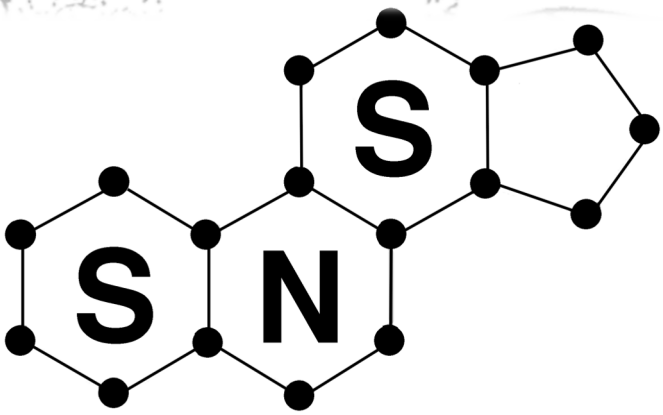
Virtual International Meeting

# STEROIDS AND NERVOUS SYSTEM




## Torino, Italy
## 11-12 and 25-26 February 2021

# ABSTRACT BOOK

**TORINO – 2021**

**ABSTRACTS OF INVITED LECTURES AND FREE CONTRIBUTIONS**

**G.C. Panzica and S. Gotti, editors**

*Conference organized with the support of*

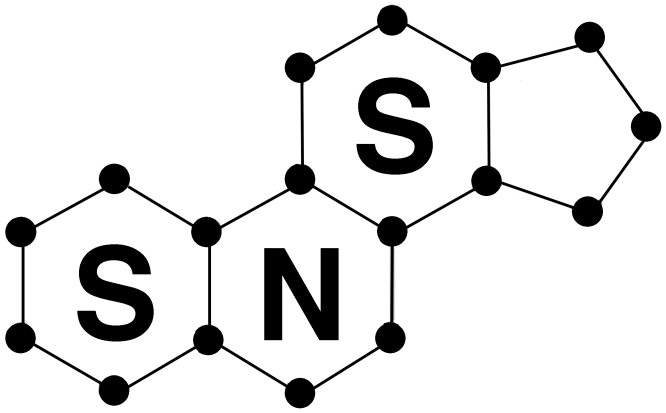
**Fondazione Cavalieri Ottolenghi, Torino**

**Università degli Studi di Milano**
**Università degli Studi di Torino**
**Scuola di Medicina, Torino**

**Dipartimento di Neuroscienze, Torino**
**Dipartimento di Scienze Farmacologiche e Biomolecolari, Milano**
**Neuroscience Institute Cavalieri Ottolenghi (NICO)**
**Istituto Nazionale di Neuroscienze (INN)**

**Journal of Neuroendocrinology (Wiley)**

***We are very grateful to Susanna Monteleone and Maria Lo Grande for their technical support***




# VIRTUAL INTERNATIONAL MEETING

# STEROIDS AND NERVOUS SYSTEM

**Torino, Italy**

**February 11-12 and 25-26, 2021**

## ABSTRACTS OF INVITED LECTURES AND FREE CONTRIBUTIONS

**G.C. Panzica and S. Gotti, editors**

**TORINO – 2021**

# PROGESTERONE ADMINISTRATION REDUCES THE NUMBER OF HYPERTROPHIC MICROGLIA/MACROPHAGES AND MODULATES THE EXPRESSION PROFILE OF M1/M2 MARKERS AND INFLAMMASOME COMPONENTS AFTER ACUTE EXPERIMENTAL SPINAL CORD INJURY

**Raggio M.C.[1,2], Coronel M.F.[3], Ferreyra S.[1], Labombarda F.[4,5], González S.L.[*]**

[1]Laboratorio de Nocicepción y Dolor Neuropático, Instituto de Biología y Medicina Experimental-CONICET, [2]present address: Biopathologie de la Myéline, Neuroprotection et Stratégies Thérapeutiques- UMRS INSERM U1119, Université de Strasbourg- Centre de Recherche en Biomédecine de Strasbourg, France, [3]Instituto de Investigaciones en Medicina Traslacional (IIMT), Universidad Austral-CONICET, Buenos Aires, Argentina, [4]Laboratorio de Bioquímica Neuroendócrina, Instituto de Biología y Medicina Experimental, CONICET, Buenos Aires, Argentina, [5]Departamento de Bioquímica Humana, Facultad de Medicina, Universidad de Buenos Aires, Buenos Aires, Argentina.
*Laboratorio de Nocicepción y Dolor Neuropático, Instituto de Biología y Medicina Experimental-CONICET, Vuelta de Obligado 2490, C1428ADN, Buenos Aires, Argentina; Departamento de Bioquímica Humana, Facultad de Medicina, Universidad de Buenos Aires, Paraguay 2155, C1121ABG, Buenos Aires, Argentina.
E-mail address: sgonzalez@dna.uba.ar

Neuroinflammation is a hallmark of central nervous system pathologies, including spinal cord injury (SCI). In particular, the acute activation of macrophages and resident microglia are critically implicated in the detrimental long-standing consequences of spinal trauma, such as the onset and maintenance of neuropathic pain [5]. Indeed, the fine-tuning of microglia/macrophage polarization from classically-activated (M1, inflammatory) towards alternatively-activated (M2, anti-inflammatory) states represents an active research focus of restorative strategies in a wide range of experimental nervous system trauma, including SCI [1], and may offer a therapeutic opportunity to prevent the risk of developing pain later. We have previously shown that progesterone, a neuroactive steroid, exhibits neuroprotective and pro-myelinating actions in experimental spinal lesions [3, 6] and could stand as a promising repositioning molecule for timely targeting the harmful aspects of acute inflammation [2, 4], while preserving anti-inflammatory and pro-reparative features. Hence, by using real time RT-PCR and immunohistochemical techniques we evaluate the hypothesis that progesterone could modulate microglia/macrophage morphology and the mRNA expression profile of cytokines, M1/M2 biomarkers and inflammasome components at the dorsal spinal cord level, a critical site for nociceptive processing, in a well-recognized rat model of spinal hemisection that develops central neuropathic pain. Here we observed that progesterone administration (16 mg/kg, daily sc injection) within the acute phase (1–3 days post-SCI) significantly reduced the injury-induced mRNA expression of several biomarkers of neuroinflammation, including critical inflammasome components NLRP3 and ASC, two related pro-inflammatory cytokines IL-1β and IL-18, ATP-gated P2X7 ion channel and inducible nitric oxide synthase, all signatures associated with M1 phenotype, while maintaining high levels of Arginase 1 and CD206, both M2-associated markers, and the anti-inflammatory cytokine TGF-β. Along with these changes, progesterone-treated animals did not change the injury-induced increase in the total number of OX-42 microglia/macrophages positive profiles, but exhibited a significantly higher number of ramified cells and a concomitant decrease in hypertrophic/ameboid phenotypes in the dorsal horn as compared to injured-animals receiving vehicle. Collectively, our results suggest that progesterone may avoid a broad suppression of microglia/macrophages, promoting a balance towards anti-inflammatory phenotypes that may underlie the anti-allodynic mechanisms of this steroid.

These findings add new evidence to further stimulate the study of neuroactive steroids-based therapies and may open novel translational perspectives for effectively modulating the acute neuroinflammatory cascade in order to prevent the harmful enduring outcomes after spinal trauma, such as central pain.

*Supported by grants from Consejo Nacional de Investigaciones Científicas y Tecnológicas (CONICET, PIP 112-201501-00266), Agencia Nacional de Promoción Científica y Técnica (PICT 2018-02152)*

**Reference List**

[1] Akhmetzyanova E, Kletenkov K, Mukhamedshina Y and Rizvanov A (2019) Different approaches to modulation of microglia phenotypes after spinal cord injury. Front. Syst. Neurosci. 13:37. doi: 10.3389/fnsys.2019.00037

[2] Coronel MF, Raggio MC, Adler NS, De Nicola AF, Labombarda F, González SL (2016). Progesterone modulates pro-inflammatory cytokine expression profile after spinal cord injury: Implications for neuropathic pain. J Neuroimmunol. 292:85-92. doi: 10.1016/j.jneuroim.2016.01.011.

[3] González SL (2020) Progesterone for the treatment of central nervous system disorders: the many signaling roads for a single molecule. Neural Regen Res 15(10):1846-1847. doi:10.4103/1673-5374.280314

[4] Gonzalez SL, Meyer L, Raggio MC, Taleb O, Coronel MF, Patte-Mensah C, Mensah-Nyagan AG (2019). Allopregnanolone and progesterone in experimental neuropathic pain: former and new insights with a translational perspective. Cell Mol Neurobiol 39:523-537

[5] Ji R-R, Xu Z-Z, Gao Y-J (2014). Emerging targets in neuroinflammation-driven chronic pain. Nat Rev Drug Discov. 13(7): 533–548. doi:10.1038/nrd4334.

[6] Labombarda F, González SL, Lima A, Roig P, Guennoun R, Schumacher M, de Nicola AF (2009) Effects of progesterone on oligodendrocyte progenitors, oligodendrocyte transcription factors, and myelin proteins following spinal cord injury. Glia 8:884-97. doi: 10.1002/glia.20814.