Is there a role for astrocytes in $VPAC_1$ receptor-mediated modulation of GABAergic transmission and synaptic plasticity by endogenous VIP?

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Abstract / MSc thesis project proposal:

Vasoactive intestinal peptide (VIP), acting on $VPAC_1$ receptors, is released during synaptic plasticity induction and influences hippocampal synaptic plasticity through modulation of disinhibition [1,2]. VIP expression was reported only in a few populations of GABAergic interneurons and VIP is known to regulate GABA release through activation of $VPAC_1$ and $VPAC_2$ receptors[3]. Astrocytes are an important cellular component of GABAergic synapses and can greatly influence synaptic GABA availability[4]. In addition, astrocytes can be activated by synaptic GABA, that enhances intracellular Ca^{2+} through several signaling pathways. This may in turn trigger the release of gliotransmitters[5]. Gliotransmitters released from astrocytes, including neuropeptides, have been described to modulate LTP induction and expression[6]. Astrocytes express both $VPAC_1$ and $VPAC_2$ VIP-selective receptors[7] but their role in VIP modulation of GABAergic transmission and synaptic GABA availability was never investigated. Likewise, the influence of these receptors in astroglial responses to GABA stimuli was never studied.

This project aims to use hippocampal astrocyte cultures to investigate: 1) The influence of $VPAC_1$ and $VPAC_2$ receptors on astroglial GABA uptake; 2) The astrocytic Ca^{2+} responses to transient GABA stimuli, as would occur at GABAergic synapses during synaptic plasticity; 3) the presence of VIP, $VPAC_1$ and $VPAC_2$ receptors in astrocyte cultures as accessed by immunocytochemistry.

The influence of $VPAC_1$ and $VPAC_2$ receptors on astroglial GABA uptake kinetics mediated by GAT-1 and GAT-3 receptors will be studied as previously described[4], using selective agonists and antagonists for these receptors. Astrocytic Ca^{2+} responses to transient GABA stimuli will be monitored using the Ca^{2+}-sensitive fluorescent dye fura-2 acetoxymethyl ester (fura-2 AM)[8]. VIP, $VPAC_1$ and $VPAC_2$ receptors will be detected in hippocampal astrocyte cultures by immunocytochemistry.

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Students selected for this project, after thesis registration, are eligible to apply to the BioISI Junior Programme (supporting 8 students with a 6-month Scholarship(BII), being the selection criterium the academic merit of the candidates.