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Editorial

The Role of GABA in Spinal Cord Injury

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See the article "Spinal Cord Injury Provoked Neuropathic Pain and Spasticity, and Their GABAergic Connection" via https://doi.org/10.14245/ns.2244368.184.

Spinal cord injury (SCI) leads to lifelong neurological disorder as well as many complications in the chronic phase.[1] Around 80% of the SCI patients suffer from chronic pain, which significantly lower their quality of life. Spasticity is another common sequalae. Finding the mechanism of chronic neuropathic pain (CNP) and spasticity after SCI is vitally important for the effective intervention.[2]

GABA is the major inhibitory neurotransmitter which is abundant in the spinal cord. There is emerging link between the GABA and the SCI neuropathic pain (NP) and spasticity. Glutamate excitotoxicity is responsible for the inhibition of GABAergic inhibitory tone. After SCI, there is GABAergic cell loss, glutamic acid decarboxylase downregulation, GABA transporters upregulation and overactivation of glutamate receptors. Upregulation of Na+ cotransporter 1 (NCC1) and downregulation of K+ cotransporter 2 (KCC2) leads to Cl- concentration imbalance, which further leads to NP and spasticity.[3] Excitotoxity as well as hypoactivation of inhibitory GABAergic tone make the imbalanced neuromodulation.

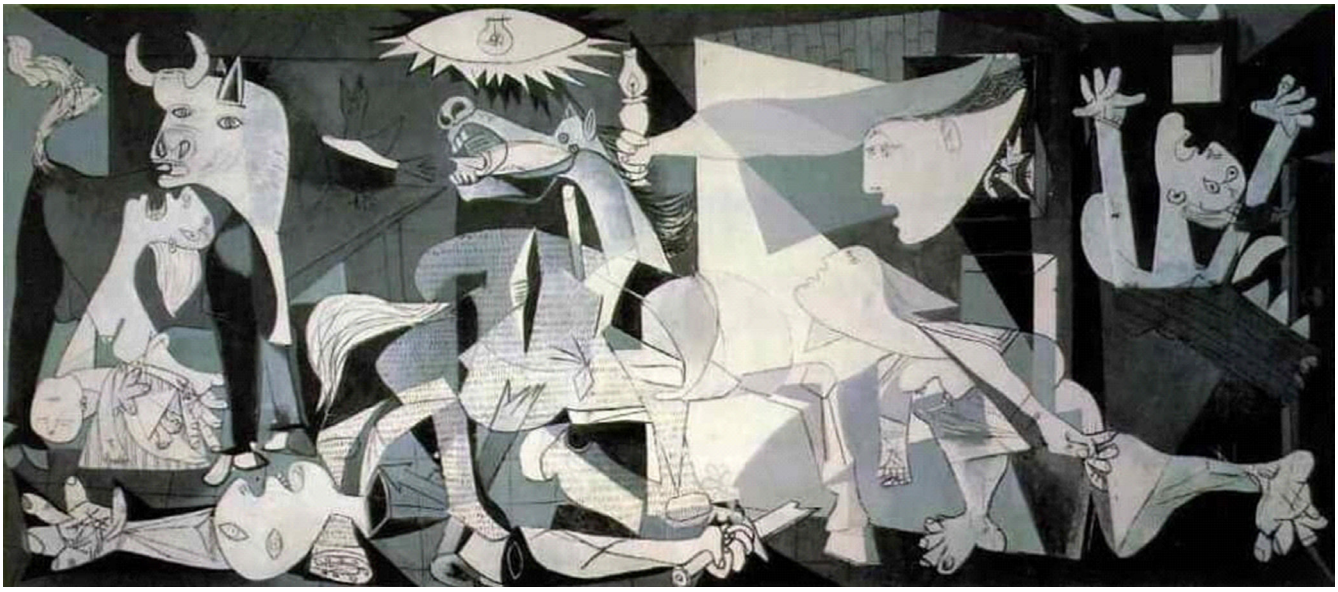
Bhagwani et al.[4] made a comprehensive survey of the literature on GABAergic in the NP and spasticity in chronic SCI. GABAergic neurotransmission in NP has 3 aspects of impact in the cellular and molecular level: neuronal hyperexcitablity, microglial activation as well as cotransporter alterations. Spasticity is caused by the motor neuron hyperexcitability induced increased muscle tone, which can be inhibited by GABA agonist Baclofen effectively. Preventing loss of GABAergic neuron and restoring the inhibitory tone is beneficial in both the NP and the spasticity. The authors summarize the preclinical and clinical study of promoting the inhibitory tone for SCI CNP and spasticity. Promising treatment includes GABAergic drugs, calcium channel blockers and cell therapy.

In this editorial, I would like to extend the concern about the GAGAergic neurotransmission to all aspects of SCI. Not only NP and spasticity were involved in the GAGAergic, but also the locomotion is involved. KCC2 expression as well as its agonist could restore locomotion by modulation of the dormant relay.[5] Treatment such as transplantation of GABA neurons not only promotes locomotive recovery but also reduced spasticity in SCI.[6] Since the neuromodulation is promising in SCI,[7] the GABAergic role in electrical stimulation in SCI to promote functional recovery is also an interesting direction that worthy to explore.

Conflict of Interest: The author has nothing to disclose.

REFERENCES

1. Gadot R, Smith DN, Prablek M, et al. Established and emerging therapies in acute spinal cord injury. Neurospine 2022;19:283-96.
2. Fan B, Wei Z, Feng S. Progression in translational research on spinal cord injury based on microenvironment imbalance. Bone Res 2022;10:35.
3. Shiao R, Lee-Kubli CA. Neuropathic pain after spinal cord injury: challenges and research perspectives. Neurotherapeutics 2018;15:635-53.
4. Bhagwani A, Chopra M, Kumar H. Spinal cord injury provoked neuropathic pain and spasticity, and their GABAergic connection. Neurospine 2022;19:646-68.
5. Chen B, Li Y, Yu B, et al. Reactivation of dormant relay pathways in injured spinal cord by KCC2 manipulations. Cell 2018;174:521-35.e13.
6. Gong C, Zheng X, Guo F, et al. Human spinal GABA neurons alleviate spasticity and improve locomotion in rats with spinal cord injury. Cell Rep 2021;34:108889.
7. Fehlings MG, Velumian AA. The impact of spinal cord neuromodulation on restoration of walking ability after spinal cord injury. Neurospine 2022;19:244-5.



Title: Guernica
Year: 1937
Artist: Pablo Picasso

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