



Presentation Abstract

Program#/Poster#: 343.19/G50

Title: The role of astrocytes in gamma oscillations in the brain

Location: Halls B-H

Presentation Time: Monday, Nov 15, 2010, 10:00 AM -11:00 AM

Authors: ***H. S. LEE**¹, A. GHETTI¹, A. PINTO-DUARTE¹, F. GALIMI¹, J. PINA-CRESPO¹, G. SANNA², I. VERMA¹, T. SEJNOWSKI¹, S. F. HEINEMANN¹;
¹The Salk Inst., LA JOLLA, CA; ²The Scripps Res. Inst., La Jolla, CA

Abstract: Glial cells have been thought to serve homeostatic functions in the brain. However, recent reports have suggested a potential role for astrocytes in neurotransmission. Various neurotransmitter receptors are expressed in astrocytes, allowing these cells to respond to exogenously applied neurotransmitters or neuronal stimulation with an increase in cytosolic calcium. Furthermore, in response to an intracellular calcium increase, astrocytes can release glutamate. The observed spreading of the calcium signals in the astrocytic network suggest that glutamate released from these cells may affect the excitability of large neuronal networks.

We have tested this hypothesis by generating a lentiviral vector aimed at targeting the expression of Tetanus toxin (TeNT) in astrocytes in hippocampal slices. Expression of the toxin in astrocytes blocks the calcium dependent release of glutamate from these cells. When astrocytic glutamate release is blocked by TeNT, the duration of gamma oscillations induced by carbachol is reduced 5 fold, compared to control slices. The effect of the toxin can be reversed by exogenously applying a glutamate receptor agonist (AMPA). These data indicate that astrocytes may have a previously unsuspected role in information processing by modulating the oscillatory behavior of neuronal networks.

To investigate the *in vivo* role of the astrocytes in gamma oscillations and the function of the gamma oscillation in behavior, the transgenic mouse line of TeNT-GFP was generated (TRE-loxP-STOP-loxP-TeNT-GFP). In this new line of mouse, the expression of TeNT-GFP is regulated regionally and temporally. In the

triple transgenic mouse of TRE-loxP-STOP-loxP-TeNT-GFP; GFAP-tTA; GFAP-CreERt2, the transactivator tTA can activate the expression of the gene under the tet-responsive element (TRE) promoter. However, in this scheme, the expression of TeNT-GFP is suppressed by the inserted translational and transcriptional inhibition sequence (STOP) until the STOP is excised by CreERt2 activated by tamoxifen injection. The expression of toxin will be stopped when tTA is deactivated by doxycycline. Both tTA and CreERt2 are expressed only in astrocytes under the human astrocytic specific promoter, gfa2.

We established a line of mice with the properly restricted expression of the toxin with tamoxifen activation and doxycycline suppression. The transgenic mice with tamoxifen injection did not show any obvious abnormality, suggesting specific expression of the toxin in astrocytes and not in neurons. *In vivo* EEG recording and the behavior of the mice are being characterized.

Disclosures: **H.S. Lee**, None; **A. Ghetti**, None; **A. Pinto-Duarte**, None; **F. Galimi**, None; **J. Pina-Crespo**, None; **G. Sanna**, None; **I. Verma**, None; **T. Sejnowski**, None; **S.F. Heinemann**, None.

Keyword(s): Astrocytes
Gamma Oscillation
mouse

Support: Salk Innovation Grant

[Authors]. [Abstract Title]. Program No. XXX.XX. 2010 Neuroscience Meeting Planner. San Diego, CA: Society for Neuroscience, 2010. Online.

2010 Copyright by the Society for Neuroscience all rights reserved. Permission to republish any abstract or part of any abstract in any form must be obtained in writing by SfN office prior to publication.