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Synaptic activation of kainate receptors gates presynaptic CB(1) signaling at GABAergic synapses.

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About the work

Neurons are capable of integrating information spatially and temporally. They can process electrical signals at specific locations called synapses, which can be excitatory or inhibitory. The information can then be built or not into an output signal, the action potential, carried by the axon. The dynamic balance between excitation and inhibition of synaptic signals is crucial for the functioning of neural circuits. An alteration of this balance can lead to pathological conditions such as epileptic states or abnormal cognitive processes. In normal brain functioning, the balance between excitation and inhibition can be highly regulated by phenomena of synaptic plasticity of excitatory or inhibitory synapses.
This study published in the Nature Neuroscience journal reflects a unique mechanism of interaction between excitatory and inhibitory synapses in the rodent hippocampus. Our work describes a new form of short-term plasticity of inhibitory synapses that involves glutamate receptors, the major excitatory neurotransmitter in the brain. These receptors are located on the terminal axons of inhibitory neurons, releasing GABA, major inhibitory neurotransmitter in the nervous system.

Our experiments show that activation of glutamate receptors leads to enhancement of the action of the endogenous cannabinoids (endocannabinoids) and their receptors (specifically cannabinoid receptor type 1). This modulation allows a local control in the release of GABA by glutamate under conditions of sustained activity of excitatory neurons. Moreover, it suggests that the efficiency of the endocannabinoids and its receptors can be regulated by the synaptic activity of glutamate receptors of a particular subtype: kainate receptors.

Thus, this study describes a new level of regulation of synaptic excitation over synaptic inhibition by an unexpected mechanism of cellular partnership. Although, new experimental models and pharmacological approaches should be designed to access the problematic of abnormal brain homeostasis, these results might pave way to new cognitive therapeutics.

About the author

I graduated in Biology at University of Coimbra in 2004. My first contact with neuroscience was as an undergraduate during a research training with Dr. Ana P. Silva and Dr. João Malva at Centre for Neuroscience and Cell Biology (Coimbra). During this period I was interested in the neuroprotective role of the neuropeptide NPY in the rodent kainate seizure model. This work has lead to the collaboration articles in journals such as FASEB Journal and Journal of Neurochemistry. In 2005 I joined the PhD programme BEB at the CNC, Coimbra. I develop my PhD project at the NeuroCentre Magendie (Bordeaux, France) under the supervision of Dr. Giovanni Marsicano and Dr. Ana P. Silva, with the close collaboration of Dr. Christophe Mulle. I used electrophysiological and pharmacological techniques in acute brain slices to study the role of the endocannabinoid system in the hippocampus and its role in modulating GABAergic synaptic plasticity along with the gating action of kainate receptors. This work led to the publication of scientific articles in high impact international peer reviewed journals, including Nature Neuroscience and Journal of Neuroscience (*in press*). And, in July of 2010 I defended my thesis at the University of Coimbra (Portugal) under the title " *Unravelling a functional interaction between kainate receptors and the endocannabinoid system".* Currently, I am a postdoctoral fellow at the laboratory of Dr. Alberto Bacci at the EBRI institute (Roma, Italy). My main research interest is GABAergic synaptic plasticity at the neocortical circuitry. I am currently focused on neocortical pyramidal neurons and how they integrate inhibitory inputs from different interneuron populations.