

Mast cells infiltrate the submucosal plexus in diverticular disease

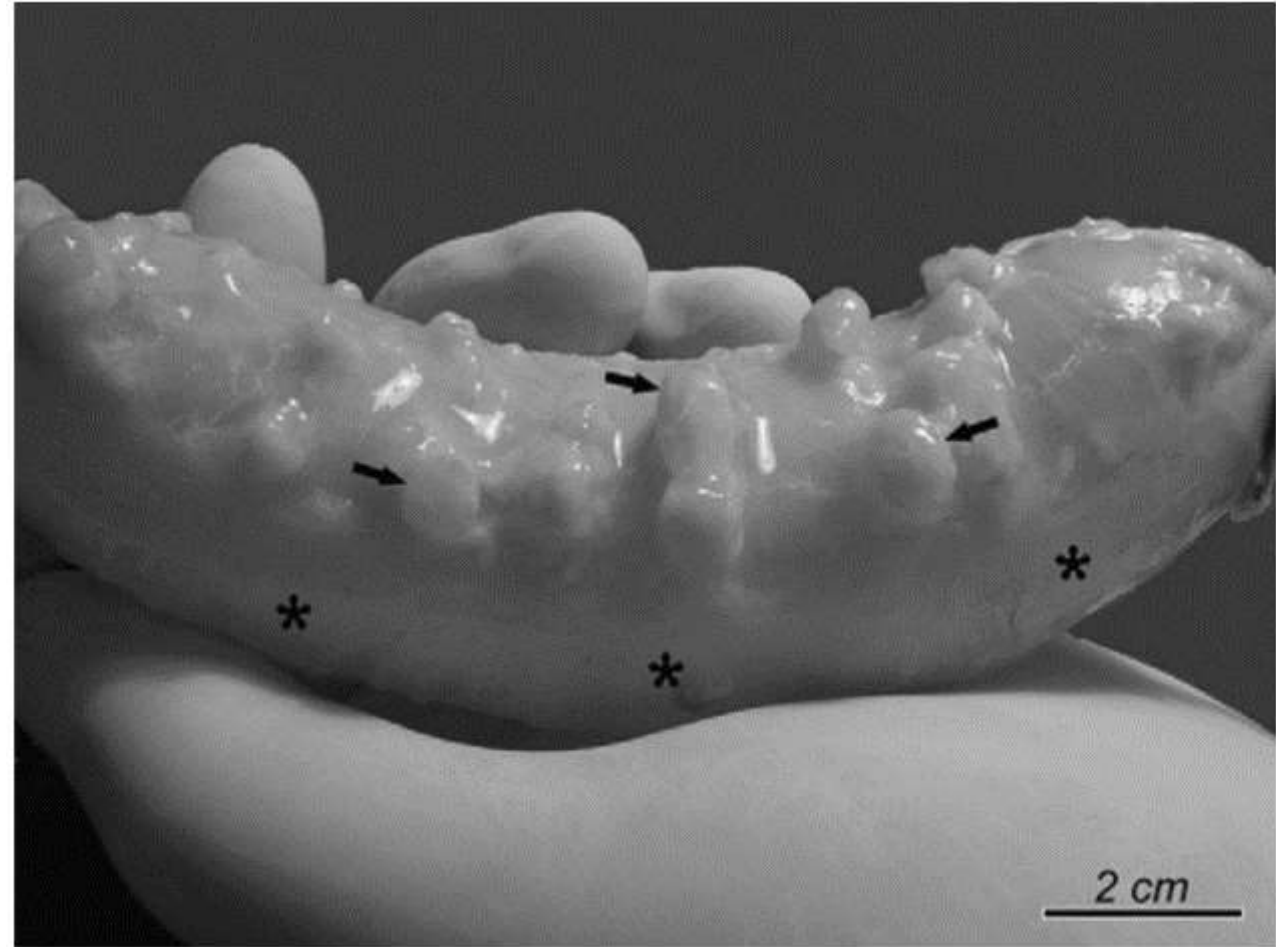
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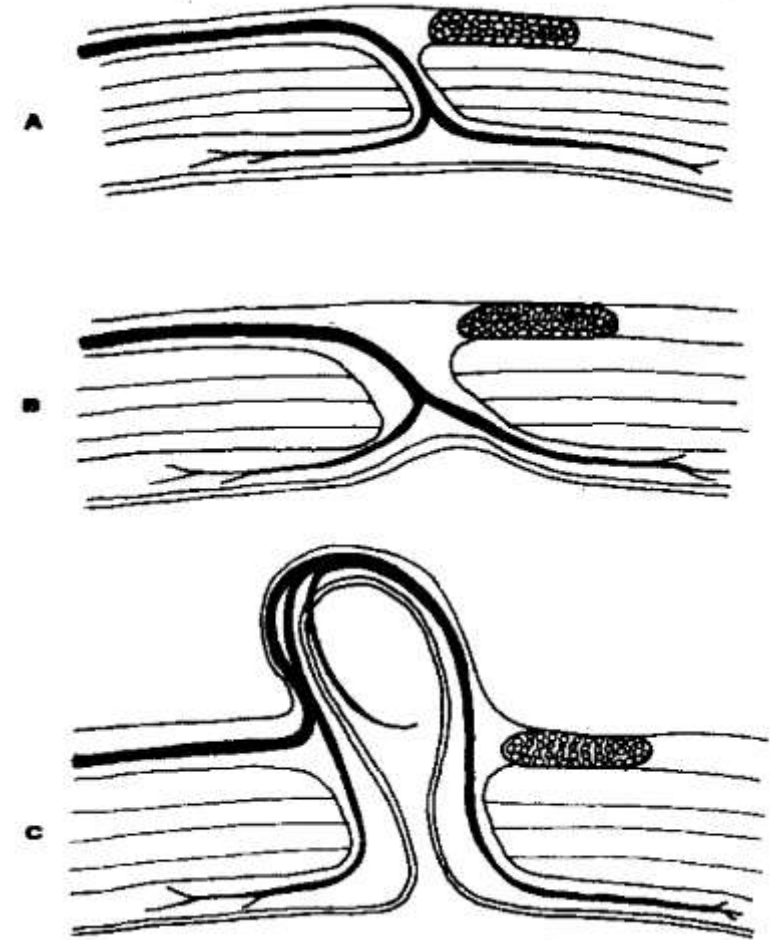
Background

- Diverticulum is a hernia of the mucosa and submucosa through the muscular layer of the colon;
- 65–80% of people over 65 yrs develop diverticula;
- Symptomatic in 20% of patients;
- Complicated in 15% of symptomatic patients.



What is known about diverticular disease?

- Risk factors – obesity, smoking, NSAIDs;
- Genes related to collagen synthesis;
- Changes in the enteric nervous system:
 - Fewer intramural ganglia;
 - Fewer neurons;
 - Immune cell infiltration;
 - Changes in smooth muscle innervation;
 - Fewer Interstitial cells of Cajal.



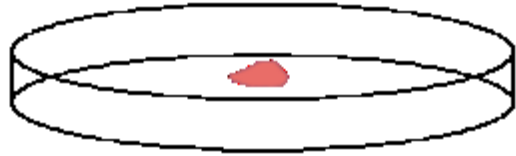
What is unknown about diverticular disease?

- Most studies use control tissue and tissue from complicated diverticulitis – hard to infer a cause-effect relationship;
- Knowledge about the relationship of tissues and cells is limited;
- Irritable bowel syndrome and diverticular disease are related, but the exact common pathophysiology remains unknown.

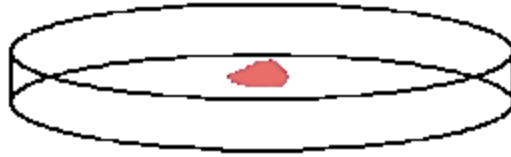
Aim of the study

Assess the ultrastructure of the enteric nervous system and its relationship to mast cells in the submucosal layer.

Materials



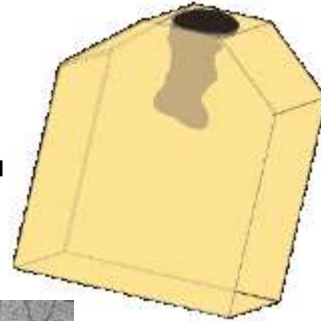
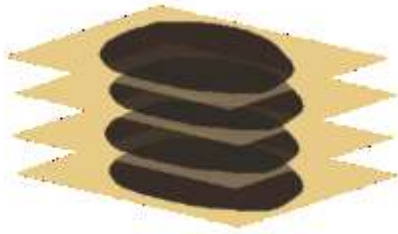
16 patients operated for non-obstructing colon cancer



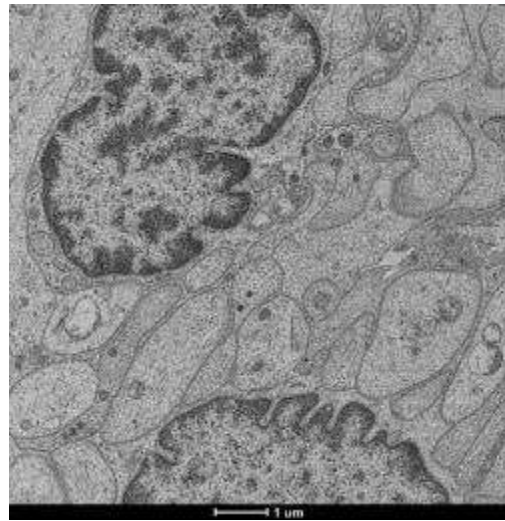
9 patients operated for recurring attacks of diverticulitis

Inner submucosal plexus sample preparation, fixation and resin molds, semithin sectioning

Thin sections



Routine staining, TEM microscopy



Age

Control (9): 58.2 (SD 13.3)

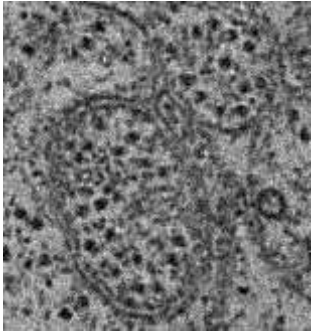
Asymptomatic diverticulosis (7): 60.9 (SD 10.4)

Complicated diverticular disease (9): 67.6 (SD 11.4)

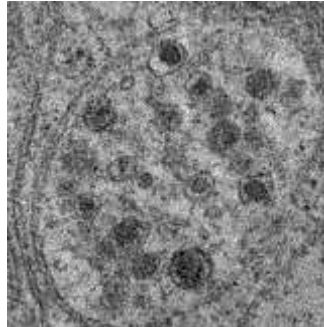
Methods

1. Nerve profile measurements with Fiji
2. Nerve profile classification based on:

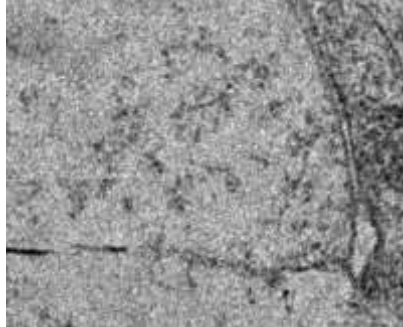
1. Cytoskeleton



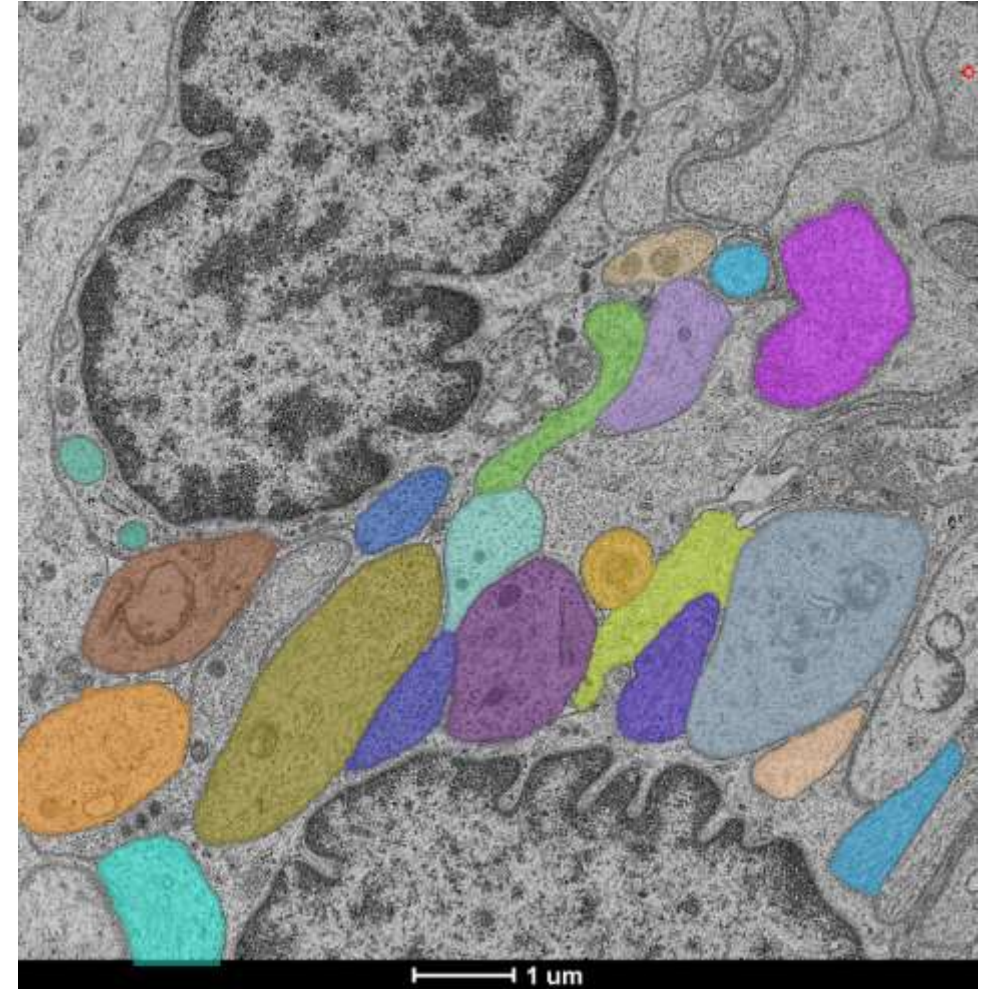
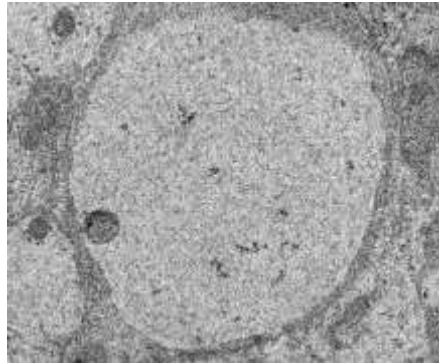
2. Vesicles



3. Membrane integrity



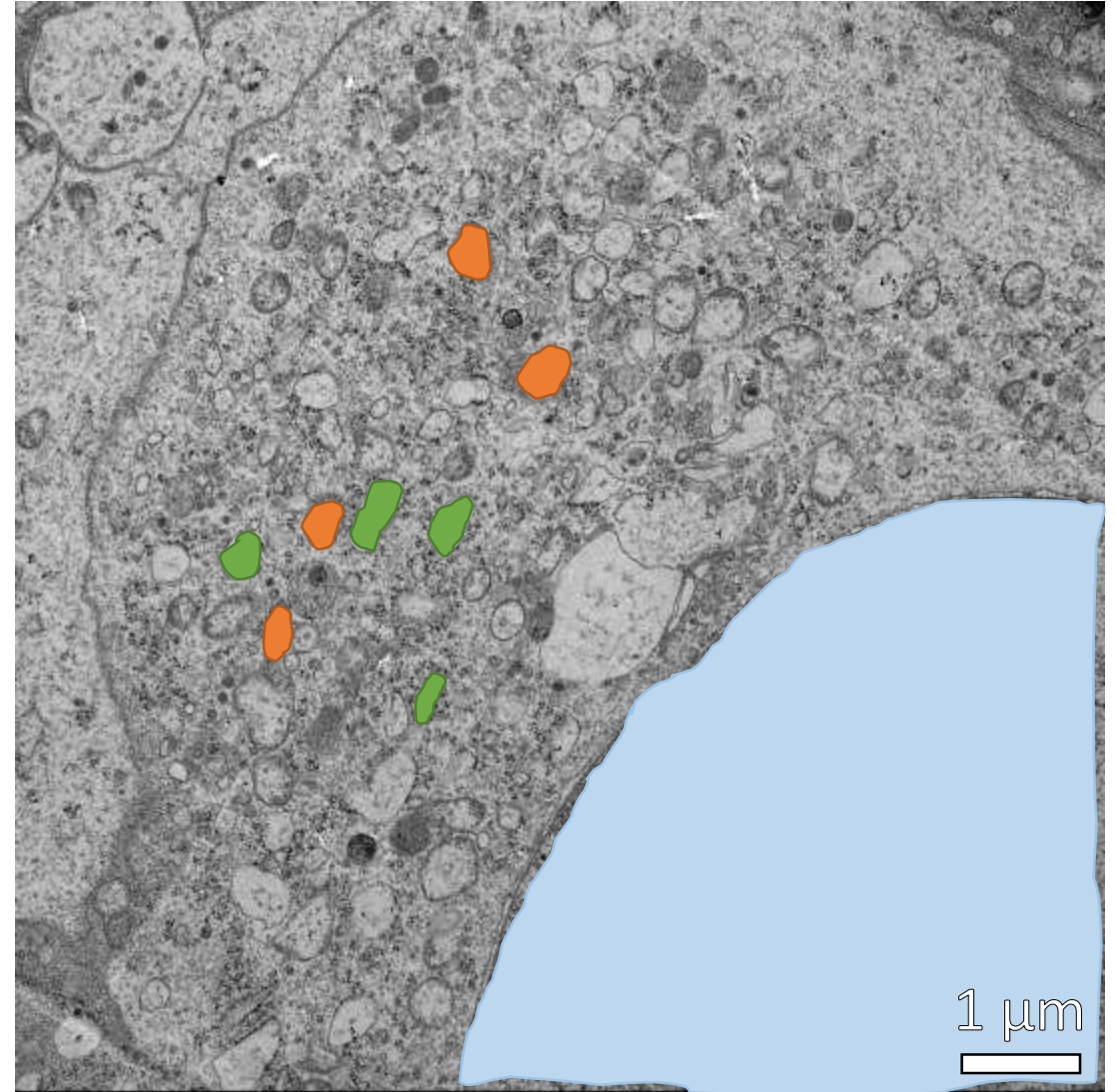
4. Profile shape



3. Mast cells were counted in a thin section of each tissue sample.

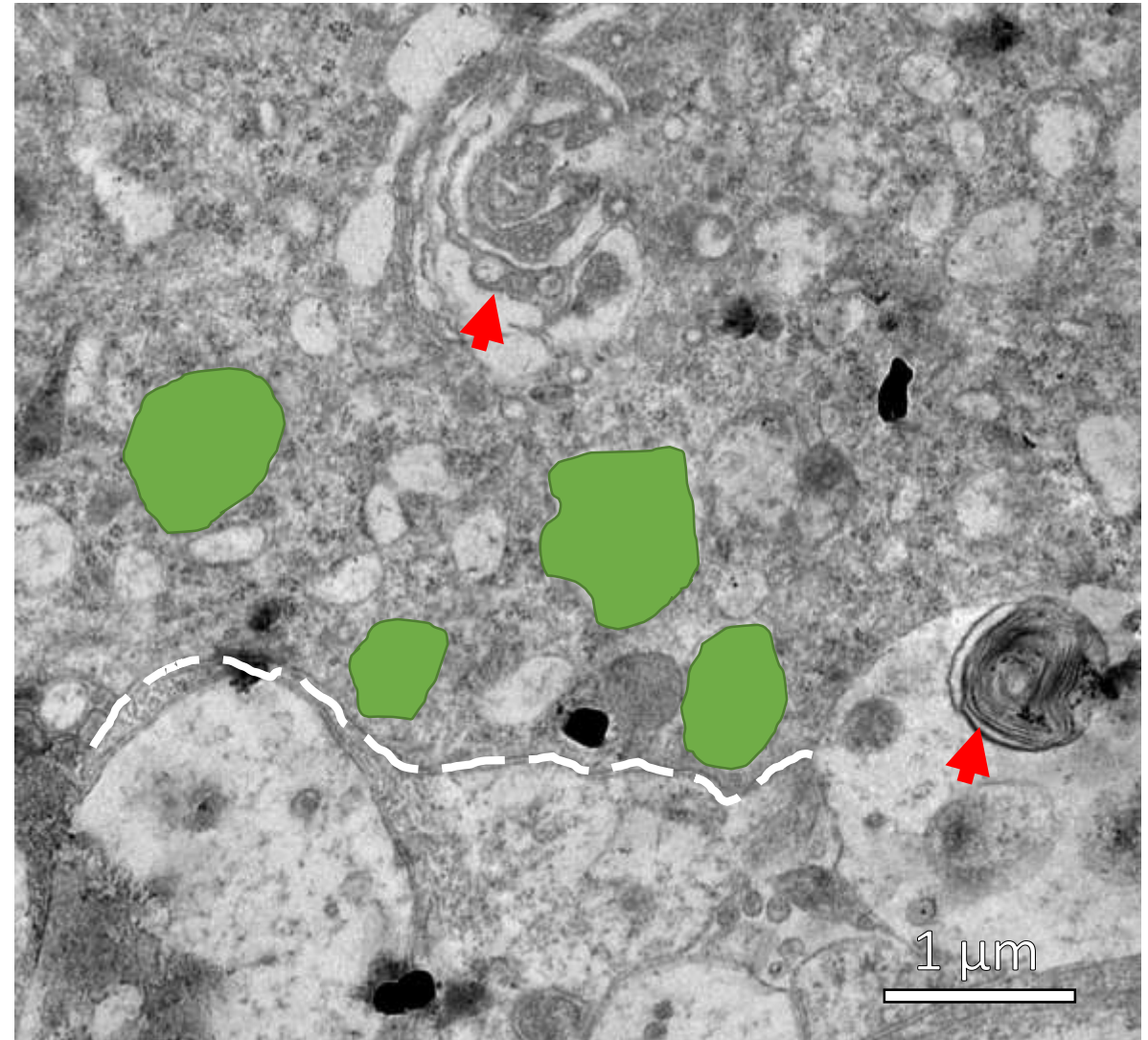
Neurons in the inner submucosal plexus

- Control and asymptomatic group neurons are ultrastructurally similar;
- rER and Golgi cisterns and mitochondria are present;
- Synapses with adjacent axons;
- Few to no lipofuscin inclusions.



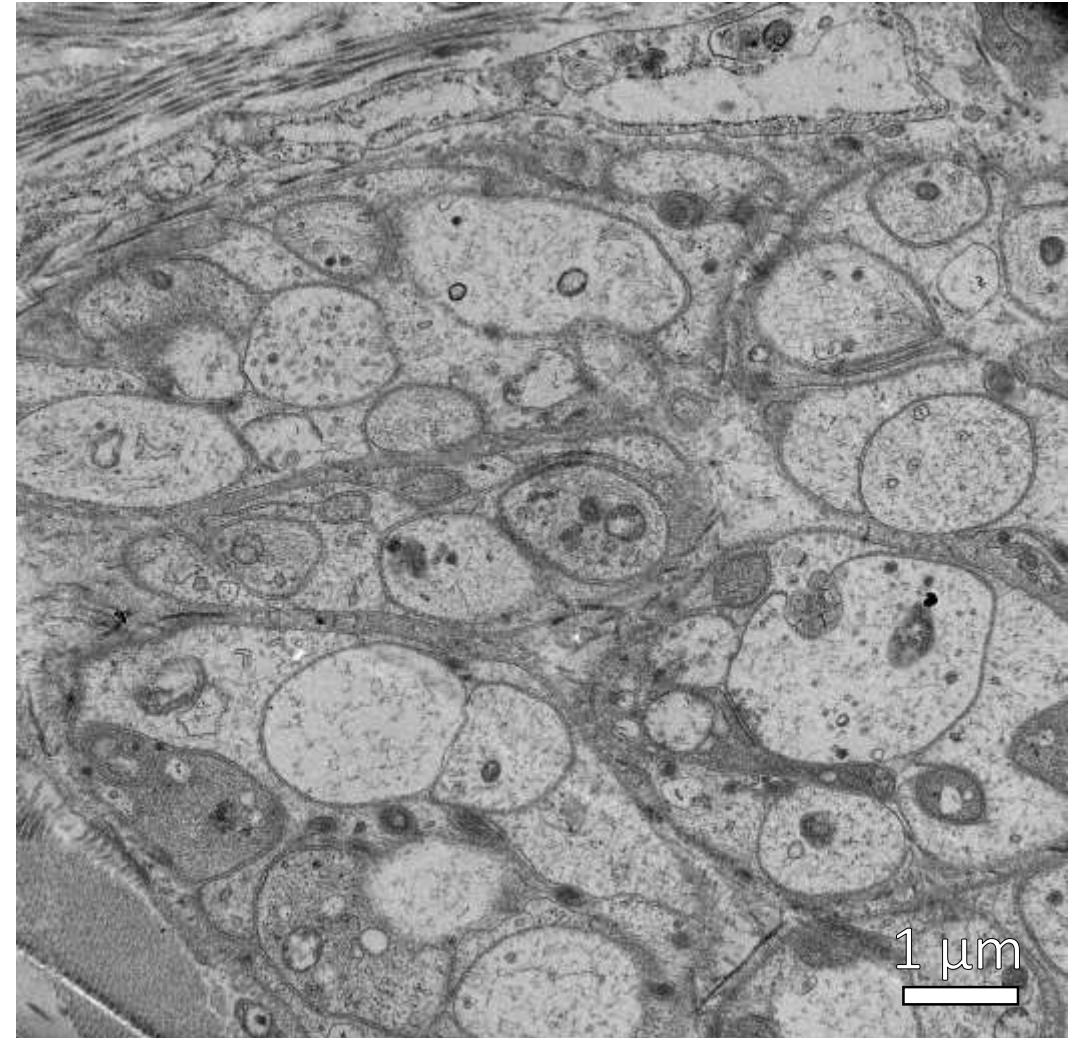
Neurons in complicated diverticular disease

- Enlarged rER and Golgi cisterns;
- Larger and more frequent lipofuscin inclusions;
- Lamellar bodies present;
- Larger contact surface with glial processes.



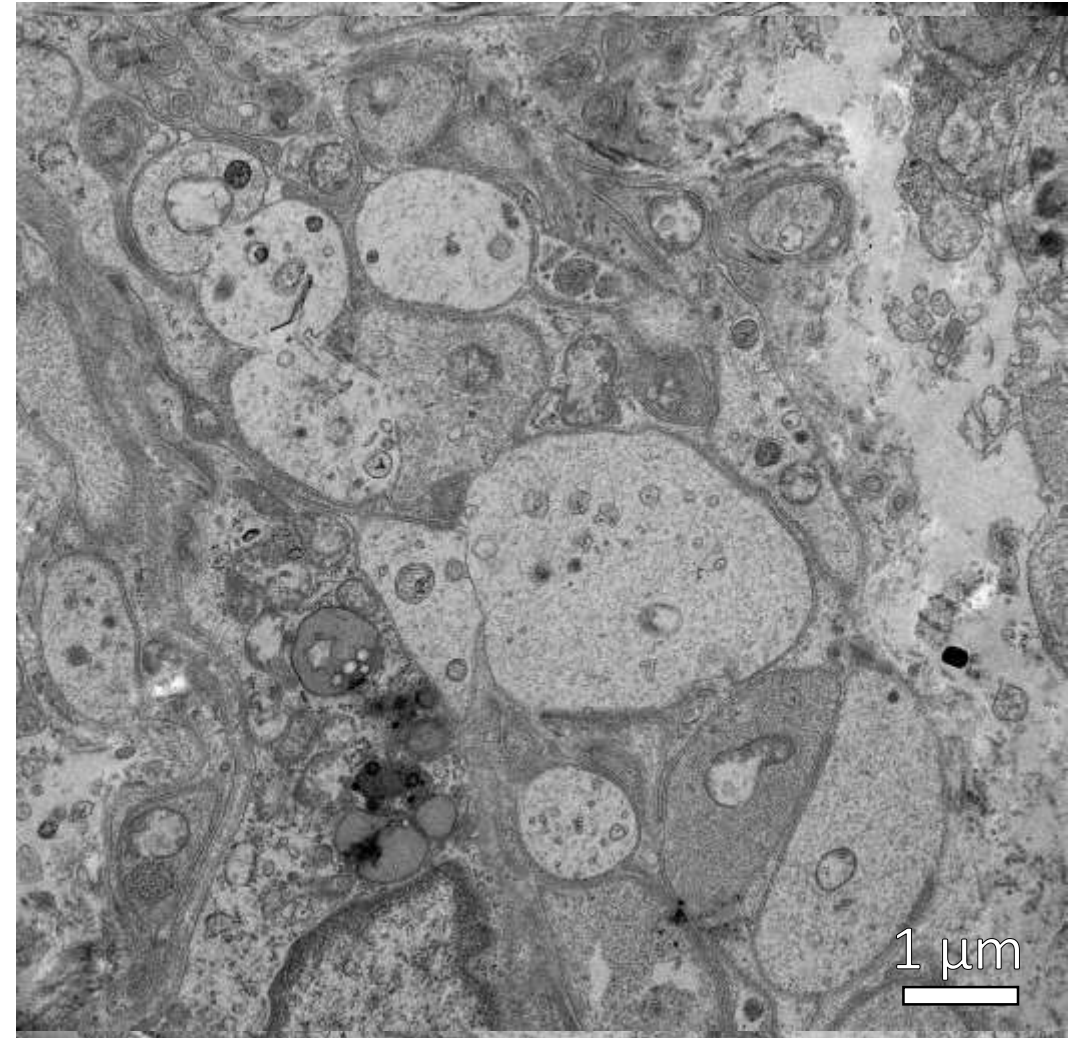
Axons and dendrites in the control group

- Few glial processes between axons;
- Differentiated neurofilaments in most axons;
- A few synapses are present between processes;
- Various vesicle shapes with neurotransmitter;
- Ganglia and nerve morphology is similar between control and asymptomatic groups.



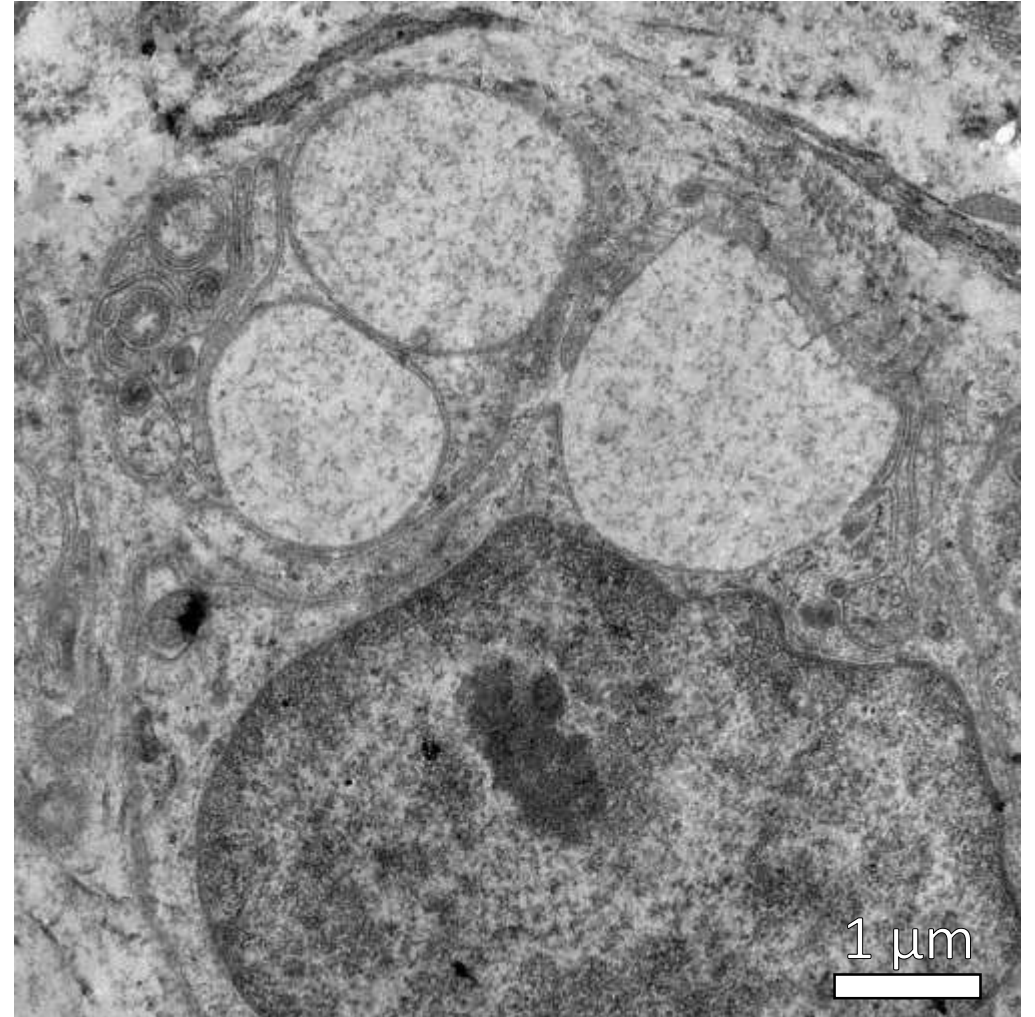
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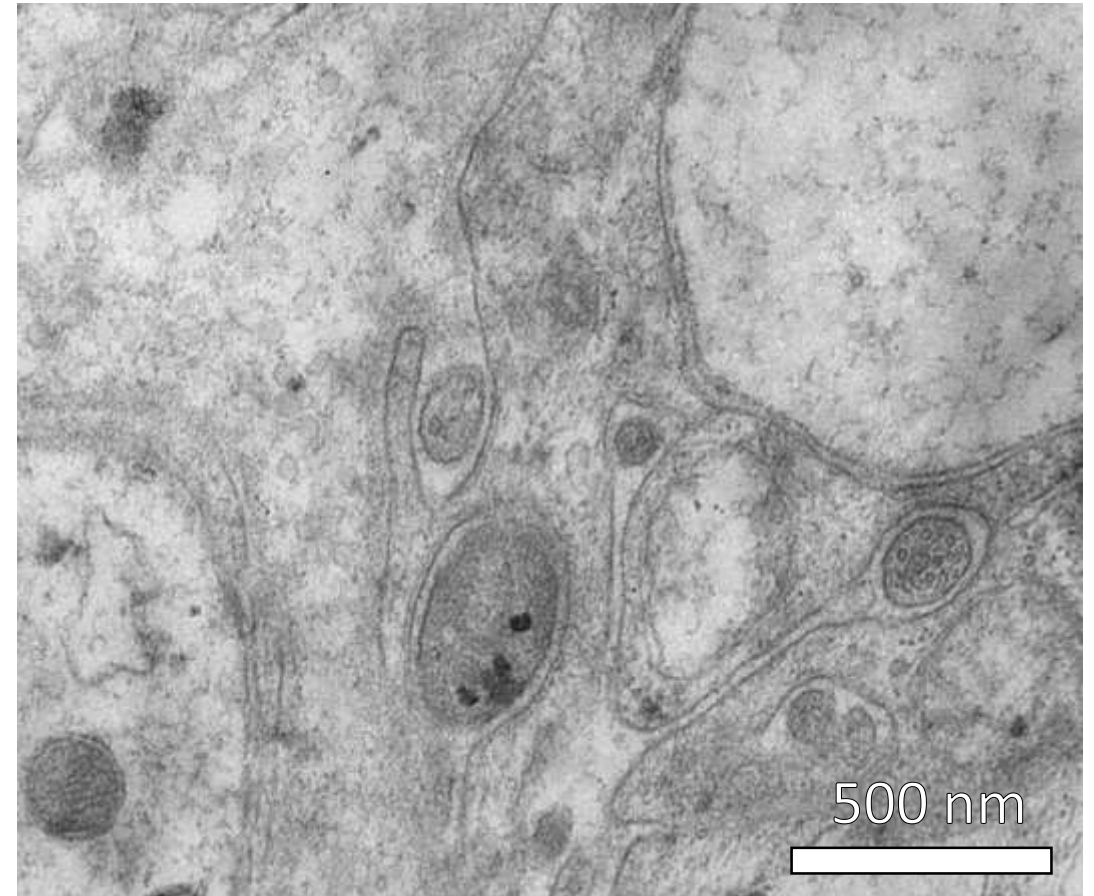
Axons and dendrites in diverticular disease

- Larger percentage of swollen nerve processes
- Fewer vesicles with neurotransmitter;
- Poorly visible or absent cytoskeleton;
- Larger glial processes;
- Fine nerve fibres more frequent.

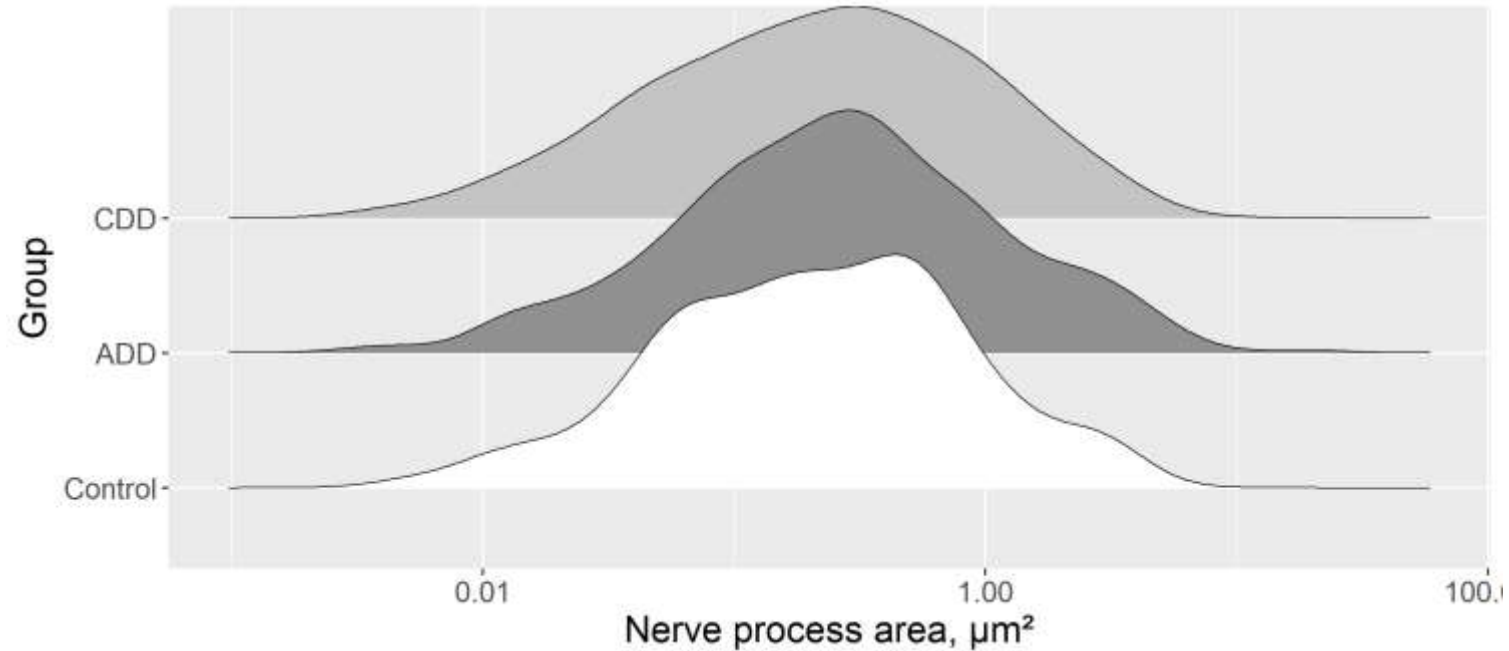
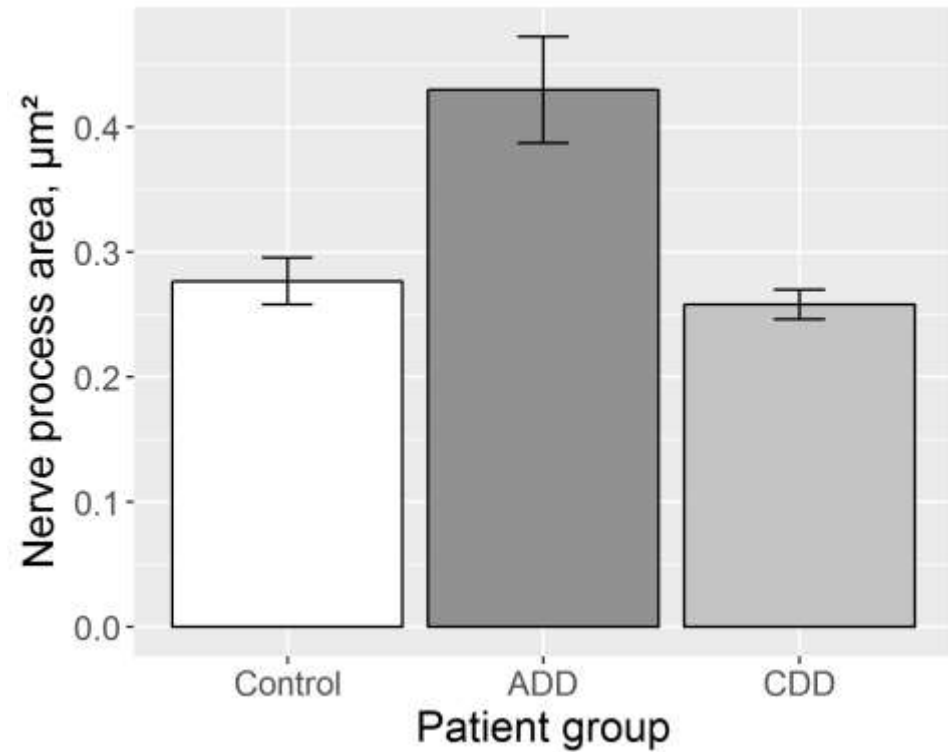


Axons and dendrites in diverticular disease

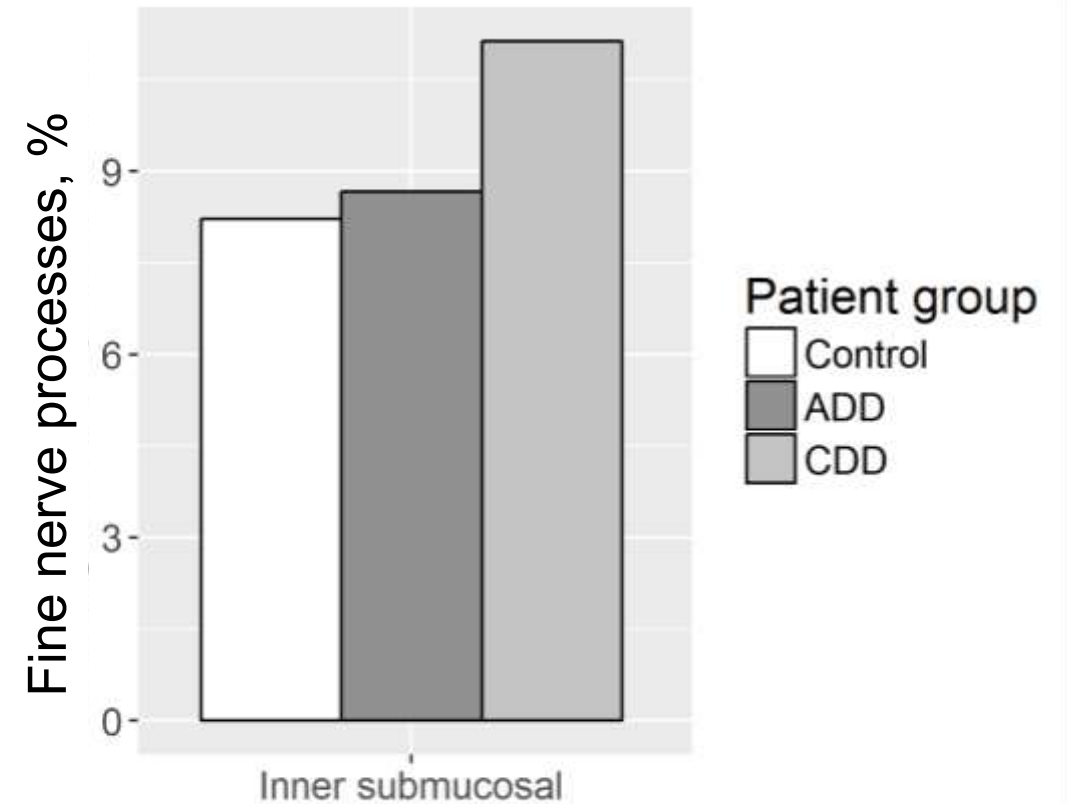
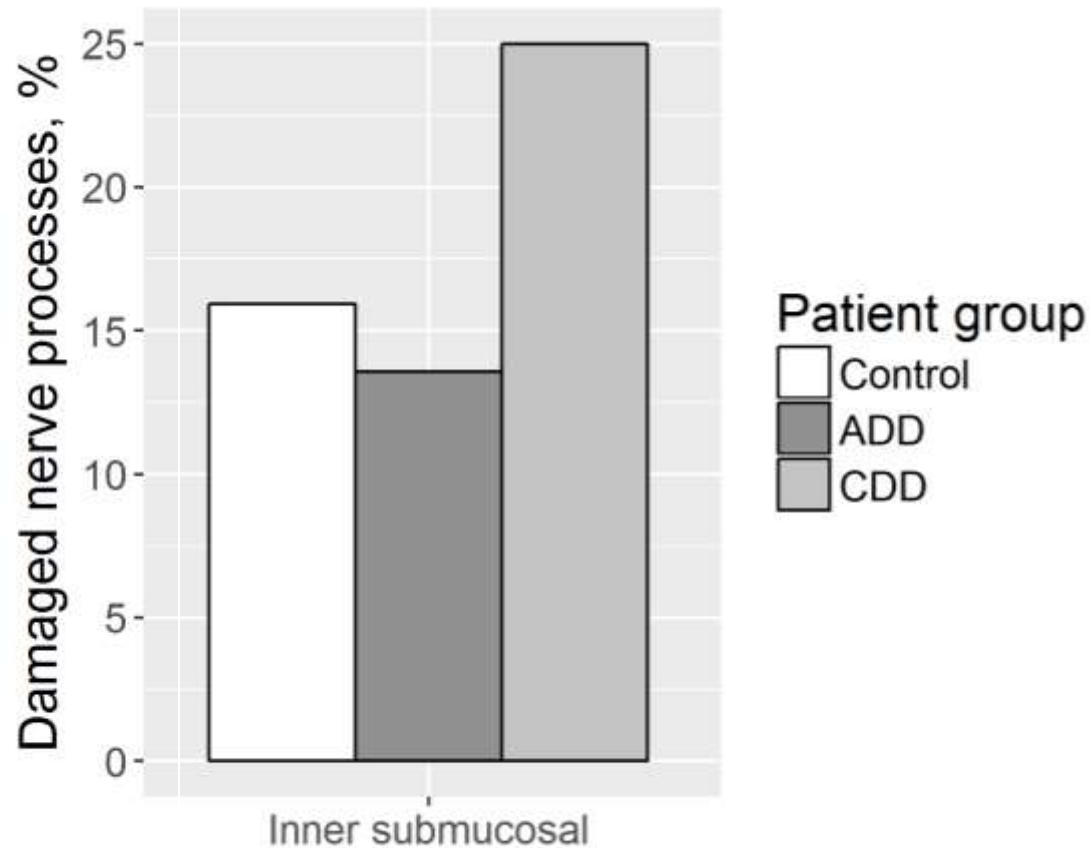
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- Fewer vesicles with neurotransmitter;
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Nerve process area in the inner submucosal plexus



Swollen and fine axons in the inner submucosal plexus



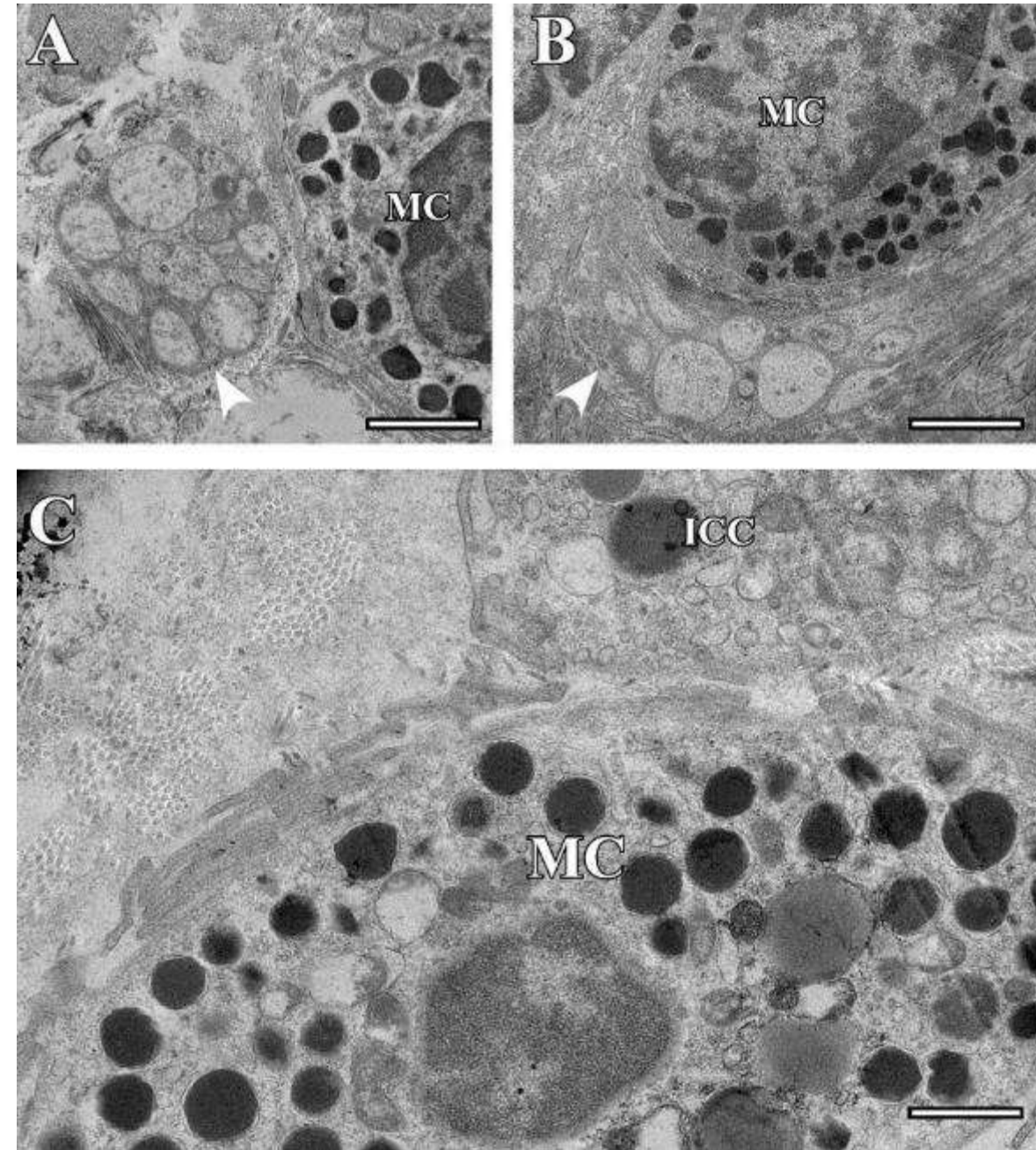
Mast cells in the inner submucosal plexus

In CDD:

- Mast cells were more frequent;
- The gap between the cells was smaller (ranged from 1.5 μm to 200 nm);
- Nerves lacked perineurium
- Contacts with ICC

Mast cell number per specimen

Patient group	Median	Minimum	Maximum
Control	1	1	4
Asymptomatic	1.5	1	2
Complicated DD	2	1	8



Conclusions and future considerations

- There is notable remodeling of the inner submucosal plexus in the colon;
- Mast cells are more frequent as well as closer to enteric nerves;
- Irritable bowel syndrome has similar symptoms as well as larger numbers of mast cells – potential cause of symptoms in DD?

Acknowledgment

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