What's New In The Lab 2?

Understanding the causes of MS symptoms

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Diverse Symptoms Typical Of MS

Partial blindness
Leg weakness
Numbness
Lost sense of balance and taste

} Relapse - Loss of function

Full recovery

Remission

Temperature-sensitive symptoms

Temperature

Tingling
Seeing dots / sparks of light with eyes shut

} Tingling

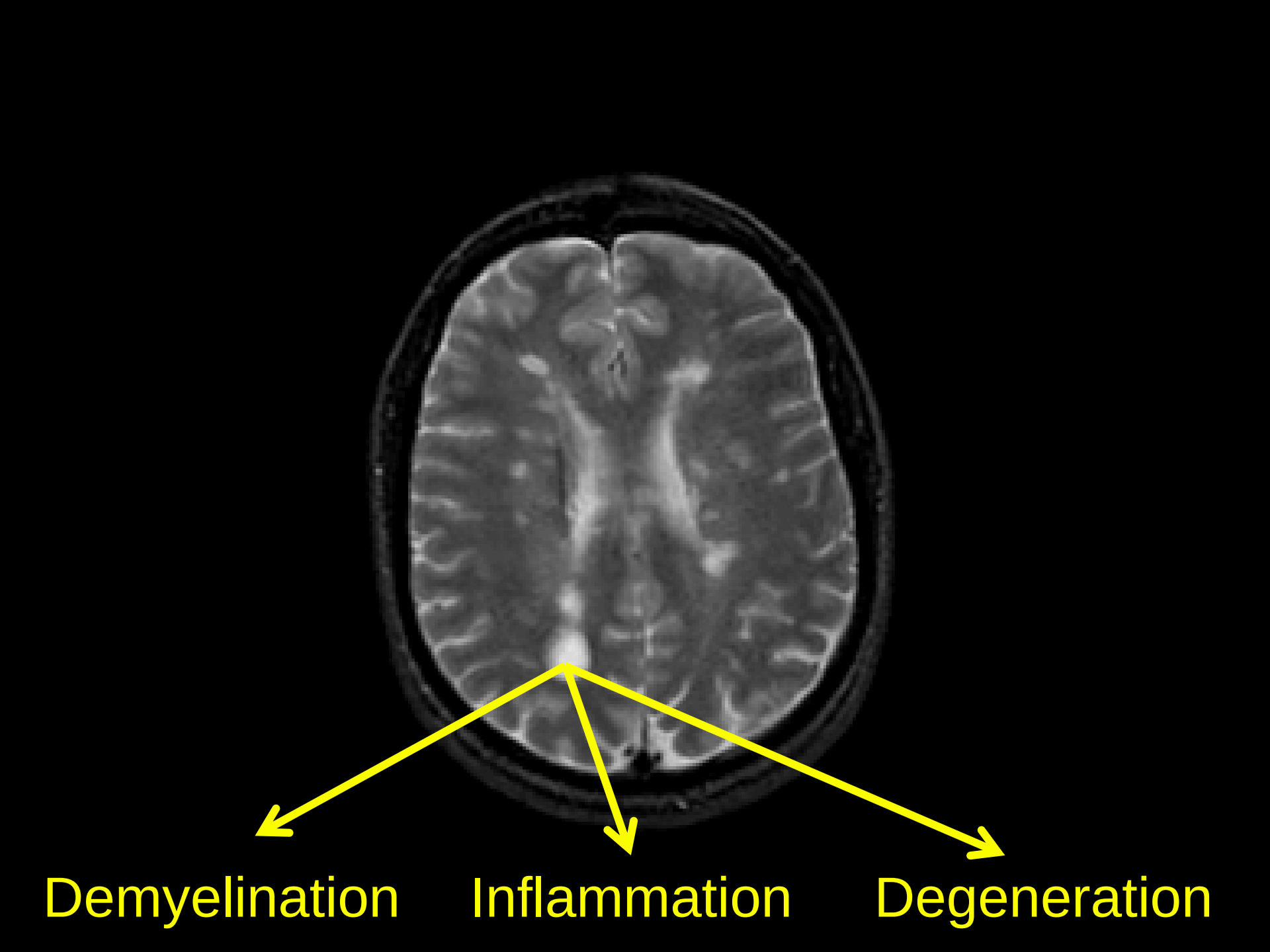
Flashes of light upon eye movement
Bending neck causes electric shock sensation

} Movement

Incomplete recovery after relapses

Progression

Diverse symptoms, different between people


Demyelination
Inflammation
Degeneration

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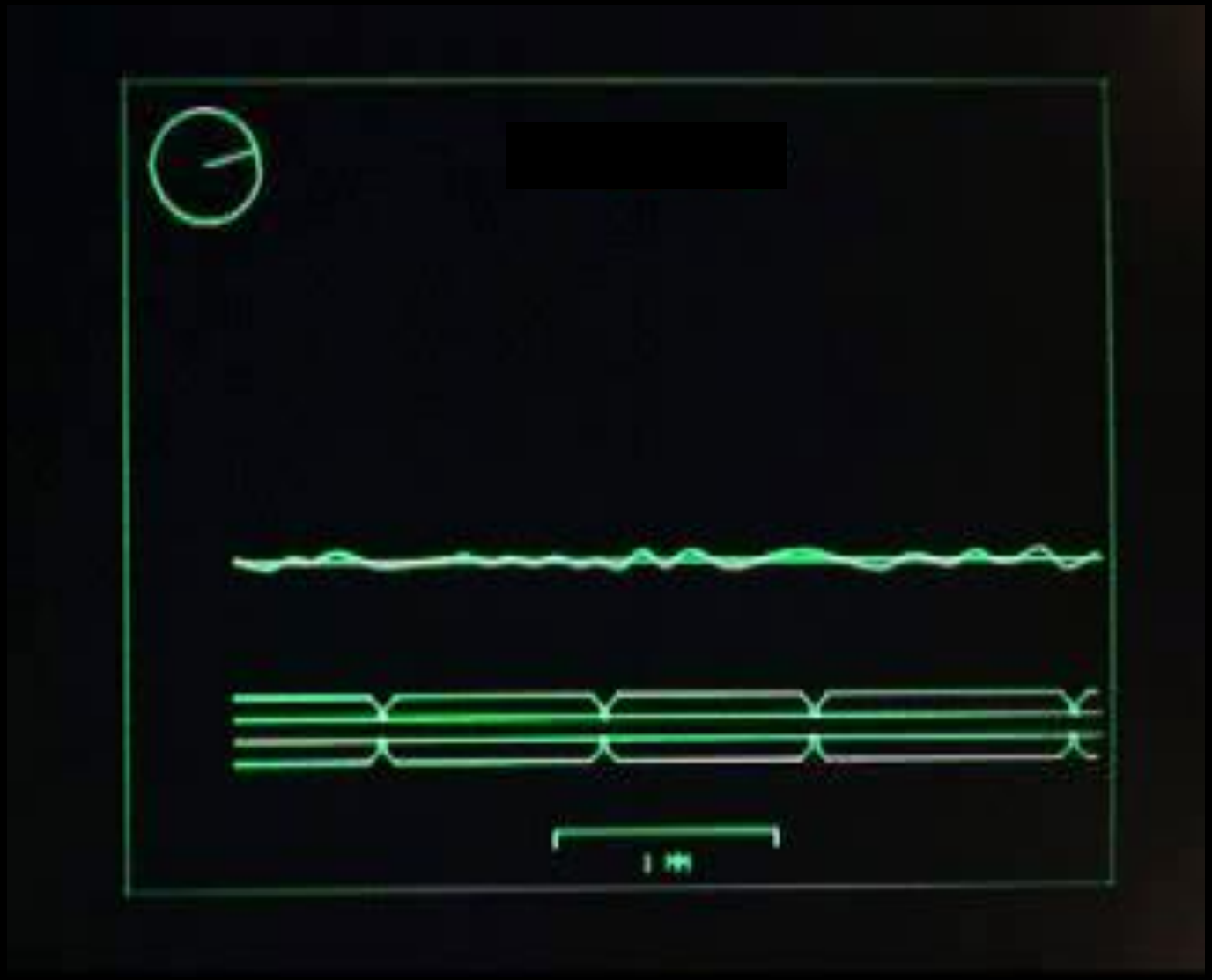
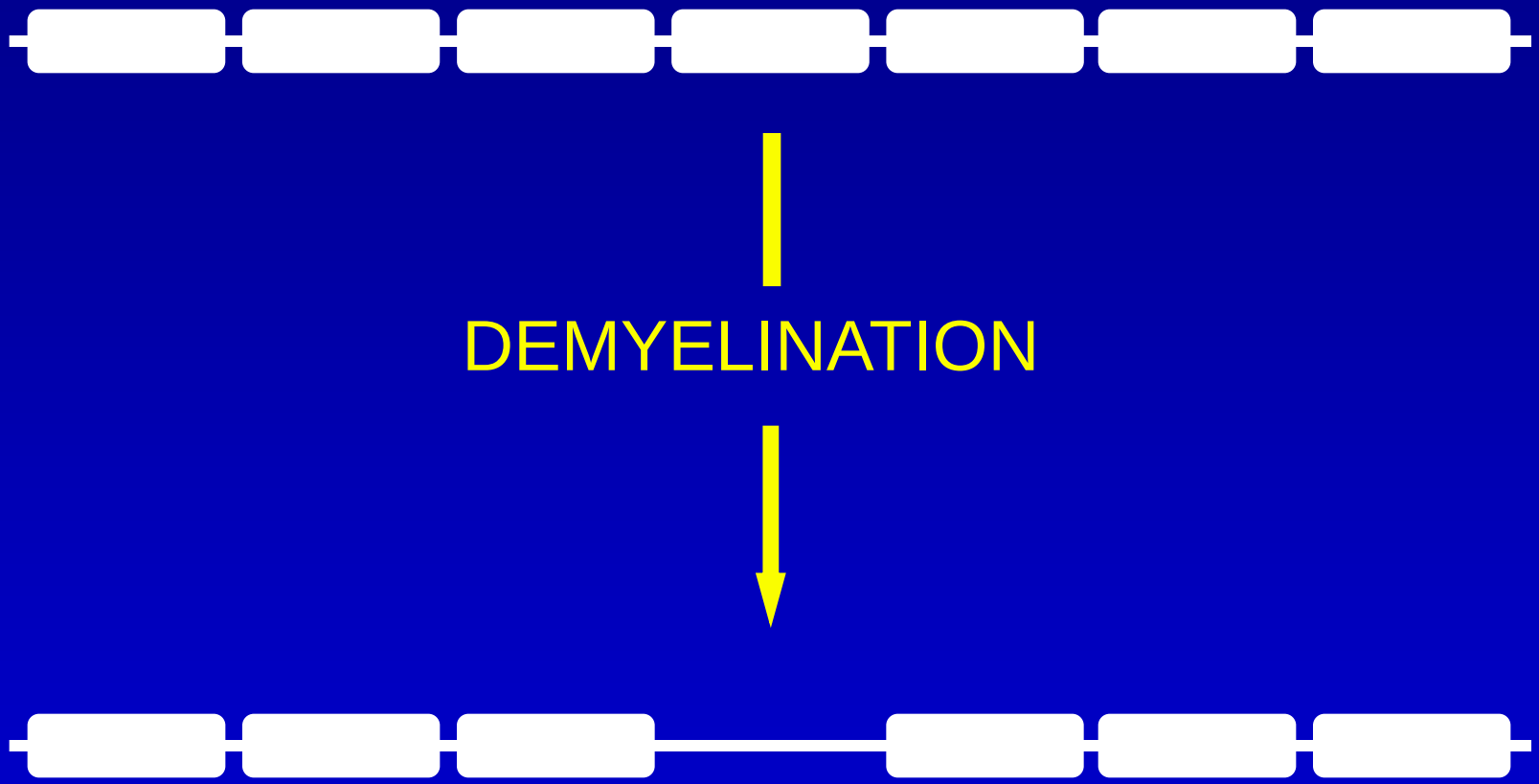
Loss of Function

1) Conduction block due to demyelination

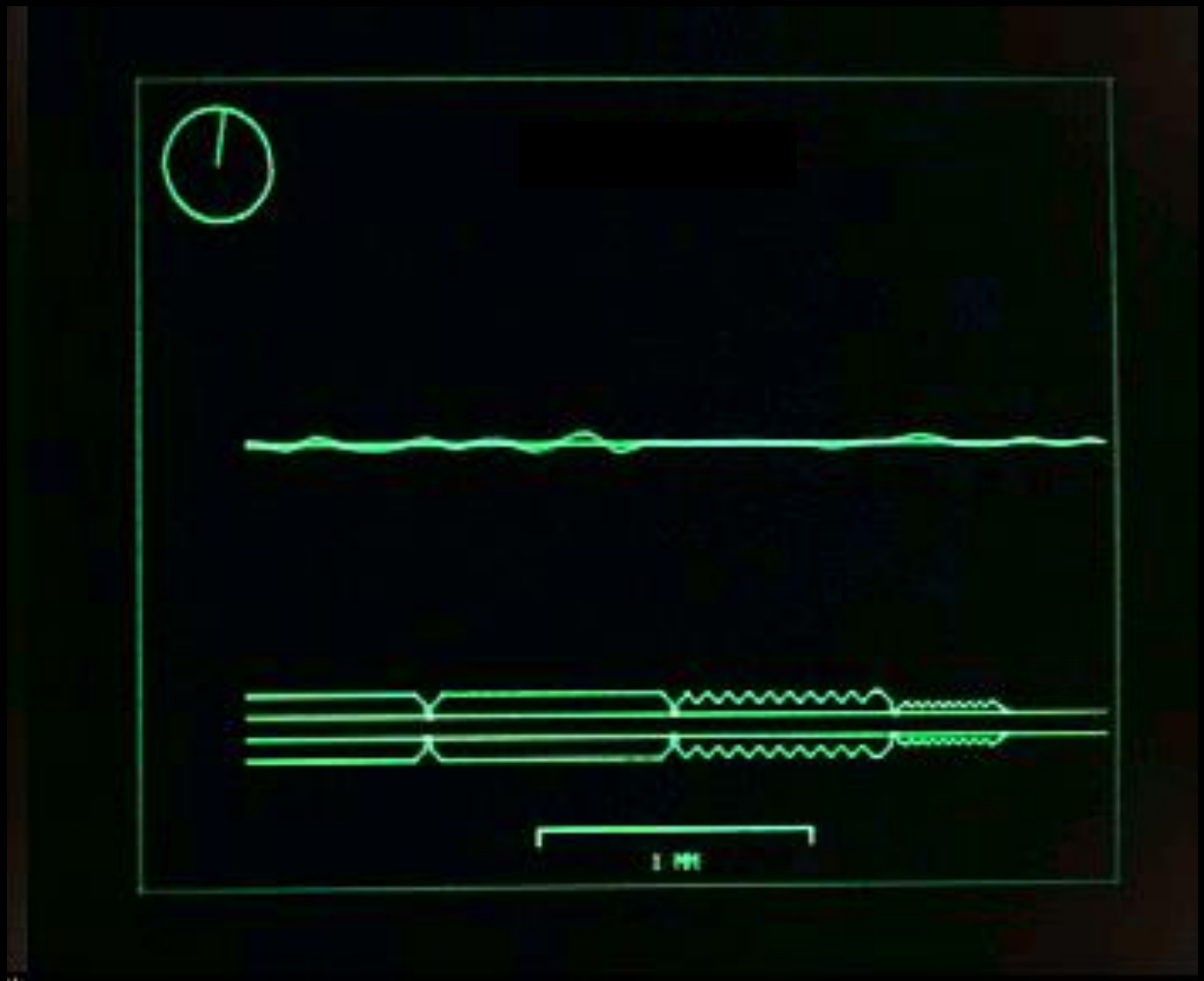
First, what do normal nerve fibres look like, and how do they conduct?

Normal Conduction




DEMYELINATION

Conduction Block Due To Demyelination



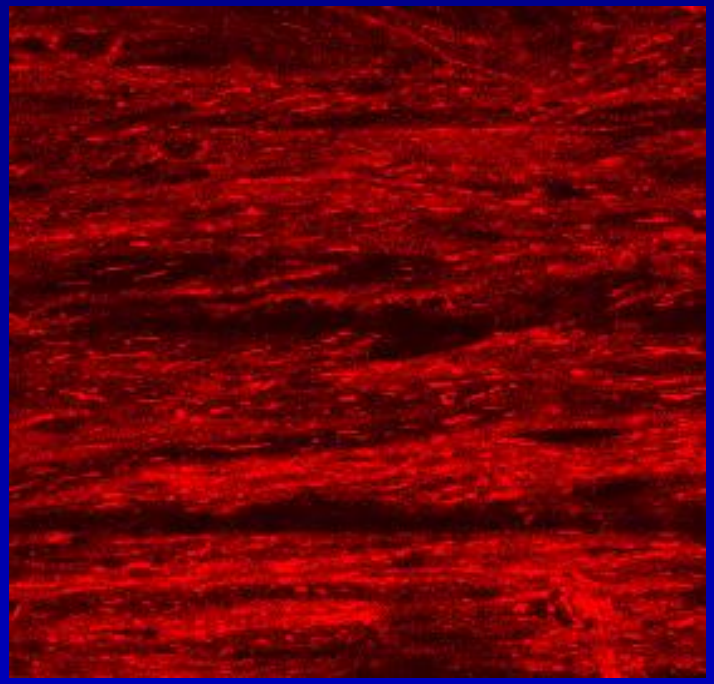
Loss of Function

1) Conduction block due to demyelination

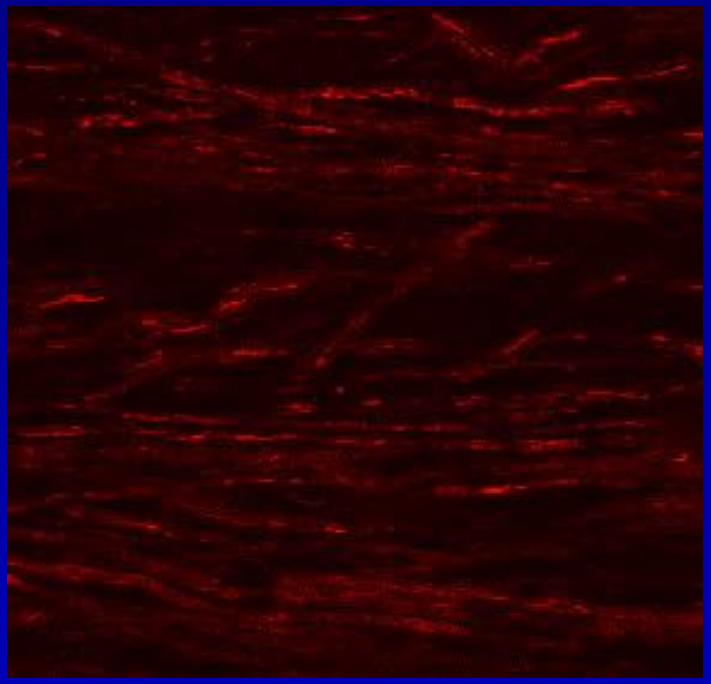
2) Conduction block due to inflammation

Mitochondria: tiny factories in cells that turn glucose from our food into energy

Examining mitochondrial function



Healthy (red) mitochondria in the normal CNS



Non-functioning mitochondria in the inflamed CNS

Only healthy mitochondria can turn glucose into energy to support impulse conduction. It is not clear why the mitochondria fail. Perhaps not enough oxygen, perhaps too much of a toxin.

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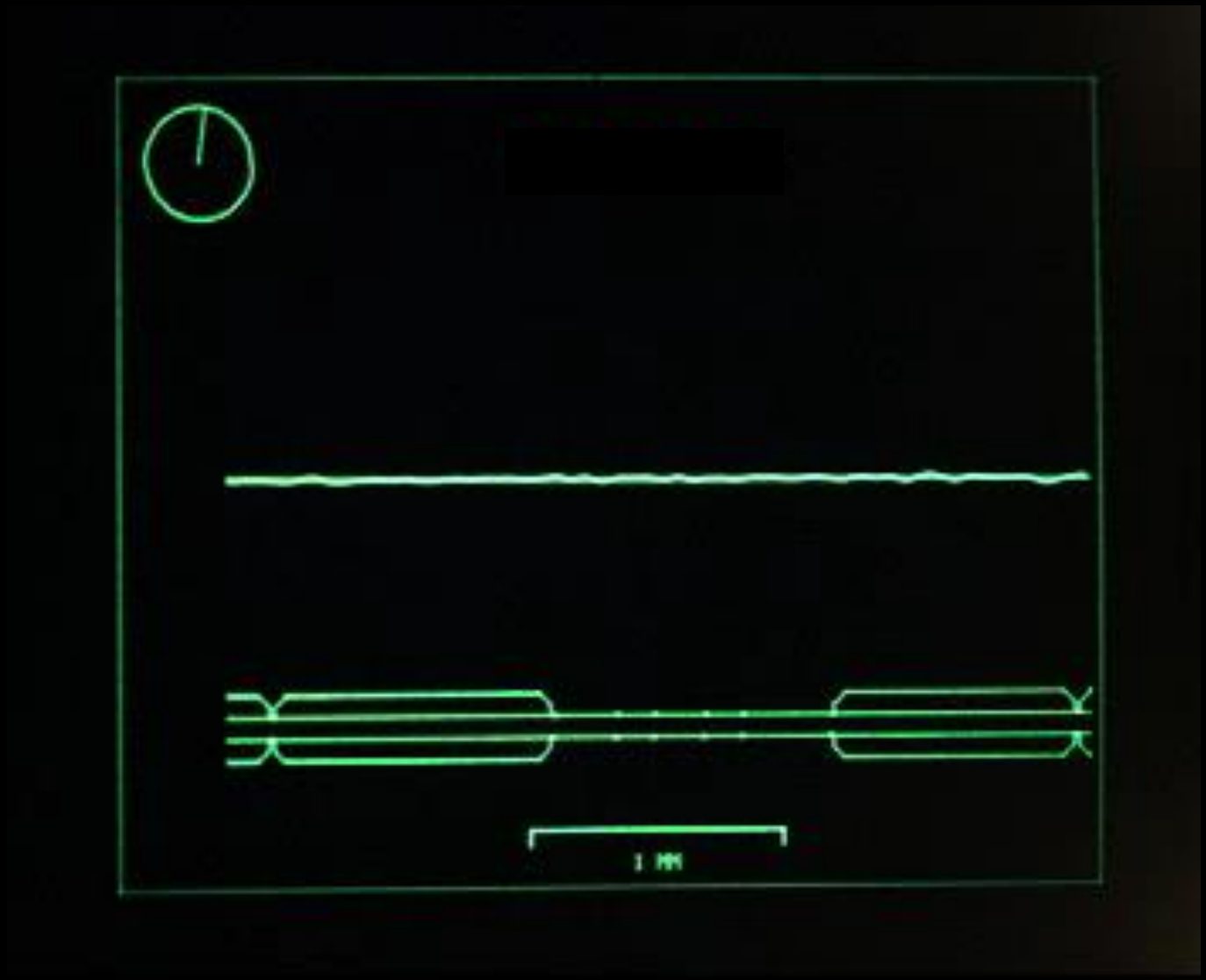
Recovery

1) Restoration of conduction to demyelinated fibres

Restored Conduction

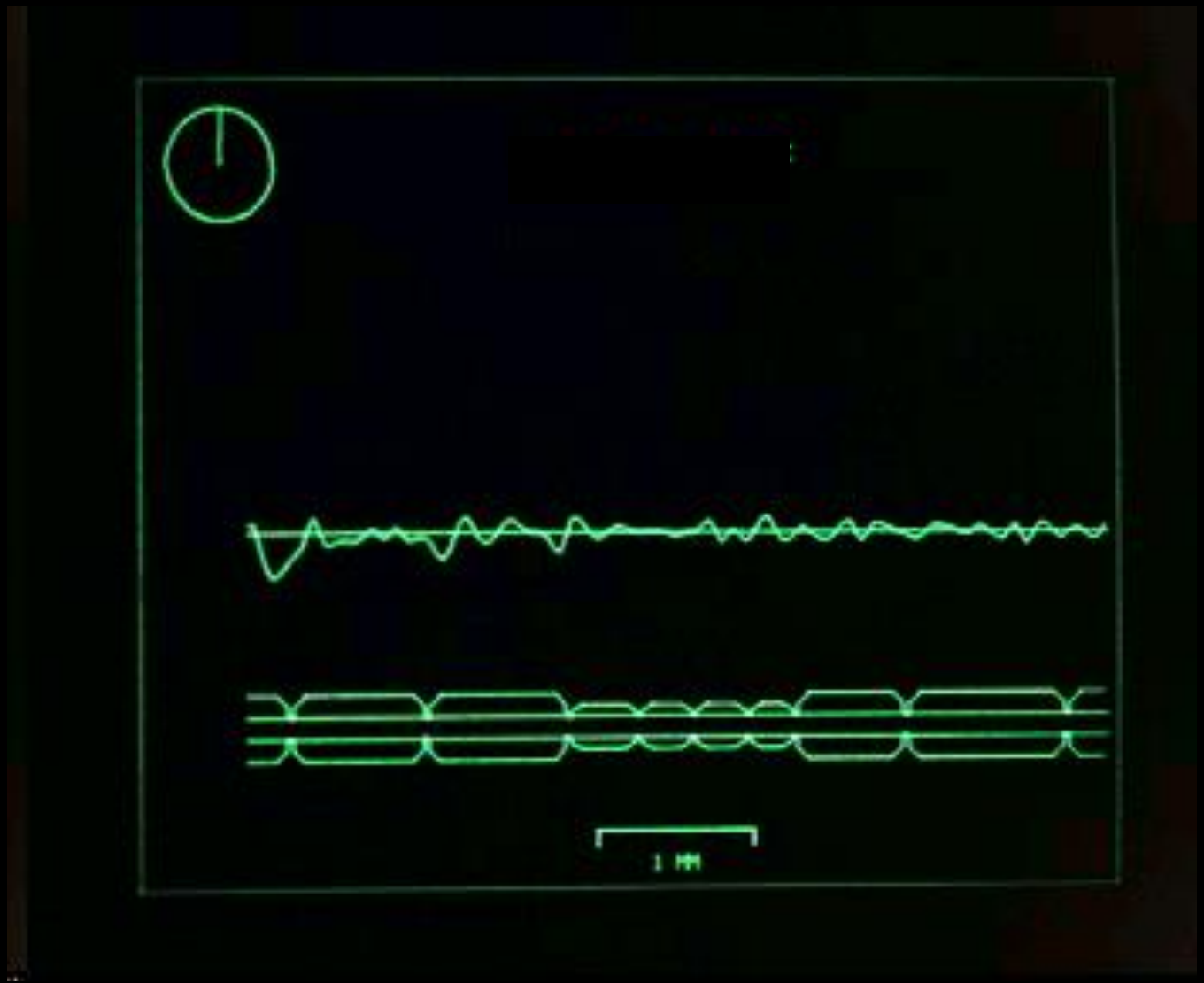


Recovery

1) Restoration of conduction to demyelinated fibres

2) Restoration of conduction by repair – remyelination

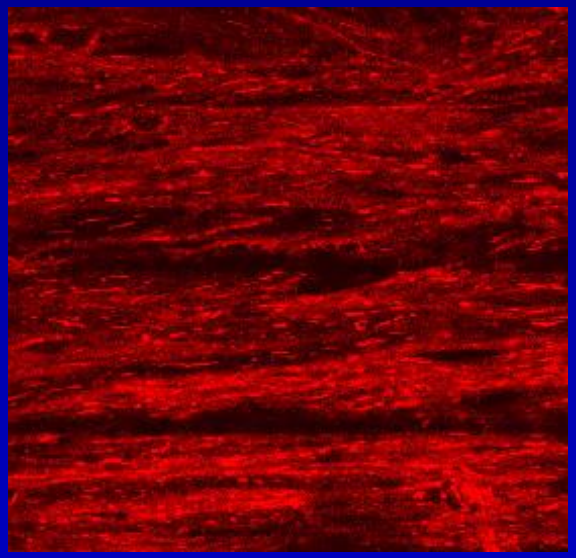
Conduction Restored By Remyelination



Recovery

1) Restoration of conduction to demyelinated fibres
2) Restoration of conduction by repair – remyelination
3) Recovery from inflammation

Imaging mitochondrial function



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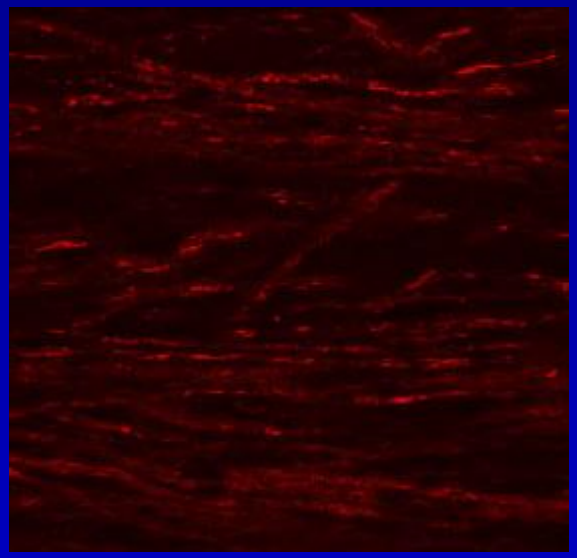

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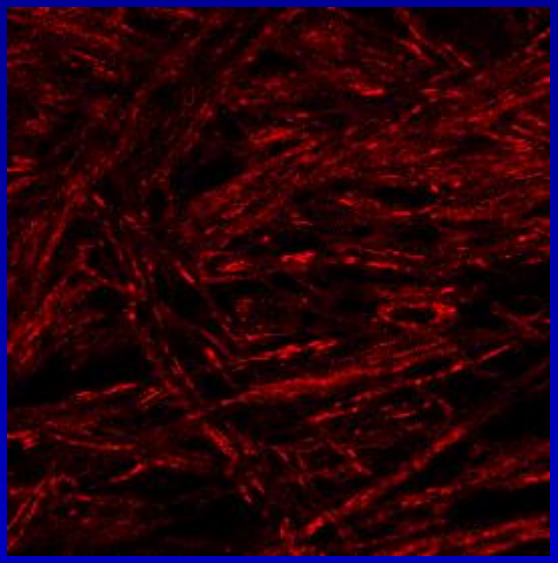
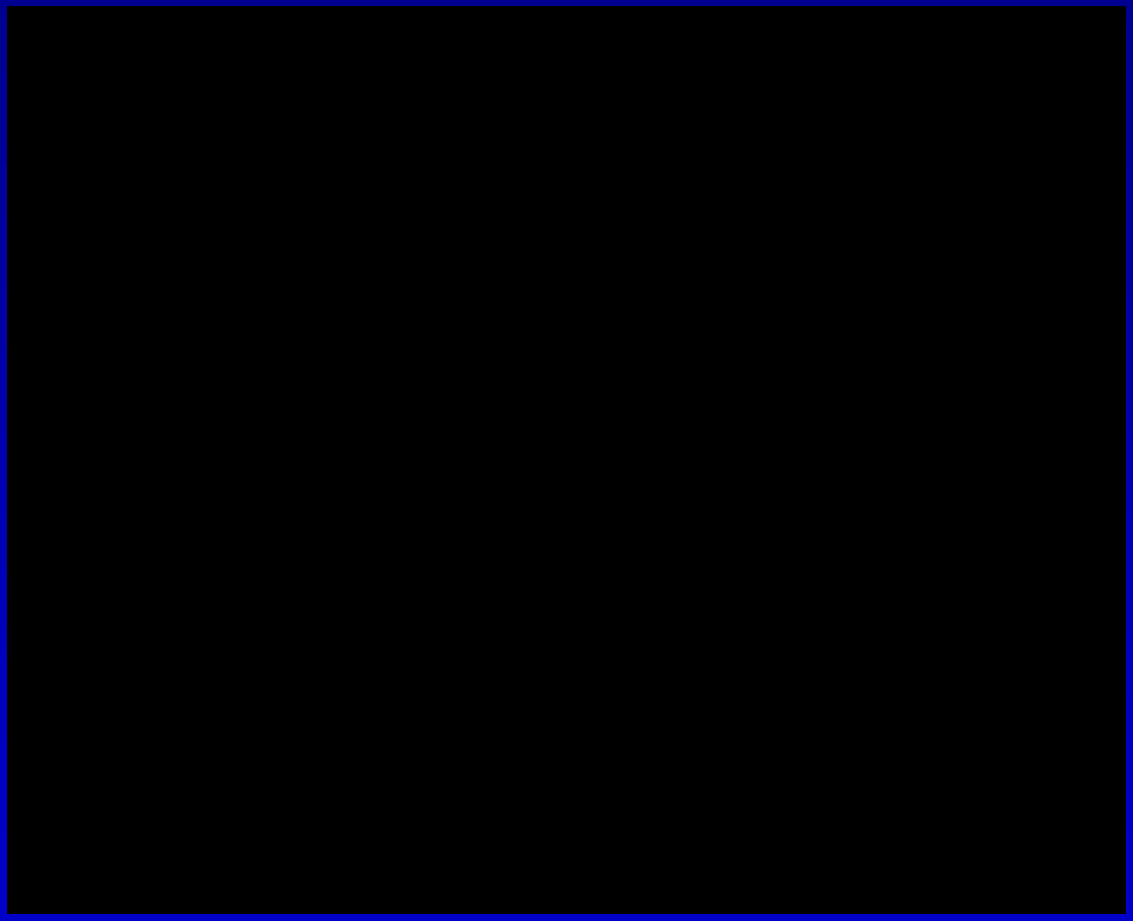


Partial recovery of mitochondria during remission

Recovery

1) Restoration of conduction to demyelinated fibres
2) Restoration of conduction by repair – remyelination
3) Recovery from inflammation
4) Rewiring – “plasticity”

Recovery By Plasticity



In MS, more brain effort is required to achieve tasks

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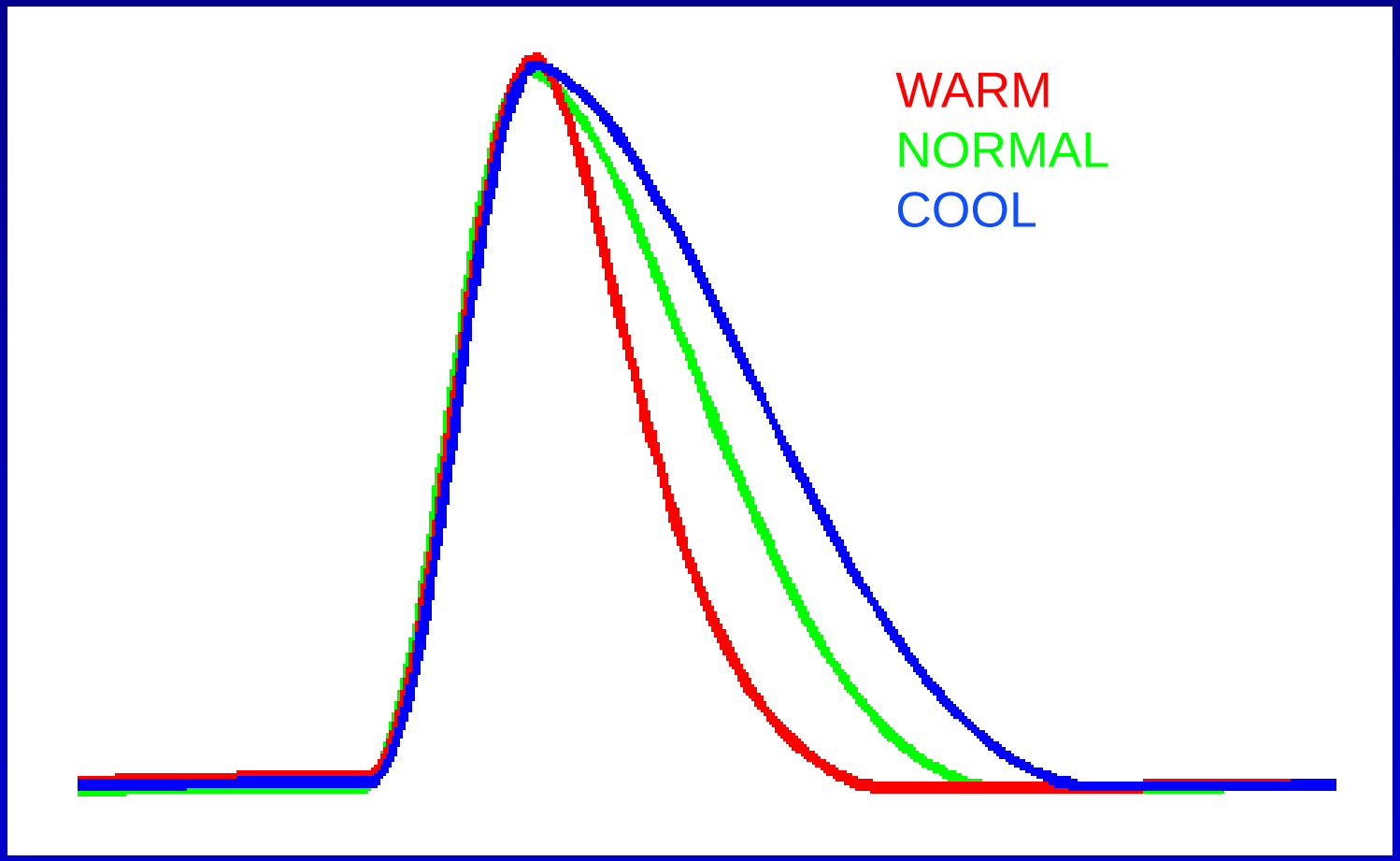
Diverse symptoms, different between different people

Body Cooling Prolongs & ‘Strengthens’ Nerve Impulses



Longer nerve impulses are more capable of exciting the demyelinated regions

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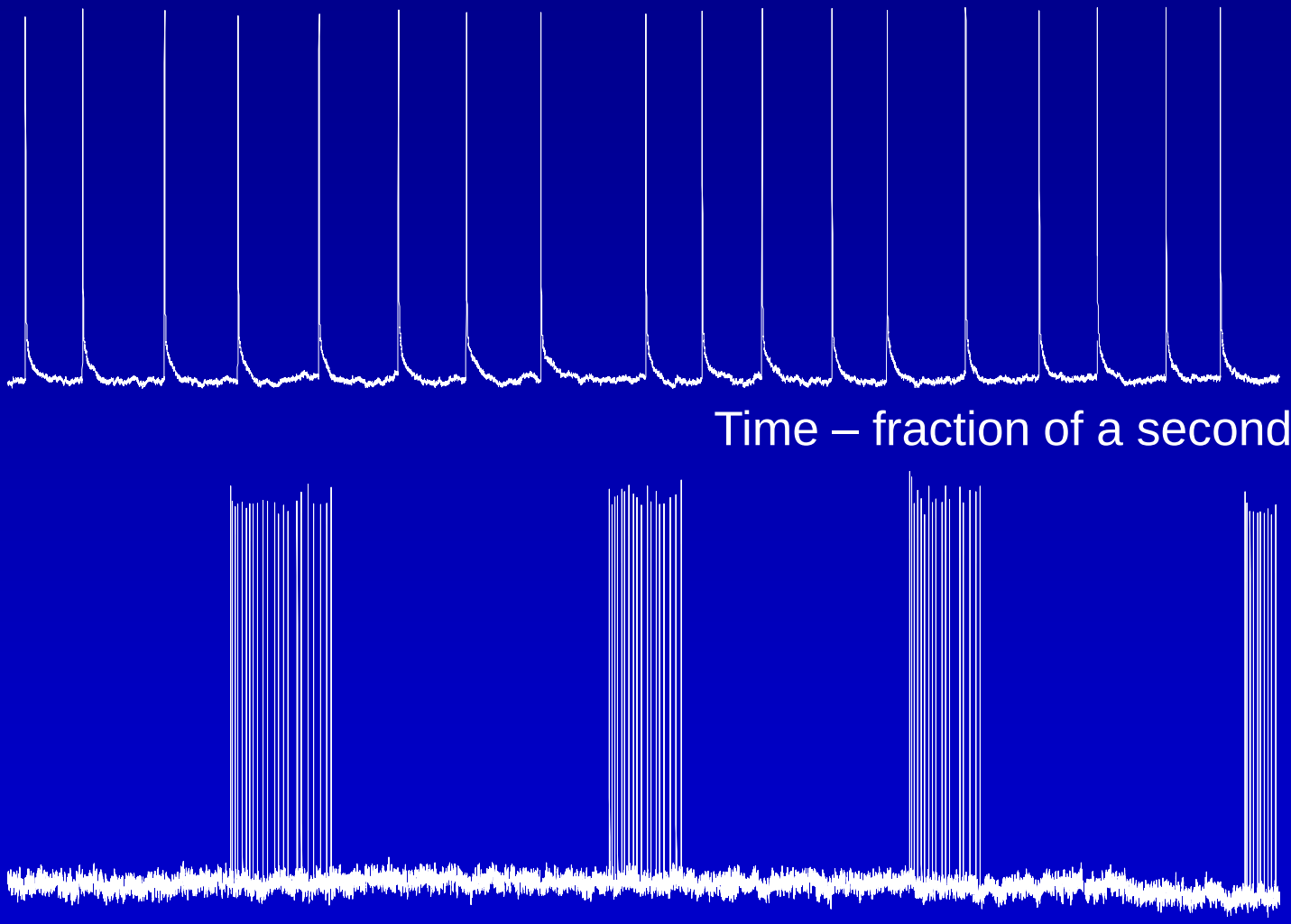
Tingling: Generation Of Meaningless Impulses



Time – fraction of a second

Up to 50 meaningless impulses generated every second by some demyelinated nerve fibres

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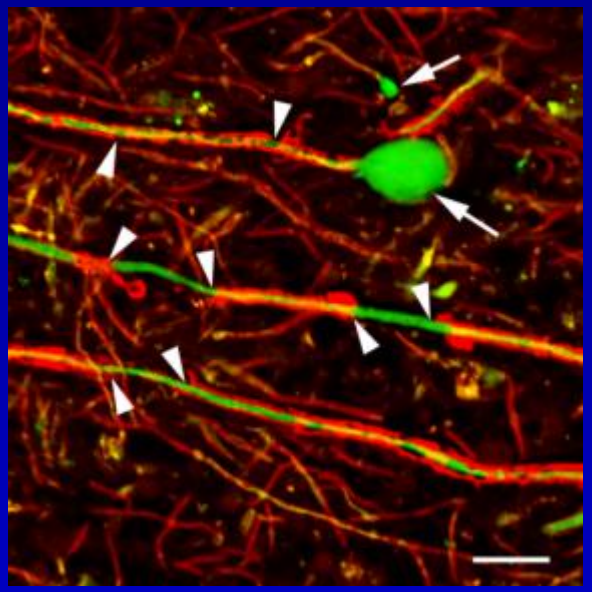
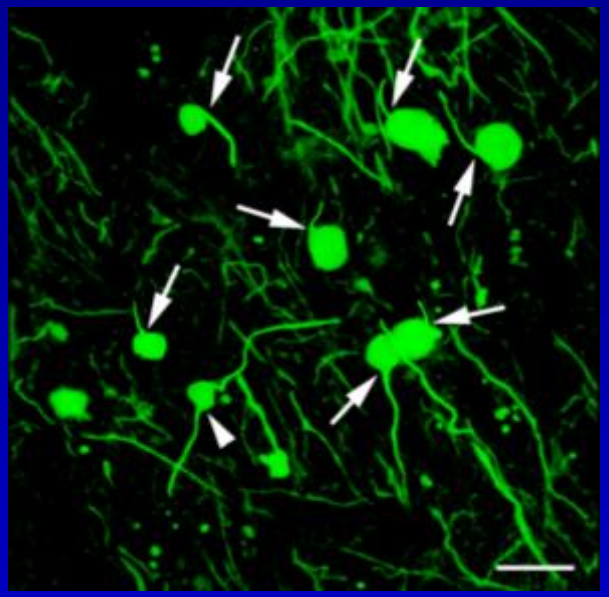
Degeneration Of Nerve Fibres: a major cause of permanent symptoms





Axons are cut within lesions. The number damaged is related to the intensity of the inflammation

Degeneration Of Nerve Fibres: a major cause of permanent symptoms

Understanding why nerve fibres degenerate, and how to protect them, are the most important current goals in MS research.

Promising lines of research:

- Possibility that degeneration is due to an energy deficit resulting from mitochondrial damage.
- Use of sodium channel blocking drugs for neuroprotection - several on-going clinical trials.
- One to watch - a role for oxygen.