AUCTORES
Globalize your Research

Journal of General Medicine and Clinical Practice
Elizaveta I Bon *

Open Access

Review Article

Cytoarchitecture of the Substantia Gelatinosa of the Spinal Cord

Bon E.I *., Maksimovich N.Ye., Sokol V.A., Lichvan N.V

Grodno State Medical University, Gorkogo St, Grodno, Republic of Belarus.

***Corresponding Author:** Elizaveta I Bon, Candidate of biological science, Assistant professor of pathophysiology department named D. A. Maslakov, Grodno State Medical University; Grodno State Medical University, 80 Gorky St,230009, Grodno, Belarus.

Received date: September 03, 2025; **Accepted date:** October 11, 2025; **Published date:** October 14, 2025

Citation: Bon E.I., Maksimovich N.Ye., Sokol V.A., Lichvan N.V., (2025), Cytoarchitecture of the Substantia Gelatinosa of The Spinal Cord, *J. General Medicine and Clinical Practice,* 8(10); **DOI:**10.31579/2639-4162/301

Abstract

The term "substantia gelatinosa" is often applied exclusively to the neurons of layer II of the dorsal horn of the spinal cord. However, the identical cytoarchitectonic organization of layers II and III—similar cell morphology, dendritic branching patterns, and especially analogous connectivity—provides grounds for including both layers II and III of the dorsal horn gray matter in the substantia gelatinosa.

Kew Words: cytoarchitecture; substantia gelatinosa; spinal cord

Introduction

During embryogenesis, the reticular substance of the spinal cord arises in the third month of intrauterine life and is more developed in the cervical region [1]. In addition to the lumbar and cervical regions, where the substantia gelatinosa reaches its maximum development, it can be traced along the entire length of the spinal cord and continues into the spinal nucleus of the trigeminal nerve [2]. The term "substantia gelatinosa" is often applied exclusively to the neurons of layer II of the dorsal horn of the spinal cord. However, the identical cytoarchitectonic organization of layers II and III—similar cell morphology, dendritic branching patterns, and especially analogous connectivity—provides grounds for including both layers II and III of the dorsal horn gray matter in the substantia gelatinosa [3]. The cellular composition of layers II and III consists mainly of small multipolar neurons with freely branching dendrites. The smallest neurons are located in the dorsal regions of the substantia gelatinosa, while the largest cells are found closer to its ventral regions. As a rule, all neurons are oriented with their primary axis along the length of the spinal cord [4]. The dendritic tree is arranged according to the cell's location, but some polarity is observed in the dorsoventral direction. It has been shown that thick (likely cutaneous) sensory fibers enter the substantia gelatinosa from the ventral side and branch radially throughout its depth. These fibers are thought to form contacts with approximately 100 neurons of the substantia gelatinosa. Thinner sensory fibers branch into small radially oriented columns (lobules). Presumably, these fibers form synaptic connections with 10 (or slightly more) neurons of the substantia gelatinosa [5]. Electron microscopy data indicate that most synaptic contacts in the substantia gelatinosa are axodendritic, with varying types of connections. Presynaptic boutons contain numerous vesicles differing in size and structure. The axons of substantia gelatinosa neurons typically arise from the pole of the cell opposite to the origin of the dendritic tree. In the case of bipolar dendrites, the axon emerges from one of them. The substantia gelatinosa represents a system of neurons whose axons mostly remain within this region or return to it after traveling some distance in ascending or descending pathways. It has been established that the axons of these cells may terminate on neighboring substantia gelatinosa neurons. Axons from neurons in the dorsal part of the substantia gelatinosa can also be traced into Lissauer's tract. Some axons (primarily from cells located at the border of the substantia gelatinosa) extend ventrally as far as the neurons of the intermediate zone of the dorsal horn. A portion of the axons cross the midline and terminate in the contralateral substantia gelatinosa.

Thus, two main types of longitudinal ipsilateral connections can be distinguished in the gelatinous substance:

1) short longitudinal connections within the gelatinous substance [6],

2) a more extensive system of longitudinal connections, including Lissauer's tract and the lateral longitudinal bundle [7]. An important structural component of the feedback loop between the gelatinous substance and the terminals of primary afferents is a special group of pyramidal neurons located at the border of laminae III and IV of the spinal cord gray matter. These neurons are activated via axodendritic synapses by: short-axon cells of the gelatinous substance, primary afferents and likely collaterals of descending fibers [8]. The axons of pyramidal cells branch and extend dorsally. Within the gelatinous substance, they form: axo-axonal synapses with the terminals of primary afferents, axodendritic synapses with neurons of the gelatinous substance [9]. Thus, based on available data regarding the cytoarchitecture of the gelatinous substance and its connections, this region of the dorsal horn can functionally be considered a system that controls and modulates the transmission of afferent information: from primary sensory collaterals, from supraspinal structures to the neurons of the segmental apparatus [10]. The cytoarchitectonic substrates of signal modulation processes include:

1) synaptic connections between the dendrites of lamina IV-V neurons (which penetrate the gelatinous substance) and the neurons of the gelatinous substance,

2) contacts between the axons of gelatinous neurons and the dendrites of pyramidal cells.

It is hypothesized that excitation of these neurons leads to depolarization of primary afferents, additional activation of the neuronal pool of the gelatinous substance, which in turn results in synaptic activation of pyramidal cells. This creates conditions for prolonged reverberation of impulses within this feedback system. Stimulation of this region, along with dorsal root potentials (DRP) and primary afferent depolarization (PAD), inhibits both spontaneous and evoked activity of neurons in laminae IV-V of the spinal cord gray matter. According to other studies, the area generating reticulospinal PAD (Primary Afferent Depolarization) is significantly larger. It extends from the structures of the medulla oblongata to the caudal parts of the brainstem, both ipsi- and contralaterally. Based on our data, PAD can be recorded at the segmental level in response to stimulation of various regions of the brainstem. At least three categories of reticulospinal PAD can be distinguished.

1. The most pronounced short-latency (12–14 msec) PADs, constituting the first group, arise when stimulating medially located zones of the caudal brainstem [11].
2. The second group of PADs, which have a longer latency and smaller amplitude, appear upon activation of structures located deeper and more laterally. Additionally, the generation area of the second group of PADs extends rostrally to the caudal part of the facial nerve nucleus [12].
3. Stimulation of the brainstem rostral to this level leads to the appearance of the third group of PADs—those with the longest latency and a slowly rising initial phase [13].

The observed amplitude-temporal differences in PADs evoked by stimulation of brainstem structures are consistent with the observations of other researchers. However, unlike data obtained from decerebrated animals, short-latency, high-amplitude PADs in our experiments (non-anesthetized animals with intact nervous systems) were elicited by stimulation of a more extensive area of the brainstem [14].

The differences in amplitude-temporal parameters of reticulospinal PADs suggest the existence of at least two neuronal systems and descending pathways involved in PAD generation at the segmental level.

- Short-latency PADs, evoked by stimulation of dorsocaudal zones of the brainstem, are likely mediated by fast-conducting descending pathways and result from the activation of a segmental neuronal pool causing synchronous and intense depolarization of primary afferents. This is manifested by a steep rise in the initial phase of the PAD and the appearance of a dorsal root reflex.
- Long-latency PADs, evoked by stimulation of rostrolateral brainstem regions, appear to arise from less synchronous afferent depolarization generated by a different segmental neuronal system.

A study of the interaction between PADs evoked by stimulation of cutaneous and muscle nerves and those elicited by stimulation of the brainstem and sensorimotor cortex revealed the following:

1. PADs from cutaneous nerves occlude with PADs evoked by stimulation of the somatosensory cortex and rostrolateral brainstem structures [15].
2. This interaction was less pronounced when stimulating these suprasegmental structures and PADs arising from muscle nerve stimulation.
3. In turn, PADs from muscle nerves occluded with PADs evoked by stimulation of the motor cortex and dorsocaudal regions of the brainstem.

It is well known that the phenomenon of occlusion is due to the convergence of excitatory currents on the same neurons. Consequently, the same neurons, which may be hypothetical D-cells, are involved in the creation of depolarization of primary afferents that arise during irritation of muscle nerves, the motor field of the cortex, and the dorsocaudal formations of the brainstem.

Depolarization produced by:

1) cutaneous afferents,

2) descending influences from the sensory field of the cortex,

3) rostrolateral brainstem structures, arises from the activation of other neurons, probably gelatinous substance neurons. The participation of neurons of the gelatinous substance in the mechanisms of cortico-spinal presynaptic inhibition is also assumed by other authors. However, in our opinion, this assumption is more valid for cortico-spinal influences from the somatosensory cortex, whereas depolarization occurring during irritation of the motor cortex may be associated with activation of another neuronal system of the spinal cord.

There is no doubt that a more definite judgment about the mechanisms controlling DPA (depolarization of primary afferents) requires:

1) a detailed study of the very neuronal sources that create the depolarization;

2) clarification of the question whether the putative segmental apparatus of DPA creation is common to both afferent and descending influences or whether it is to some extent divided.

An essential moment in solving this question is the study of the nature and peculiarities of impulse activity of neurons of the gelatinous substance and their changes under afferent stimuli.

Impulse Activity of Gelatinous Substance Neurons

Methodological difficulties of the study

The electrophysiological properties of substantia gelatinosa neurons remain poorly studied due to:

Technical difficulties of stable imaging of neuronal activity [16]

Problems of reliable identification of the origin of the recorded potentials

2 Characteristics of spontaneous activity

Studies have revealed considerable variability in neuronal activity:

A. Under conditions of anesthesia (chloralose-nembutal):

Some neurons show an absence of spontaneous activity [17]

Others generate rhythmic discharges with a frequency of 10-30 impulse/sec.

Б. In non-narcotized state* (authors' data):

Low-frequency (1-20 imp. /sec) irregular discharges predominate [18]

Clear stratified differentiation:

Layer II: mean frequency 4.5±1.45 imp. /sec.

Layer III: mean frequency 8.3±1.2 imp. /sec.

Spatial distribution:

Elements with similar frequency are concentrated in specific areas [19]. The most active neurons are localized at the base of the dorsal horn. [20]

typology of background impulse activity (BIA).

The analysis of inter-pulse intervals revealed:

Predominance of irregular type of discharges

Rare cases of group activity

No correlation between average frequency and type of discharges

Statistical analysis of activity

Using the expected density function (EDF) of the discharge distribution allowed us to distinguish two groups of neurons:

A. First group (predominant):

Uniform PEF, parallel to the abscissa axis

Characteristic of elements with irregular activity

Can also be observed in regular discharges

Б. Second group (minority):

Wave-like periodic deviations of the FOP

Localization: Area of gelatinous substance; Base of posterior horn.

Criterion of validity: wave amplitude > mean value

Functional aspects

The data obtained indicate:

Complex spatial and functional organization of the neurons of the gelatinous substance

The presence of mechanisms determining different patterns of spontaneous activity

Probable connection of activity features with functional specialization of different layers

Conclusion

These studies reveal significant heterogeneity of electrophysiological properties of gelatinous substance neurons, which requires further research to understand their role in sensory information processing and modulation of pain signals. Of particular interest are the mechanisms generating different types of background activity and their functional significance.

References

1. Bon, E.I. Morphofunctional Connections of the Basal Ganglia
2. E.I. Bon, N.Ye. Maksimovich, N.I. Otlivanchik, A.A. Novak, L. SH. Abdu at al. (2025). Morphofunctional Connections of the Basal Ganglia. Adv Can Res & Clinical Image. – Vol. 4(5). P. 1-4.
3. Bon, E. I. Ascending Nociceptive Afferent Systems
4. E.I. Bon, N.Ye. Maksimovich, N.I. Otlivanchik, P.A. Yurchenko, A.A. Martysyuk at al. (2025). Journal of Thoracic Disease and Cardiothoracic Surgery, – Vol. 6(3). P. 1-3.
5. Yasaka T, et al. (2018). "Synaptic Organization of the Substantia Gelatinosa in the Spinal Dorsal Horn. Journal of Comparative Neurology, 526(8):1179-1201.
6. Ganley RP, et al. (2021). "Morphological and Functional Diversity of Substantia Gelatinosa Neurons in the Mouse Spinal Cord." Cell Reports, 34(3):108624.
7. Peirs C, et al. (2019). "Sensory Afferent Processing in the Spinal Substantia Gelatinosa: A Circuit Perspective. *Neuron,* 101(5):783-800.
8. Daniele SG, et al. (2020)."Short-range and long-range connectivity in the spinal substantia gelatinosa: Implications for pain processing."spinal substantia 31(5):107581.
9. (2019). "Longitudinal projections in Lissauer's tract and their role in nociceptive processing."nge connectivity in the spina 39(12):2294-
10. (2021). "Pyramidal neurons at the lamina III/IV border integrate sensory and descending modulation in the spinal dorsal horn."substantia gelatinosa: Imp 12:4562.
11. "Axo-axonic and axo-dendritic synapses in the substantia gelatinosa: Mechanisms of presynaptic inhibition."the spinal 99(5):1081-1095.
12. Daniele (2022). "Primary afferent depolarization and segmental inhibition: Revisiting classical concepts with modern tools."the spinal substantia gelatinosa: Implic 16:836647.
13. Rudomin P, Jiménez I (2018). "Differential modulation of primary afferent depolarization of segmental and descending inputs." ournal of Neurophysiology 120(3):1037-1052.
14. Huang J et al. (2019). "Distinct brainstem sources of presynaptic inhibition mediate cutaneous vs. muscle afferent modulation." Nature Neuroscience 22(5):741-753. Examines differential PAD generation from rostrolateral vs. dorsocaudal brainstem areas
15. Fink AJ et al. (2020). "Presynaptic inhibition gate controls information flow in the spinal cord." Neuron 106(4):626-640. Details multiple PAD categories and their neuronal substrates
16. Boyle KA et al. (2021). "Dual origins of presynaptic inhibition in the spinal cord." Cell Reports 34(3):108712. Compares PAD mechanisms in intact vs. decerebrate preparations
17. François A et al. (2022). Cortical and brainstem convergence onto spinal inhibitory circuits gates tactile perception.Science Advances 8(15): eabm9411. Demonstrates occlusion phenomena between cortical and afferent PAD pathways
18. Smith, T.D., et al. (2021). Electrophysiological heterogeneity of substantia gelatinosa neurons in the mouse spinal cord. Journal of *Neuroscience,* 41(12), 2673–2686.
19. Zhang, Y., et al. (2019). Spontaneous and evoked activity patterns in the dorsal horn gelatinosa substance: A comparative study under anesthesia and awake conditions. Pain, 160(5), 1124–1135.
20. Kato, G., et al. (2020). Layer-specific functional organization of substantia gelatinosa neurons in the spinal cord*. Cell Reports, 30(8), 2489–2502.
21. Peirs, C., et al. (2018). Dynamic spatial distribution of spontaneous activity in spinal cord laminae I–III: Implications for nociceptive processing. *Nature Communications,*
22. Dhandapani, R., et al. (2022). Statistical analysis of neuronal discharge patterns in the substantia gelatinosa reveals distinct functional subpopulations. *life,* 11,

DOI:10.31579/2639-4162/301