



Mechanical allodynia in tenascin-X - deficient mice associated with the Ehlers-Danlos syndrome

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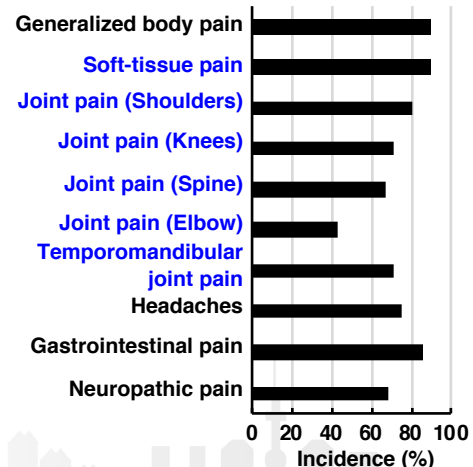


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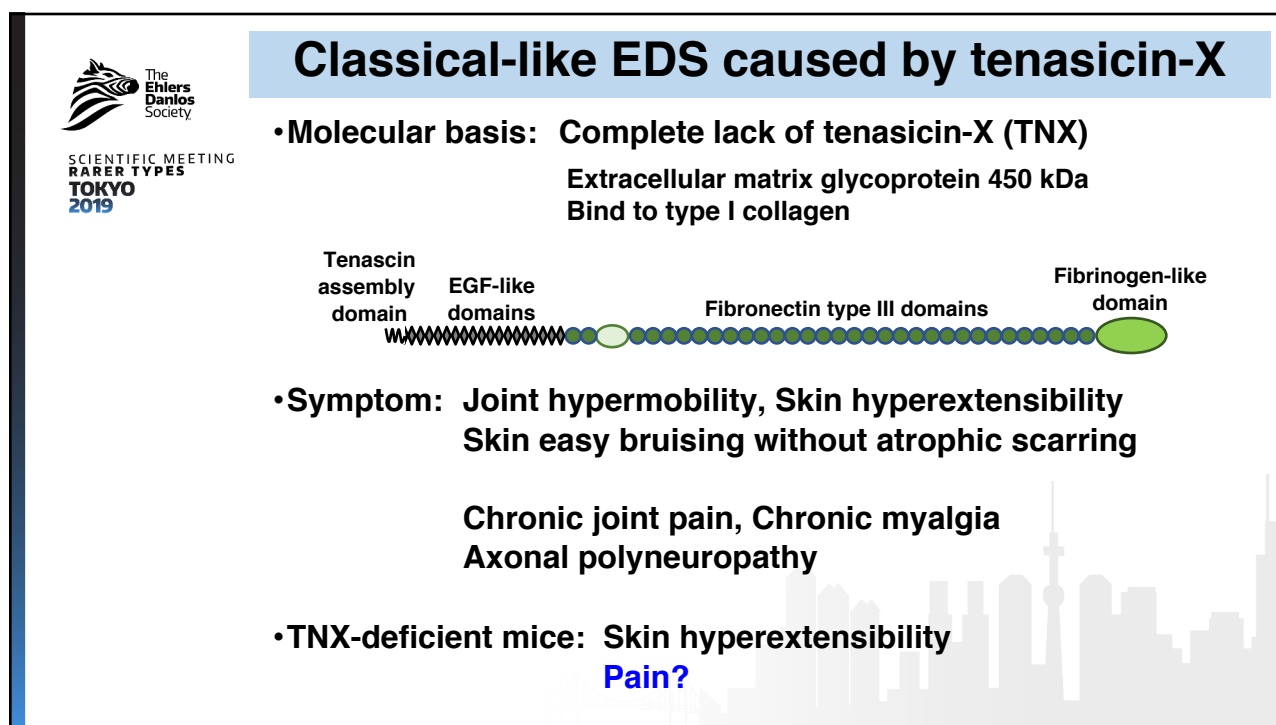
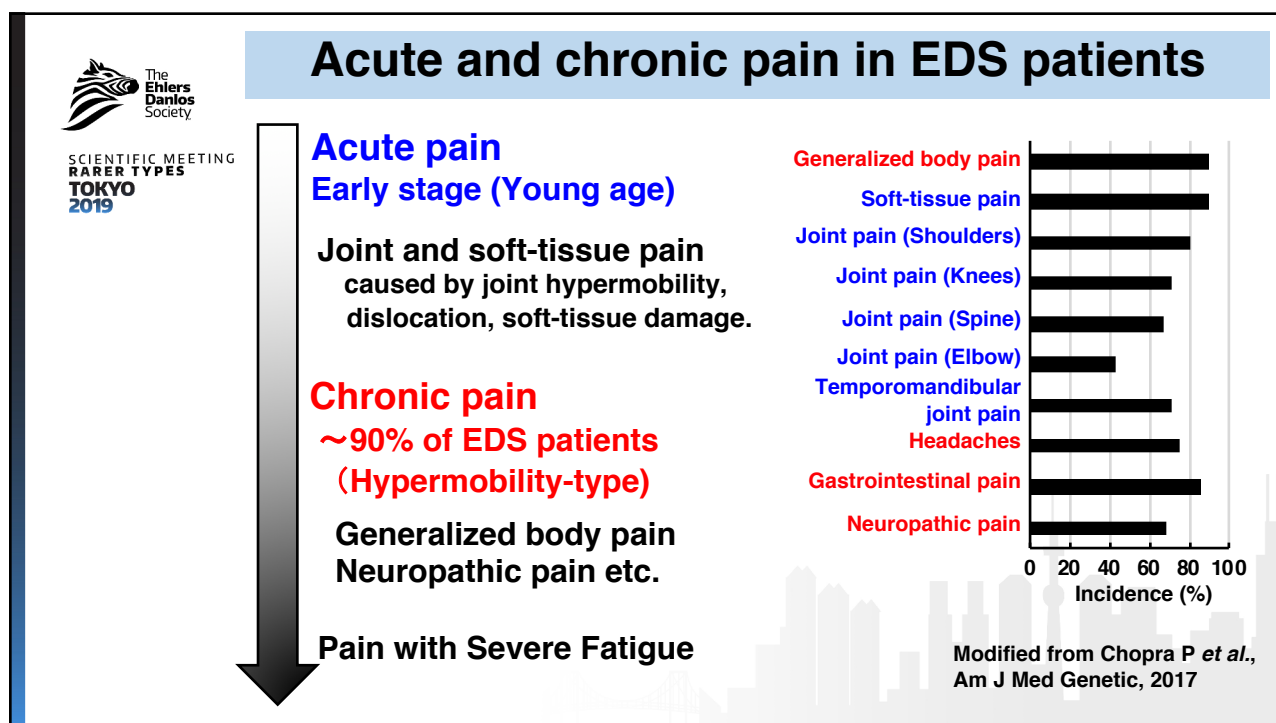
Acute and chronic pain in EDS patients

Acute pain Early stage (Young age)

Joint and soft-tissue pain
caused by joint hypermobility,
dislocation, soft-tissue damage.



Modified from Chopra P *et al.*,
Am J Med Genetic, 2017





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Mechanical allodynia in tenascin-X-deficient mice associated with the Ehlers-Danlos syndrome

1. Pain behaviors in $TNX^{-/-}$ mice

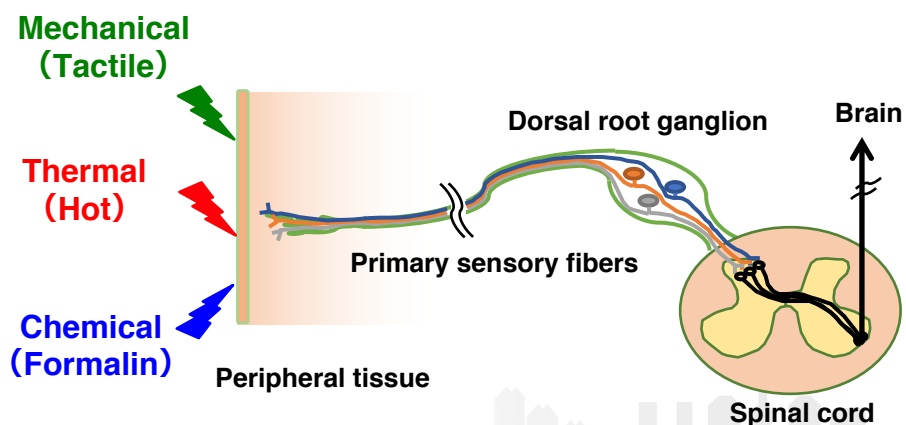
2. Mechanisms of pain in $TNX^{-/-}$ mice

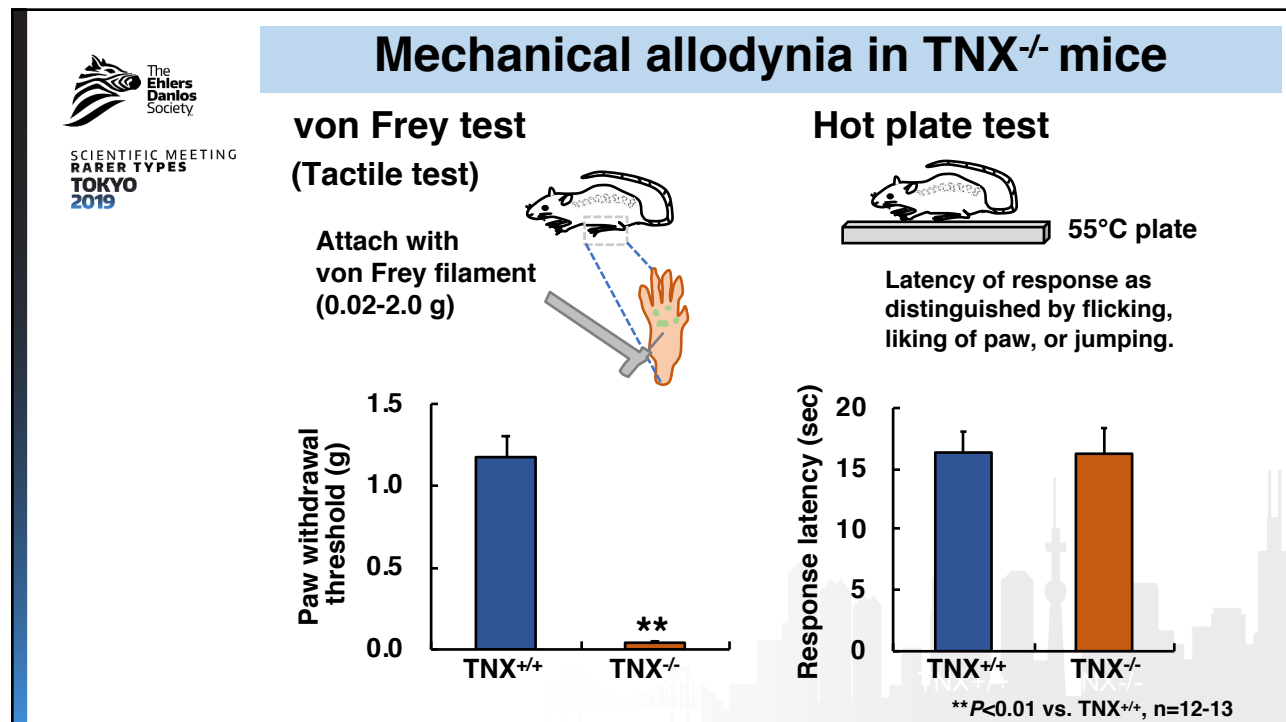
- Primary sensory fibers
- Central sensitization



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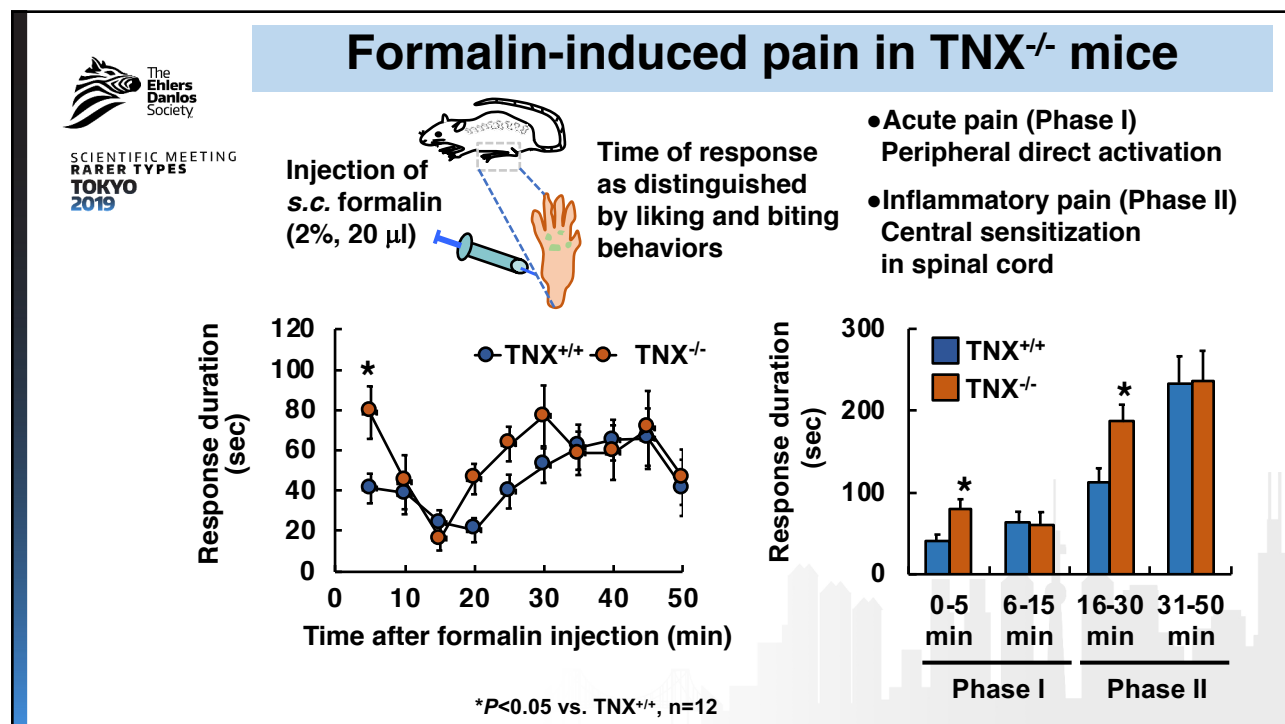
Analysis of pain behaviors in $TNX^{-/-}$ mice





1. Pain behaviors in TNX^{-/-} mice

- **Mechanical stimulus:**
High sensitivity to light-touch stimuli
→ Mechanical allodynia
- **Thermal stimulus:**
Normal response to heat stimuli



The Ehlers Danlos Society
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1. Pain behaviors in TNX^{-/-} mice

- **Mechanical stimulus:**
High sensitivity to light-touch stimuli
→ Mechanical allodynia
- **Thermal stimulus:**
Normal response to heat stimuli
- **Chemical stimulus:**
High pain sensitivity to formalin stimuli
→ Hyperalgesia
Aggravation of early inflammatory pain evoked by formalin



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1. Pain behaviors in TNX^{-/-} mice

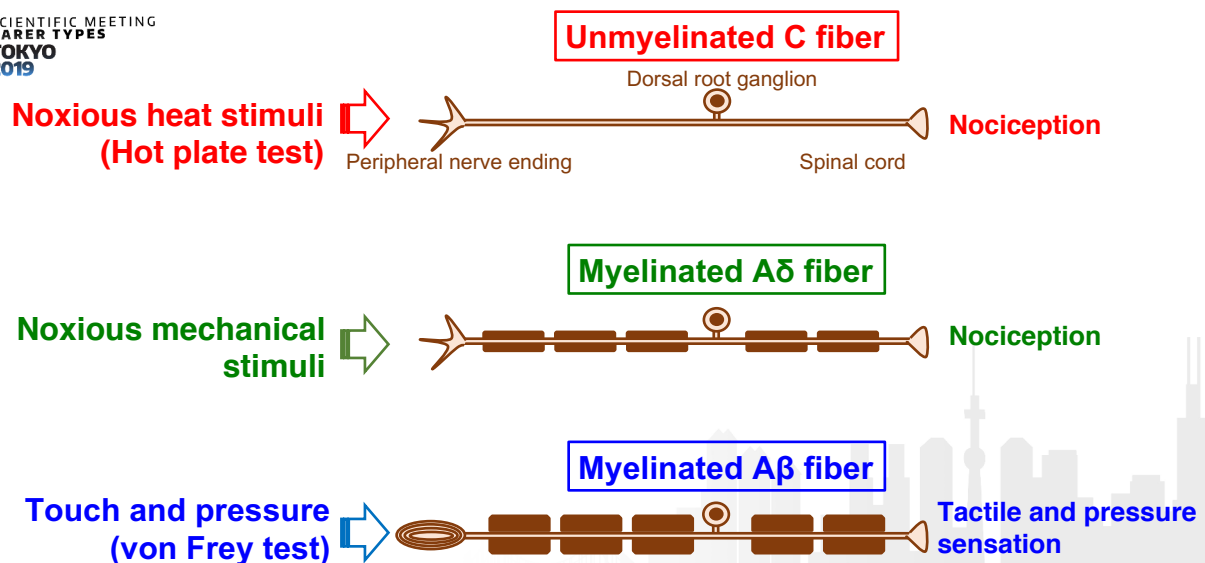
2. Mechanisms of pain in TNX^{-/-} mice

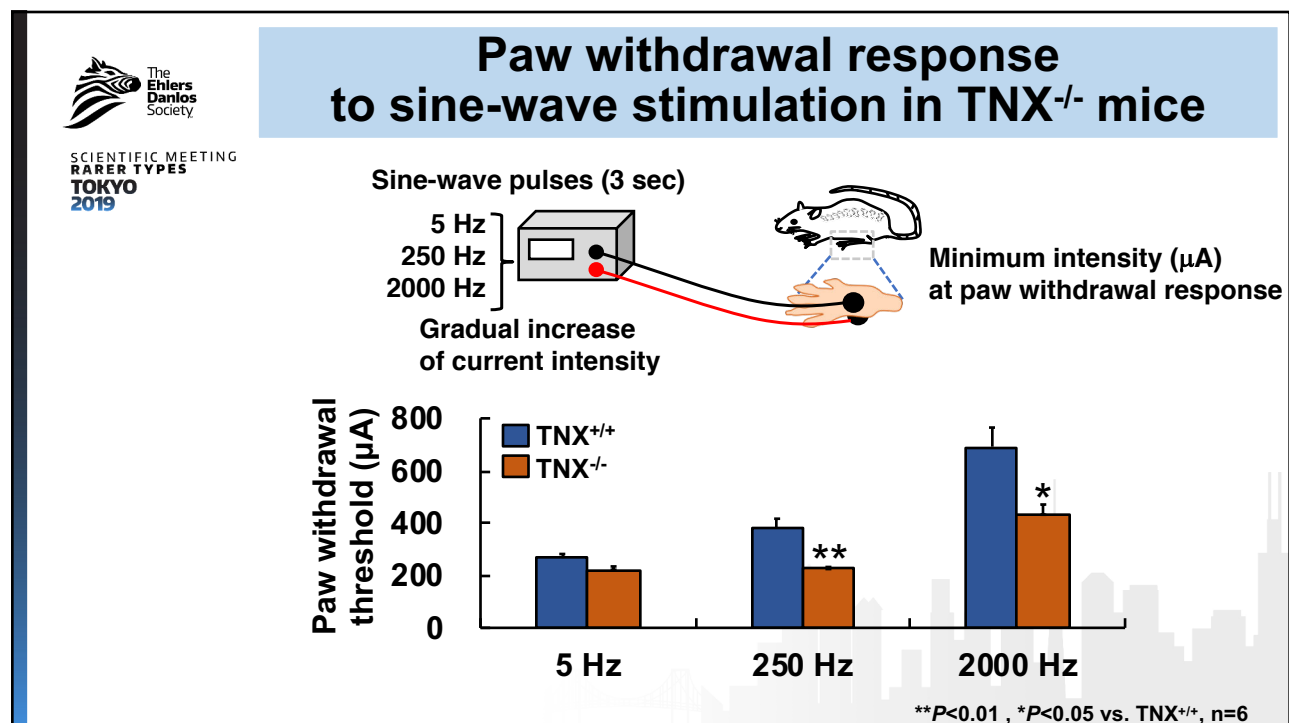
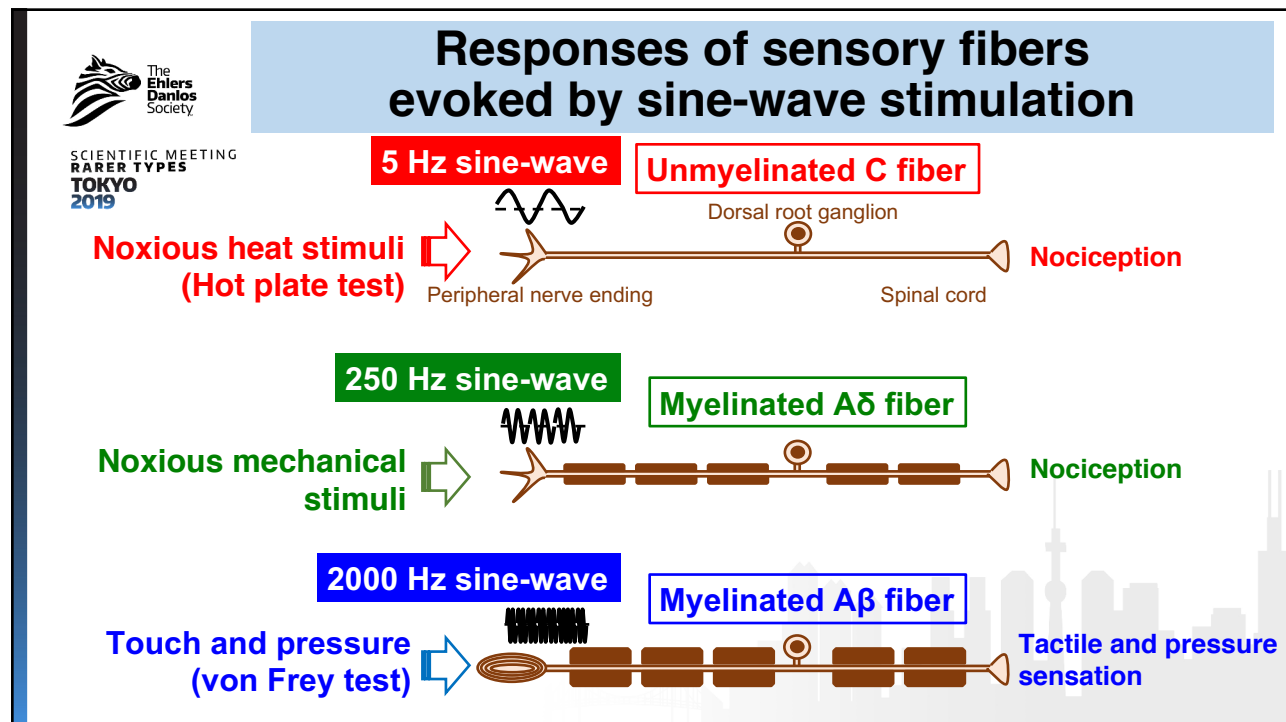
- Primary sensory fibers
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Responses of sensory fibers evoked by sine-wave stimulation







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2. Mechanisms of pain in TNX^{-/-} mice

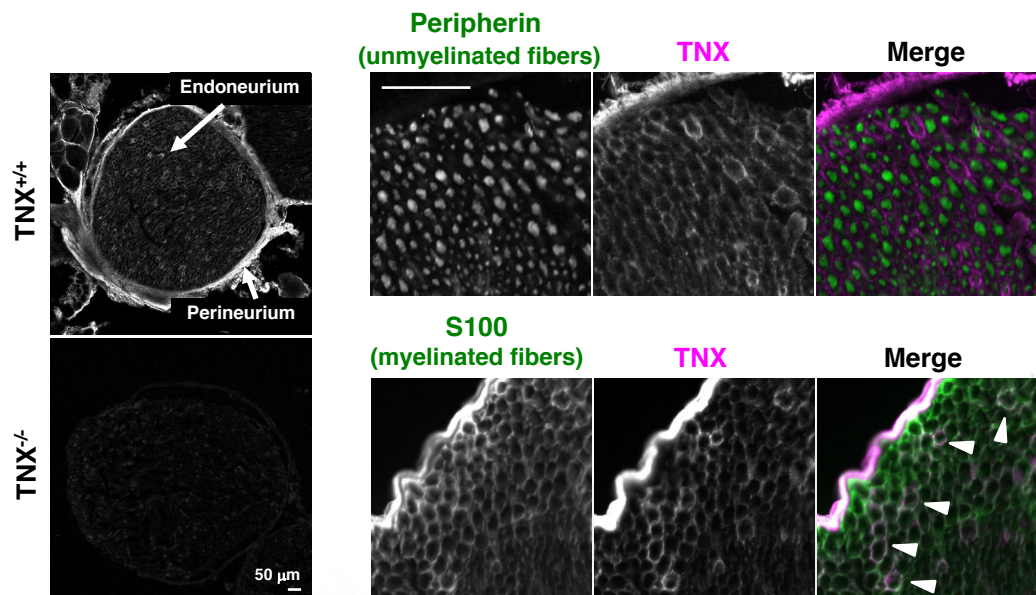
- **Primary sensory fibers:**

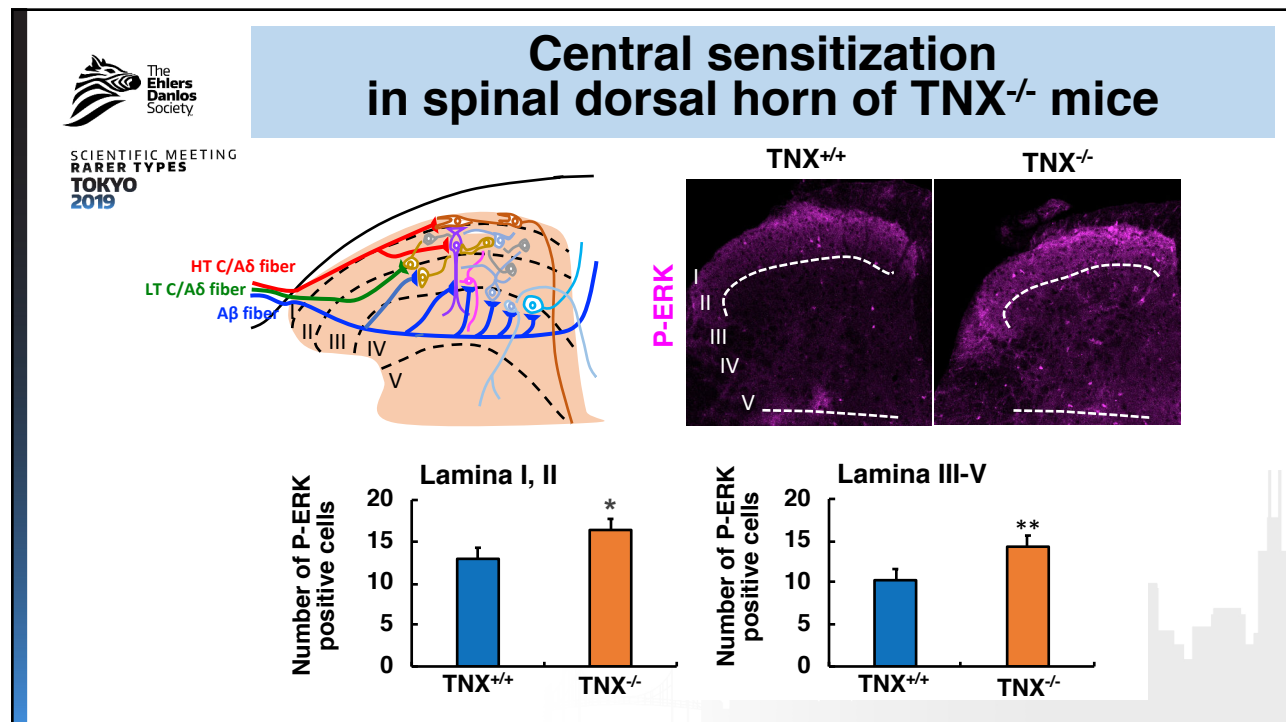
Hypersensitivity of myelinated A δ -fiber and A β -fiber, but not unmyelinated C-fiber



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Expression of TNX in myelinated fibers





2. Mechanisms of pain in TNX^{-/-} mice

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- **Primary sensory fibers:**
Hypersensitivity of myelinated Aδ-fiber and Aβ-fiber, but not unmyelinated C-fiber
- **Central sensitization :**
Increase of neuronal ERK activation in spinal dorsal horn



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Conclusions

1. **TNX deficiency induced mechanical allodynia, formalin-induced hyperalgesia, and aggravation of inflammatory pain.**
2. **TNX deficiency induced hypersensitization of myelinated A fibers and central sensitization of spinal cord.**

This work was supported by JSPS KAKENHI Grant number 17K09045.



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