

# EXPLORING PNS IN FABRY DISEASE

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# FD:

- X linked
- 1/1 000 000
- alpha galactosidase A deficit
- lysosomal accumulation of GL3
- 7 genes, 670 mutations, polymorphism
- classical phenotype in male (early or late)
- variable phenotype in female (X inactivation)



# FD:

- angiokeratoma and reddish-purple skin lesions
- cornea verticillata
- length-dependent (small fiber) peripheral neuropathy
- hypo/hyperhidrosis, GI disturbances, deafness and vertigo
- nephropathy
- cardiopathy
- (cerebro)vasculopathy

# SFN DD:

- Diabetes Mellitus
- Systemic or hereditary Amyloidosis
- OH
- Gougerot-Sjögren, Lupus, Sarkoidose
- HIV, CVH
- Paraneoplastic
- Friedreich, Tangier



# PUBMED:

- Small Fiber Neuropathy & Fabry disease: 29 from 1982 !

# CONTROVERSIES:

- fiber (MF, UF)
- topography (DRG, AGC, nerve, sensorial organ, endo/exocrine)
- ANS
- vasa nervorum
- diagnosis & follow-up
- ERT efficacy



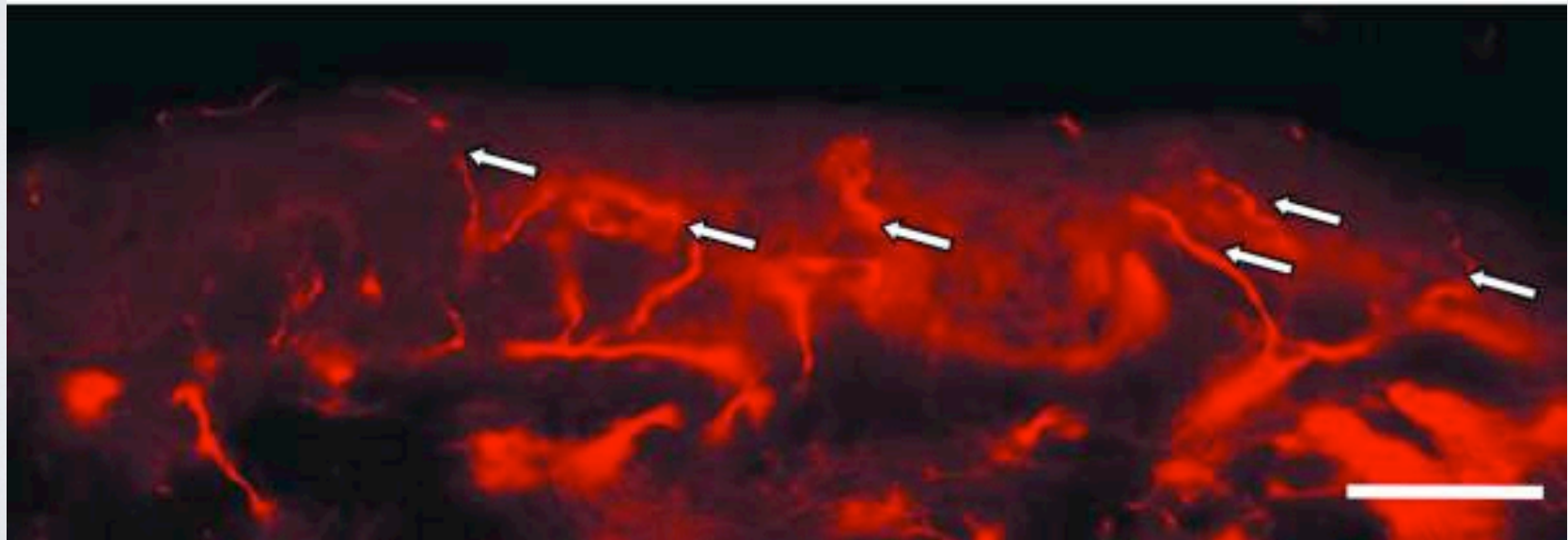
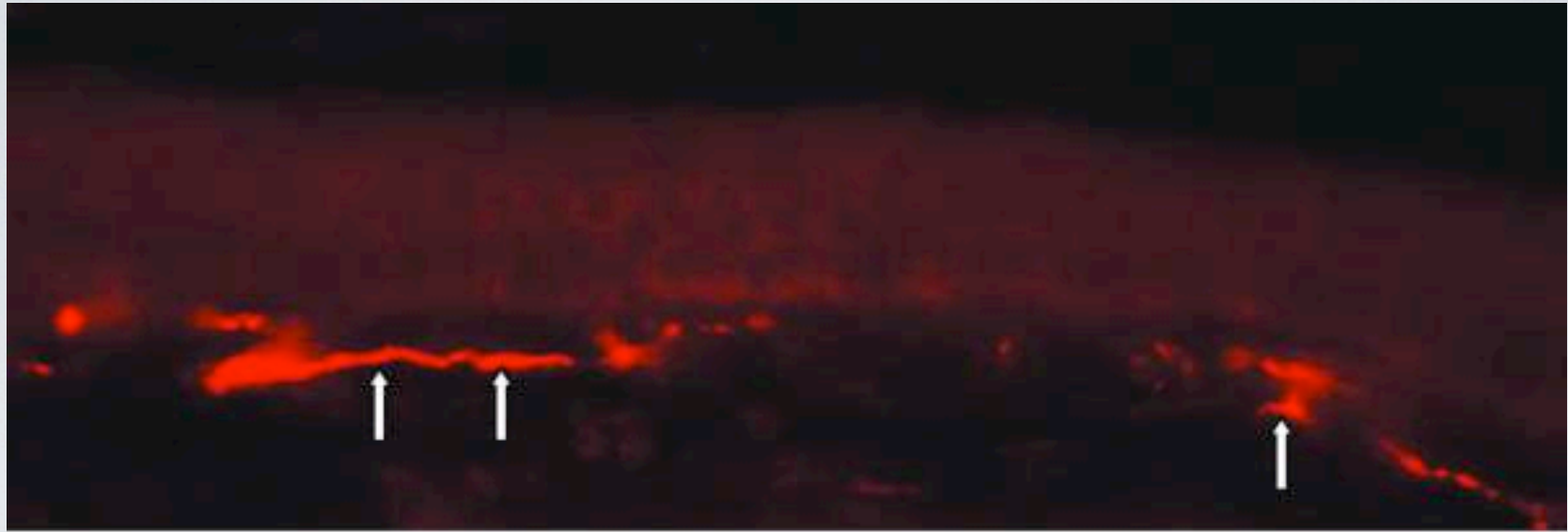
# WHY ?

- first symptom is neuropathic pain (Fabry crisis and chronic burning & tingling pain)
- childhood in male (9y for 60 to 80 %), adolescent in female (16y for 40 to 60 %)
- most impact in QOL and depression prognosis
- mostly irreversible
- efficacy of treatment (complains, IENFD if no renal involvement)

# HOW ?

- QST (cold/warm, pain, vibration treshold) (...)
  - NCV (carpal tunnel syndrome in 27%)
  - SCR
  - R-R
  - Tilt-Test
- Need for more investigation (...)
- LEP (IENFD correlation, Camdessanché 2011)
  - Skin biopsy (Intra Epithelial Nerve Density Fiber; fibers/mm)
  - Nerve biopsy («Gold Standard» ?)

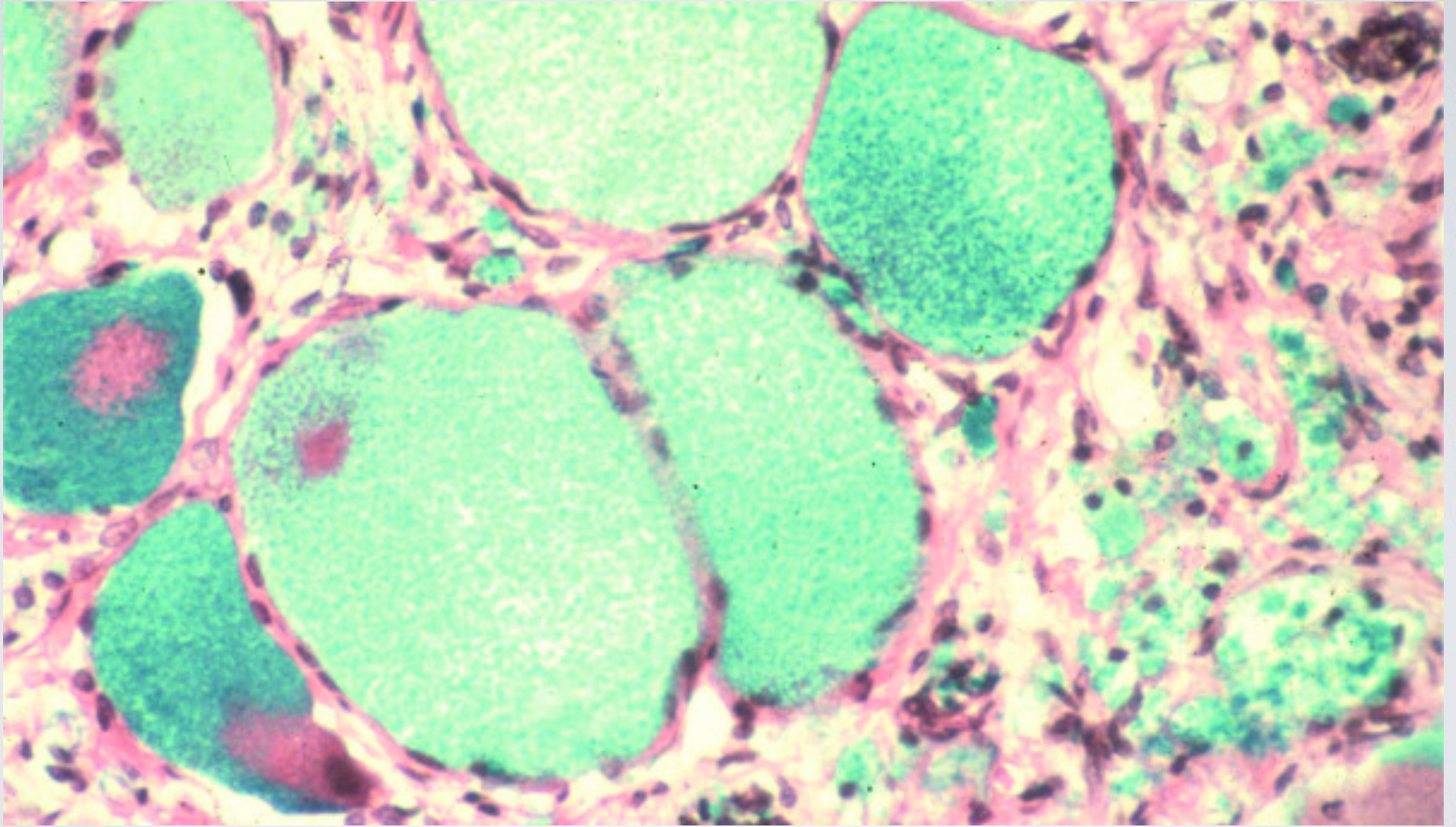




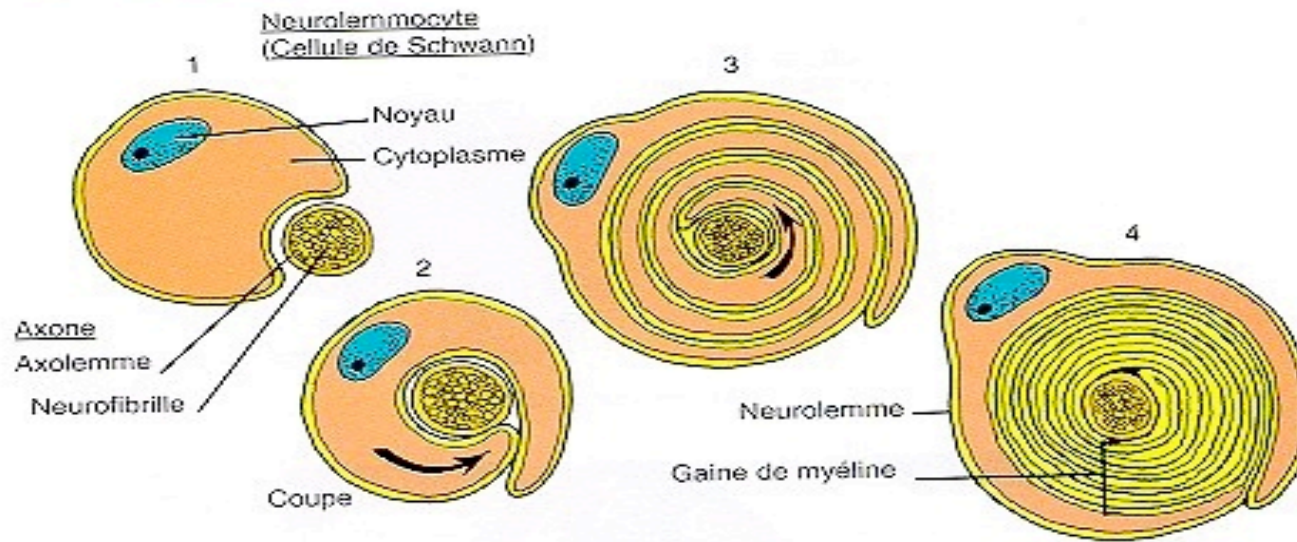
# GL:

- Neuronal (spinal ganglion)
- Schwann cell
- Perineurial and Endoneurial cells
- Sensory Receptors
- Vasa Nervorum (endothelial cell)
- Smooth muscle cell
- Sudoripar Glands









a) Étapes de formation d'une gaine de myéline

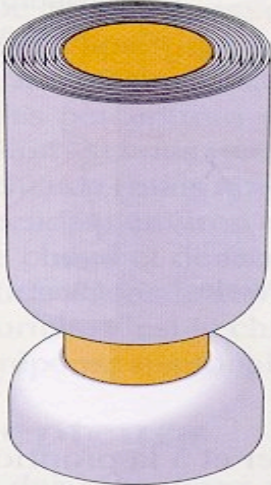





b) Micrographie électronique d'une coupe d'axone myélinisé



# FACTS:

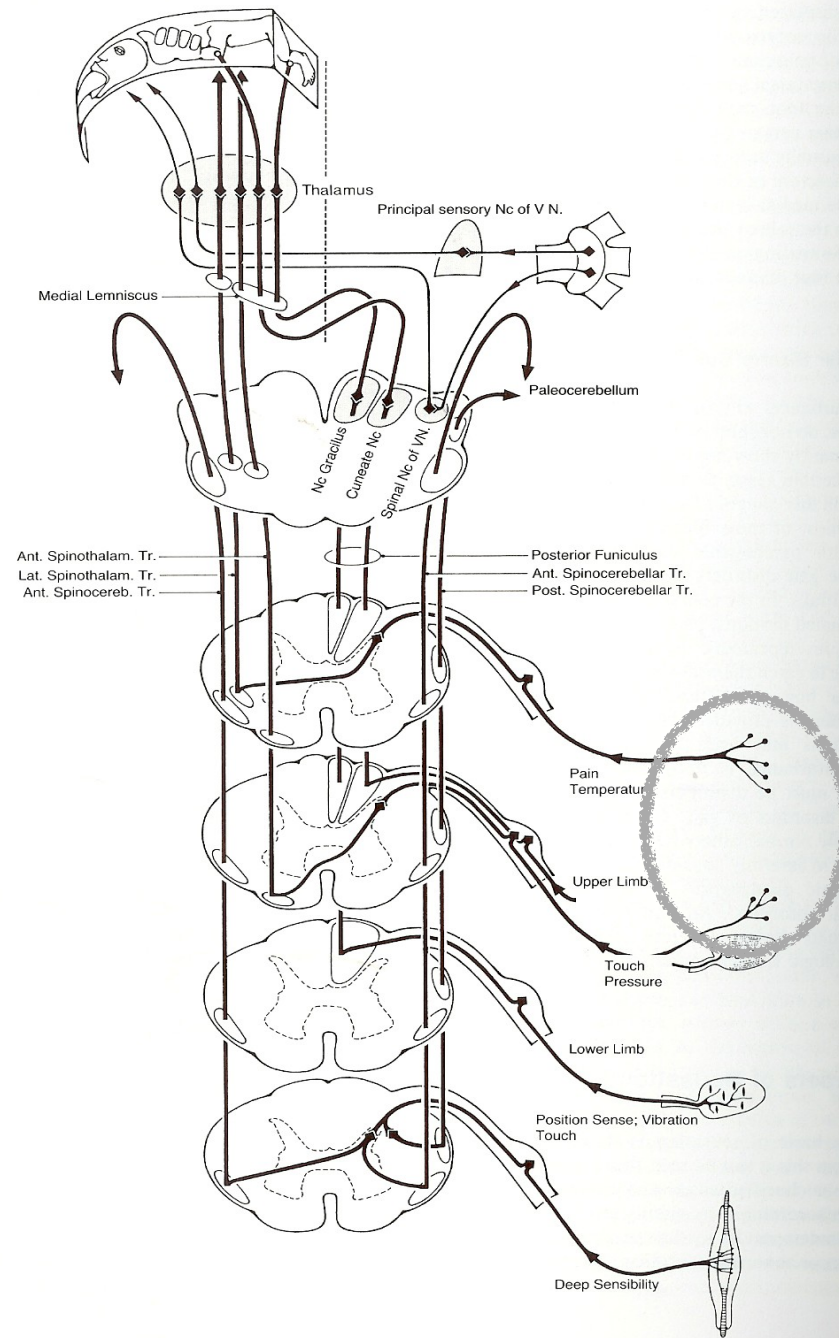
- Cold treshold
- A-delta  $\gg$  C  $>$  A-béta/alpha
- Length-dependent
- Protection of the BBB
- Nearly no A-delta in ANS (male sexual dysfunction,...)
- Pain and Neuropathy progression are not linear (sensitization)

Axones sensoriels	A $\alpha$	A $\beta$	A $\delta$	C
Axones des fibres sensorielles musculaires	Groupe I	II	III	IV
				
Diamètre (μm)	13–20	6–12	1–5	0,2–1,5
Vitesse (m/s)	80–120	35–75	5–30	0,5–2
Récepteurs sensoriels	Propriocepteurs des muscles squelettiques	Mécanorécepteurs de la peau	Douleur, température	Température, douleur, démangeaisons

**Différentes tailles des axones des afférences primaires.** Les axones sont représentés à l'échelle les uns par rapport aux autres, mais leur taille est ici environ 2000 fois supérieure à la normale. Le diamètre de l'axone est corrélé avec sa vitesse de conduction, et avec le type de récepteur sensoriel avec lequel il est connecté.

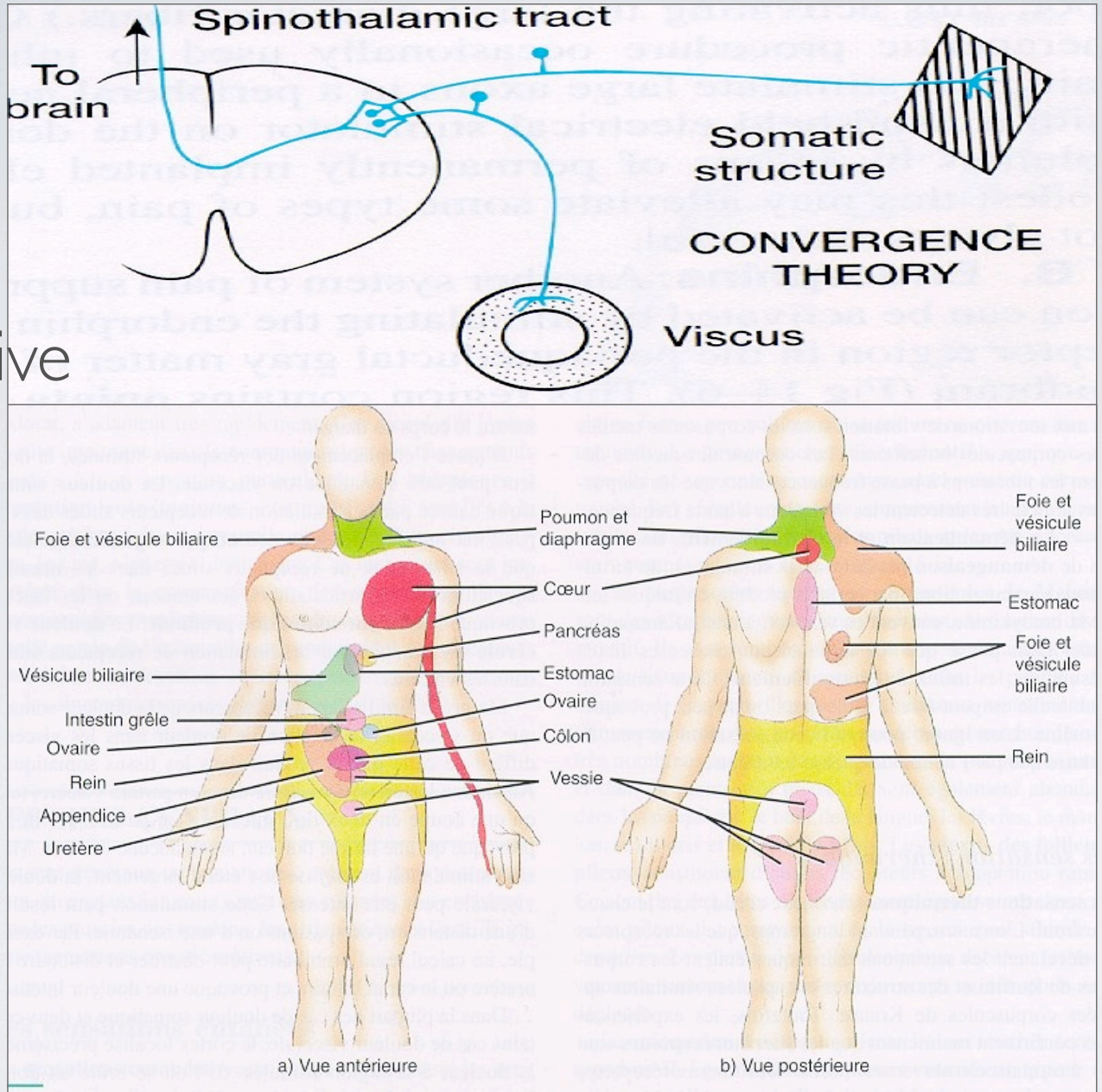


# Exteroceptive



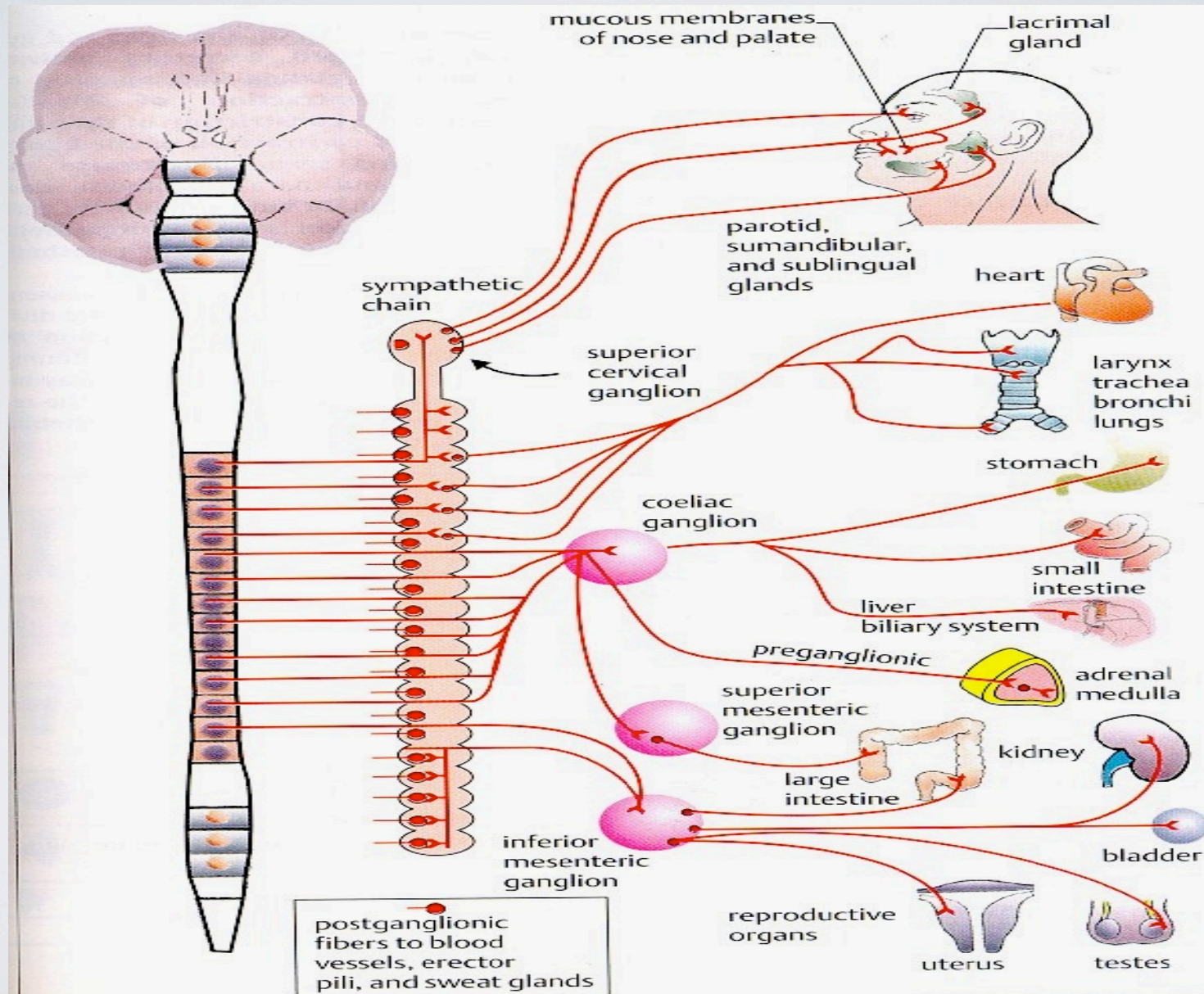
Sensory pathways from the periphery through the spinal cord to the postcentral gyrus

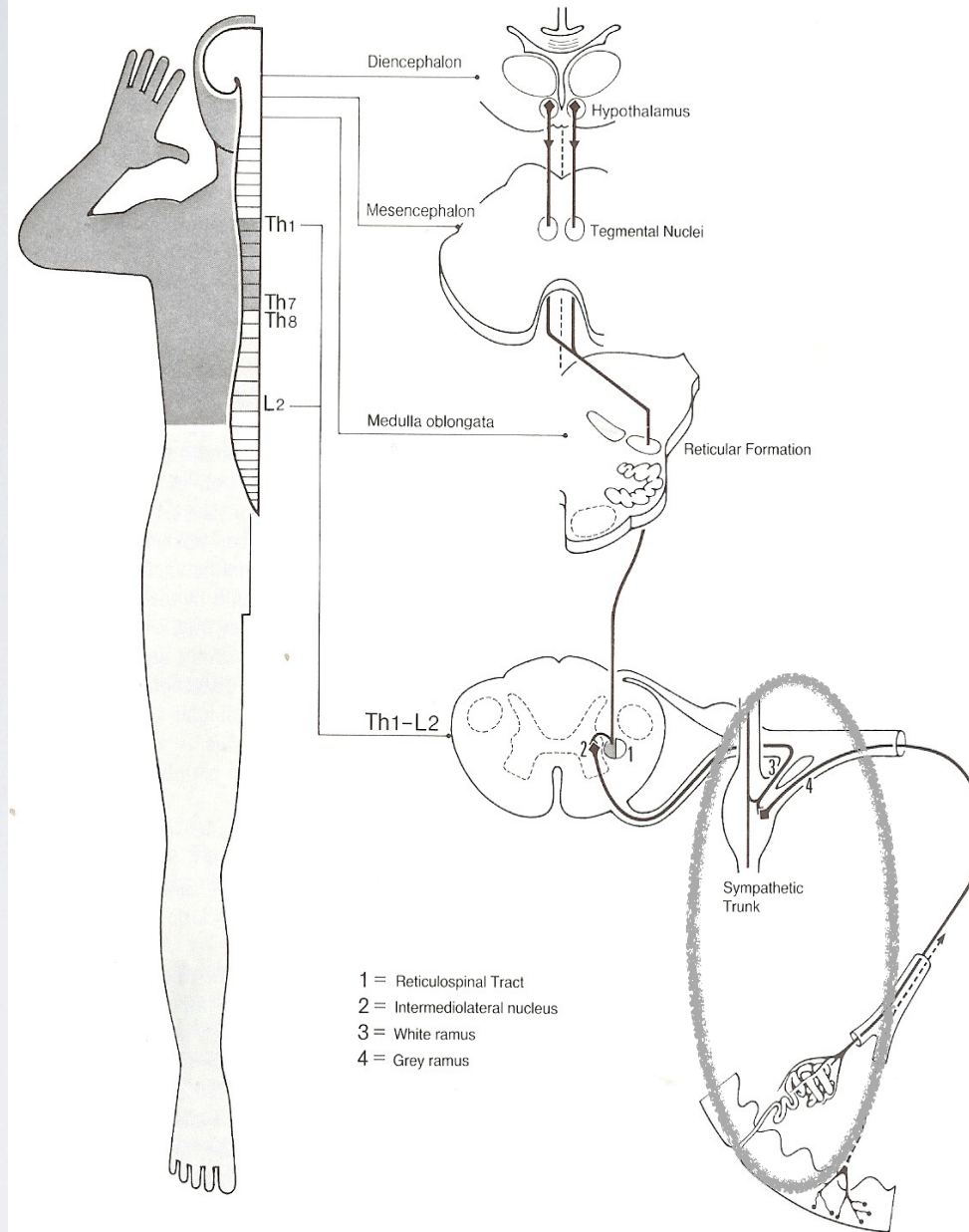
Interoceptive





# OS:

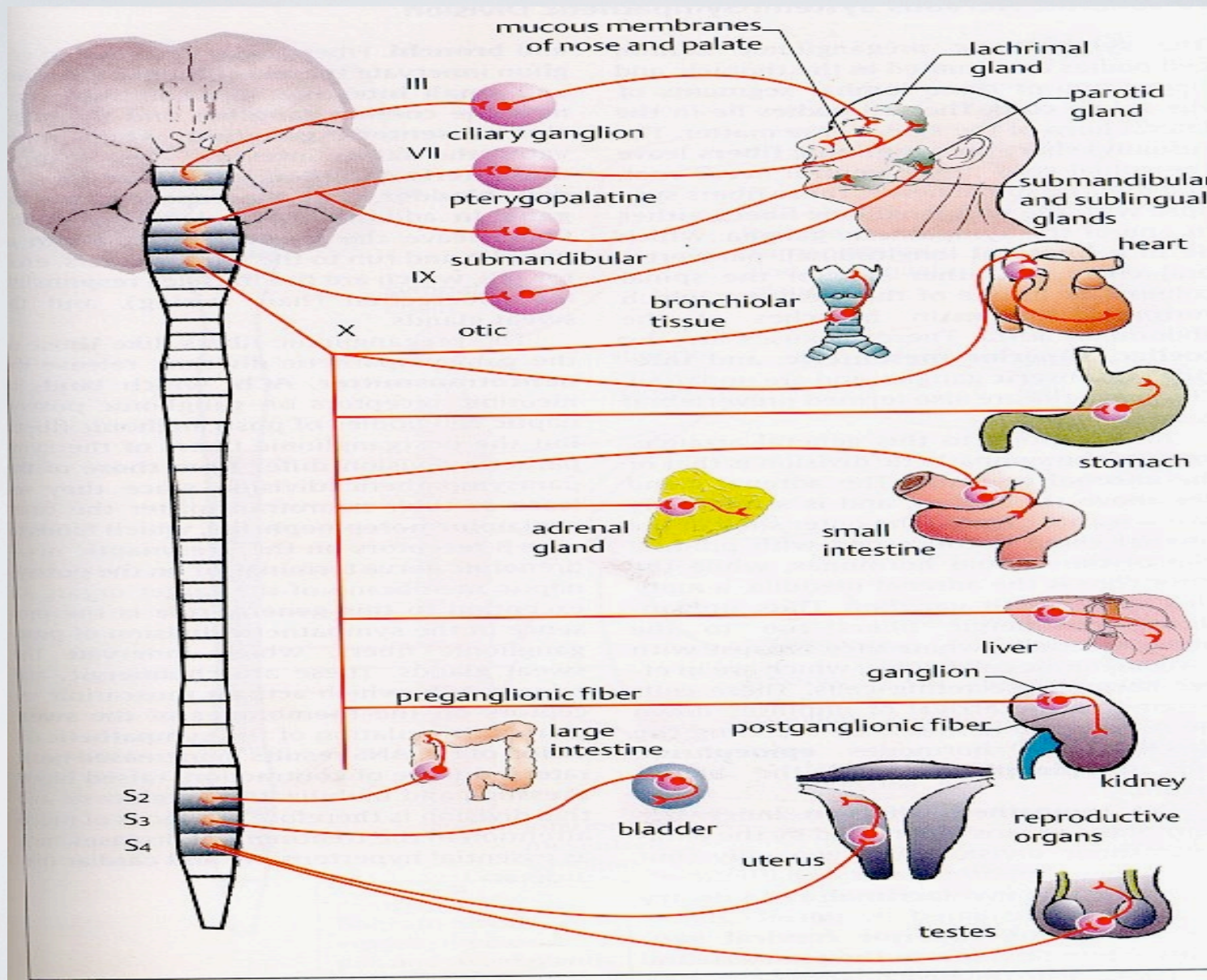




Neuroanatomic basis of sweating. Note that in the spinal cord the vegetative neurons are situated only in the portion of the intermediolateral nucleus between T1 and L2. The appropriate efferent pathways leave the spinal cord only from those segments and then are distributed via the sympathetic paravertebral chain to the entire body surface



# PS:



# RED FLAGS:

- Childhood in male, Adolescent in female or Young Adult
- Limb Pain Crisis (after fever, stress or physical activity)
- Neuropathic Pain, symmetric and distal, MI > MS
- Abdominal Disturbance, especially Unexplained Pain
- Hypohidrosis



# DIAGNOSIS OF A LDADFPN:

- Cold sensation (hand in ice < 30'' and highly painful)
- QST ssi
- IENFD ssi
- SCR, R-R, T-T, PEL ?

[Fabry\\_disease.](#)

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