



HAL
open science

Endocannabinoids mediate spike-timing dependent potentiation and depression: a model-based experimental approach

Yihui Cui, Vincent Paille, Bruno Delord, Stéphane Genet, Elodie Fino,
Laurent Venance, Hugues Berry

► To cite this version:

Yihui Cui, Vincent Paille, Bruno Delord, Stéphane Genet, Elodie Fino, et al.. Endocannabinoids mediate spike-timing dependent potentiation and depression: a model-based experimental approach. Twenty Second Annual Computational Neuroscience Meeting: CNS 2013, Jul 2013, Paris, France. 14 (Suppl 1), O1 (1 p.), 2013. hal-00842299

HAL Id: hal-00842299

<https://inria.hal.science/hal-00842299v1>

Submitted on 8 Jul 2013

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

ORAL PRESENTATION

Open Access

Endocannabinoids mediate spike-timing dependent potentiation and depression: a model-based experimental approach

Yihui Cui^{1,2,3}, Vincent Paille^{1,2,3}, Bruno Delord^{3,4}, Stéphane Genet^{3,4}, Elodie Fino^{1,2,3}, Laurent Venance^{1,2,3*}, Hugues Berry^{5,6*}

From Twenty Second Annual Computational Neuroscience Meeting: CNS*2013
Paris, France. 13-18 July 2013

Activity-dependent long-term potentiation (LTP) and depression (LTD) of synaptic strength underlie multiple forms of learning and memory. Endocannabinoids (eCBs) have consistently been described as mediators of short- or long-term synaptic depression through the activation of the endocannabinoid-type-1 receptor (CB1R) or the transient receptor potential vanilloid-type-1 (TRPV1). Here we investigated whether eCBs could also promote long-term potentiation, an essential requirement for eCBs to be a genuine bidirectional system and to fully encode for learning and memory.

To this aim, we combined *in vitro* spike timing-dependent plasticity (STDP) protocols in rodents and a biophysical model of the signaling pathways likely to be involved. The model describes the temporal dynamics of three main signaling systems: the postsynaptic NMDAR-CaMKII pathway (adapted from [1]), the postsynaptic mGluR-PLC β system (adapted from [2]) as well as postsynaptic eCB synthesis and subsequent activation of postsynaptic TRPV1 and presynaptic CB1R in a retrograde fashion. Using the model to drive the experiments, we uncovered the existence of an eCB-mediated spike-timing dependent potentiation (eCB-LTP). This eCB-LTP is homosynaptic, astrocyte-independent and expressed in young and adult animals and across various brain regions (cortex and striatum), supporting its role as a widespread signaling system for spike-based plasticity. We deciphered the signaling pathways (pre- and postsynaptic receptors

and enzymes) involved in this new form of plasticity and demonstrated that eCB plasticity has a postsynaptic induction and a presynaptic maintenance. On the postsynaptic side, our results show that the dynamics of free cytosolic calcium is a key element for eCB-LTP induction. eCB-LTP is triggered when eCB transients reach sufficiently high levels. Since the enzymes that synthesize eCBs are calcium-activated, eCB-LTP induction requires large levels of cytosolic calcium. On the presynaptic side, eCBs encode for bidirectional plasticity via a triad composed of eCB levels, presynaptic PKA and presynaptic CaN: intermediate eCB levels promote presynaptic CaN activity, that yields eCB-LTD, whereas large eCB amplitudes favor presynaptic PKA activity, which leads to eCB-LTP. Both effects are predicted to rely on the inhibition exerted by activated CB1R on presynaptic adenylate cyclase and P/Q-type voltage-gated calcium channels. Moreover, we show that eCB-LTP and eCB-LTD can be induced sequentially in the same neuron, depending on the cellular conditioning paradigm. Therefore, our results demonstrate that eCBs, just like glutamatergic or GABAergic signaling, form a generic system able to encode for bidirectional plasticity and capable of genuine homeostasis.

Lastly, we found that eCB-LTP is triggered by very few paired spikes (5 to 10 post-pre spikes at 1 Hz are enough). Thus, eCB-LTP provides synapses with a mechanism able to react to the very first occurrences of incoming activity. This ability strongly contrasts with NMDAR-dependent LTP which, in a classical (1 Hz) STDP context, requires the iteration of at least 75-100 paired stimulations to be expressed, at odds with the observations that new associative memories and behavioral rules can be learned within few or even a single trials in mammals (e.g. [3]). Our

* Correspondence: laurent.venance@college-de-france.fr; hugues.berry@inria.fr

¹Team Dynamic and Pathophysiology of Neuronal Networks, Center for Interdisciplinary Research in Biology (CIRB), CNRS UMR7241/INSERM U1050, Collège de France, 75005 Paris, France

⁵Team Beagle, INRIA Rhone-Alpes, 69603 Villeurbanne, France

Full list of author information is available at the end of the article

results suggest that eCB-LTP may represent a neuronal substrate for such rapid learning abilities.

Author details

¹Team Dynamic and Pathophysiology of Neuronal Networks, Center for Interdisciplinary Research in Biology (CIRB), CNRS UMR7241/INSERM U1050, Collège de France, 75005 Paris, France. ²Memolife Laboratory of Excellence and Paris Science Lettres Research University, Paris, France. ³University Pierre et Marie Curie, ED 158, 75005 Paris, France. ⁴Institute of Intelligent Systems and Robotics (ISIR), 75005 Paris, France. ⁵Team Beagle, INRIA Rhone-Alpes, 69603 Villeurbanne, France. ⁶University of Lyon, LIRIS UMR5205, 69621 Villeurbanne, France.

Published: 8 July 2013

References

1. Graupner M, Brunel N: STDP in a bistable synapse model based on CaMKII and associated signaling pathways. *PLoS Comput Biol* 2007, **3**:e221.
2. De Pittà M, Goldberg M, Volman V, Berry H, Ben-Jacob E: Glutamate regulation of calcium and IP3 oscillating and pulsating dynamics in astrocytes. *J Biol Phys* 2009, **35**:383-411.
3. Pasupathy A, Miller EK: Different time courses of learning-related activity in the prefrontal cortex and striatum. *Nature* 2005, **433**:873-876.

doi:10.1186/1471-2202-14-S1-O1

Cite this article as: Cui et al.: Endocannabinoids mediate spike-timing dependent potentiation and depression: a model-based experimental approach. *BMC Neuroscience* 2013 **14**(Suppl 1):O1.

Submit your next manuscript to BioMed Central
and take full advantage of:

- Convenient online submission
- Thorough peer review
- No space constraints or color figure charges
- Immediate publication on acceptance
- Inclusion in PubMed, CAS, Scopus and Google Scholar
- Research which is freely available for redistribution

Submit your manuscript at
www.biomedcentral.com/submit

