

- **In the future**
  - Evaluate this model and comparing it to other models such as NODDI, DKI and RSI
  - Microglial activation and cell density quantification (ongoing)
  - In vivo experiments in newborns and children

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Welcome to view other abstracts from our labs:

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