



## Seminars *in* Neuroscience

2019 - 2020

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**Title: Electroconvulsive Shock Enhances Responsive Motility and Purinergic Currents in hippocampal Microglia**

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**Title: The role of astrocyte calcium microdomains in prolonged LTP maintenance in the perirhinal cortex**

***December 12, 2019 @ 4 pm***

*Dipartimento di Scienze della Vita e Biologia dei Sistemi  
Via Accademia Albertina 13 - Aula C*





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## Dr. Stefano Vicini

*Department of Pharmacology and Physiology  
Georgetown University, Washington DC, USA,  
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### Electroconvulsive Shock Enhances Responsive Motility and Purinergic Currents in hippocampal Microglia

Microglia are in a privileged position to both affect and be affected by neuroinflammation, neuronal activity and injury, which are all hallmarks of seizures and the epilepsies. Hippocampal microglia become activated after prolonged, damaging seizures known as status epilepticus (SE). However, since SE causes both hyperactivity and injury of neurons, the mechanisms triggering this activation remain unclear, as does the relevance of the microglial activation to the ensuing epileptogenic processes. In this study, we use electroconvulsive shock (ECS) to study the effect of neuronal hyperactivity without neuronal degeneration on mouse hippocampal microglia. Unlike SE, ECS did not alter hippocampal CA1 microglial density, morphology, or baseline motility. In contrast, both ECS and SE produced a similar increase in ATP-directed microglial process motility in acute slices, and similarly upregulated expression of the chemokine C-C motif chemokine ligand 2 (CCL2). Whole-cell patch-clamp recordings of hippocampal CA1sr microglia showed that ECS enhanced purinergic currents mediated by P2X7 receptors in the absence of changes in passive properties or voltage-gated currents, or changes in receptor expression. This differs from previously described alterations in intrinsic characteristics which coincided with enhanced purinergic currents following SE. These ECS-induced effects point to a “seizure signature” in hippocampal microglia characterized by altered purinergic signaling. These data demonstrate that ictal activity per se can drive alterations in microglial physiology without neuronal injury. These physiological changes, which up until now have been associated with prolonged and damaging seizures, are of added interest as they may be relevant to electroconvulsive therapy (ECT), which remains a gold-standard treatment for depression.



## Dr. Gabriele Losi

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### The role of astrocyte calcium microdomains in prolonged LTP maintenance in the perirhinal cortex

Intracellular  $\text{Ca}^{2+}$  transients in astrocytes play a key role in the modulation of synaptic transmission and plasticity in brain circuits. Until recently  $\text{Ca}^{2+}$  signaling in fine processes was hampered by technical limitations. With the advent of genetically encoded calcium indicators and multi-photon laser scanning microscopy, it is now possible to study the  $\text{Ca}^{2+}$  microdomains in astrocytic thin processes. Of note, genetic tools to selectively reduce astrocyte  $\text{Ca}^{2+}$  signals in vivo are also available nowadays. We took advantage of these tools to study the role of astrocytic  $\text{Ca}^{2+}$  dynamics on TBS induced prolonged LTP maintenance mediated by glial BDNF recycling (Vignoli et al 2016). To allow LTP maintenance the release of astrocyte recycled BDNF must occur in a restricted time window after LTP induction. We here studied  $\text{Ca}^{2+}$  signals before, during and soon after LTP induction with TBS during the critical time window. We used 2P-laser microscopy in layer II/III astrocytes of perirhinal cortex in slices. We found that in basal conditions  $\text{Ca}^{2+}$  events were restricted to microdomains in thin processes. TBS afferent stimulation for LTP induction induced transient, large, TTX-sensitive  $\text{Ca}^{2+}$  events that involved all astrocytic compartments. Soon after the TBS, and during the critical window after TBS, astrocytes recovered their basal  $\text{Ca}^{2+}$  activity in microdomains. To selectively inhibit astrocyte  $\text{Ca}^{2+}$  transients, we used novel genetic tools such as the IP3-sponge p130PH and the calcium extruding human plasma membrane  $\text{Ca}^{2+}$  pump (hPMCA). Following p130PH or hPMCA expression we found that both  $\text{Ca}^{2+}$  transients and the long-lasting LTP were reduced. In conclusion our data reveal that astrocyte  $\text{Ca}^{2+}$  microdomains in thin processes play a crucial role for LTP maintenance, unveiling a novel function of this form of  $\text{Ca}^{2+}$  activity for brain function.

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**Host: Serena Bovetti & Alessandra Fiorio Pla**