

Patricia Bonnavion, PhD

F.R.S.-FNRS ULB-UNI Research Associate

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The Waking Brain team Principal Investigator. Lab of Neurophysiology, ULB Neuroscience Institute, Brussels, Belgium

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### Personal statement

As a neuroscientist, I am driven by my ambition to untangle sleep and arousal brain circuits and understand how their interplay generates unique behavioral and cognitive abilities, and how they contribute to mental illnesses.

### Education training

2014-2019: **Postdoctoral training.** *Université Libre de Bruxelles ULB, Belgium.*

2009-2013: **Postdoctoral training.** *Stanford University, USA.*

2004-2008: **PhD in Physiology and Physiopathology.** *Sorbonne Université Paris 6, France.*

2002-2004: **Master in Cellular Biology/Physiology & Neurosciences (DEA).** *Sorbonne Université.*

2001-2002: **Bachelor (Licence) Integrative Biology.** *Université Paris Diderot, France.*

### Positions & research

- **2019- Present F.R.S.-FNRS Research associate “Chercheuse Qualifiée”.** *The Waking Brain team Principal Investigator. ULB Neuroscience Institute, Brussels, Belgium.*

**Monoaminergic-basal ganglia interplay in arousal functions.** Our research interests focus on the monoamine-basal ganglia (BG) interplay in arousal functions in healthy and pathological mouse models of BG impairments. We employ state of the art approaches -opto- and chemo-genetics, and in vivo measurement of neuronal circuits dynamics- to untangle monoamines and BG contributions to arousal and cognitive dysfunctions occurring in numerous neurodegenerative and psychiatric disorders. We notably question the role of sleep disturbances and arousal dysregulations as premature risk factors.

- **2014-2018 European Marie Skłodowska-Curie Actions independent postdoctoral fellow.** *Laboratory of Neurophysiology directed by Prof. Serge Schiffmann. ULB-UNI, Brussels, Belgium.*

**Reappraisal of the striatal mode of operation.** This study is bringing substantial proofs revising the canonical model of striatal motor control identifying neurons co-expressing dopaminergic D1 and D2 receptors as a third striatal pathway that is stabilizing striatal motor control and critical in conveying motor responses to dopaminergic drugs. This study has a large impact on dopamine central actions in the striatum/caudate putamen and on motor diseases associated with impairments of the BG system.

**Circuit-based deconstruction of Attention deficit and Hyperactive disorder with optogenetic control.** This work identified the circuits and mechanisms through which psychostimulants exert therapeutical paradoxical calming effects involving specific dysfunctions of the BG, which are associated with attention deficits, impulsivity and hyperactivity.

- **2009-2013 Stanford University postdoctoral fellow, California, USA.** *Department of Psychiatry and Behavioral Sciences. Supervisor: Prof. Luis de Lecea.*

**Interrogation of monoaminergic pontine and hypothalamic circuits controlling arousal, stress and hypervigilance.** My postdoctoral research resulted in two major publications refining the role and circuits of hypothalamic arousal systems in controlling brain sleep/wake switches and arousal states notably leading to pathological levels of hyperarousal associated with generalized stress and anxiety. (NARSAD young investigator grant).

- **2004-2008 PhD in Physiology and Physiopathology, Sorbonne Université Paris 6, France.** *Unité INSERM U677 directed by Prof. Michel Hamon. Supervisors: Joëlle Adrien & Véronique Fabre.*

### ***Brainstem monoaminergic systems regulating vigilance states: role of the serotonergic neurotransmission.***

My PhD work led to highlight a high level of functional heterogeneity amongst serotonergic (5-HT) neurons and provided a comprehensive map of 5-HT inhibitory connections in the control of sleep and wakefulness identifying a new circuit involving a pontine-hypothalamic loop conveying both spatial information and arousal (3 distinguished PhD prizes).

#### Grants, honors & awards

- 2021** Fonds d'Encouragement à la Recherche ULB FER grant (50,000€).
- 2020** Fonds d'Encouragement à la Recherche ULB FER grant (50,000€).
- 2019** Fonds de la Recherche Scientifique F.R.S.-FNRS Crédit de Recherche CDR grant (60,000€).
- 2019** F.R.S.-FNRS Crédit de Recherche CDR **starting grant** (20,000€).
- 2018** F.R.S.-FNRS **Scientific Collaborator individual contract** (31,700€).
- 2017** Belgium Society for Neuroscience (BSN) **best presentation award**.
- 2016** European Marie Skłodowska-Curie Actions (MSCA) **individual grant** (180,000€).
- 2014** ULB International chair **postdoctoral grant** (CCCI, ex BRIC) (27,000€).
- 2013** NARSAD **Young investigator award**. American Brain and Behavior Foundation (\$60,000).
- 2010** Hilda and Preston Davis Foundation **postdoctoral grant** (\$135,000).
- 2009** IBRO **Research grant** (35,000€).
- 2009** Albert Sézary **Distinguished PhD research Prize**. Académie Nationale de Médecine.
- 2008** **Distinguished PhD Research Prize** from the Singer-Polignac Foundation.
- 2008** **Distinguished PhD research Prize**. Association Française des Femmes Diplômées des Universités.
- 2008** French Medical Research Foundation (FRM) **PhD grant** (34,000€).
- 2004** French National Institute (MRT) **PhD grant** (72,000€).

#### Publications et Communications

##### • **Articles and Scientific Reviews**

1. Cutando L, Puighermanal E, Castell L, Tarot P, Bertaso F, ***Bonnaïon P***, de Kerchove d'Exaerde A, Isingrini E, Galante M, Dallerac G, Pascoli V, Lüscher C, Giros B, Valjent E (2020). Regulation of GluA1 phosphorylation by d-amphetamine and methylphenidate in the cerebellum. *Addiction Biology* (in press)
2. ***Bonnaïon P\*#***, Pozuelo-Fernández E\*, Varin C, de Kerchove d'Exaerde A# (2019). It takes two to tango: the direct and indirect pathways orchestration of motor learning and behavioral flexibility. *Neurochem Int*, 124:200-214. \*co-first authors. #co-corresponding authors.
3. Chazalon M, Dumas S, Bernard JF, Sahly I, Tronche F, Hamon M, Adrien J, Fabre V\*, ***Bonnaïon P\**** (2018). The GABAergic Gudden's dorsal tegmental nucleus: a new relay for serotonergic regulation of sleep-wake behavior in the mouse. *Neuropharm*, 138:315-330. \*co-last authors, co-corresponding author.
4. ***Bonnaïon P\*#***, Fujita A\*, Wilson MH, Mickelsen L, Bloit J, de Lecea L, Jackson A# (2017) Hypothalamic Tuberomammillary Nucleus Neurons: Electrophysiological Diversity and Essential Role in Arousal Stability. *J Neurosci.*, 37:9574-92. \*co-first authors, #co-corresponding authors.
5. ***Bonnaïon P***, Mickelsen L, Fujita A, de Lecea L, Jackson A (2016) The hubs and spokes of the lateral hypothalamus: cell-types, circuits and behavior. *J physiol* (doi:10.1113/JP271946)
6. Rolls A\*, Pang WW\*, Ibarra I\*, Colas D, ***Bonnaïon P***, Korin B, Heller HC, Weissman IL, de Lecea L (2015) Sleep disruption impairs hematopoietic stem cell transplantation in mice. *Nat Comm*: 8516.
7. ***Bonnaïon P***, Jackson AC, Carter ME, de Lecea L (2015) Antagonistic interplay between hypocretin and leptin in the lateral hypothalamus regulates stress responses. *Nat Comm*: 6266.
8. Kiyasova V, ***Bonnaïon P***, Scotto S, Fabre V, Sahly I, Tronche F, Deneris E, Gaspar P, Fernandez S (2012) A subpopulation of serotonergic neurons that do not express the 5-HT<sub>1A</sub> autoreceptor. *ACS Chemical Neuroscience* 4(1): 89-95.
9. Carter ME, Brill J, ***Bonnaïon P***, Huguenard JR, Huerta R, de Lecea L (2012) A mechanism for Hypocretin-mediated sleep-to-wake transitions. *PNAS* 109(39): 2635-44.
10. ***Bonnaïon P***, de Lecea L (2010) Hypocretins in the control of sleep and wakefulness. *Curr Neurol Neurosci Rep* 10 (3): 174-9. (review)
11. ***Bonnaïon P***, Bernard JF, Hamon M, Adrien J, Fabre V (2010) Heterogeneous distribution of the 5-HT<sub>1A</sub> receptor mRNA in chemically identified neurons of the mouse rostral brainstem. *J Comp Neurol* 518 (14): 2744-70.

12. Kallupi M, Cannella N, Economidou D, Ubaldi M, Ruggeri B, Weiss F, Massi M, Marugan J, Heilig M, **Bonnavion P**, de Lecea L, Ciccocioppo R (2010) Neuropeptide S facilitates cue-induced relapse to cocaine seeking through activation of the hypothalamic hypocretin system. *PNAS* 107 (45): 19567-72.
13. Loucif AC, **Bonnavion P**, Macri B, Golmard JL, Boni C, Melfort M, Leonard G, Lesch KP, Adrien J, Jacquin TD (2006) Gender-dependent regulation of G-protein-gated inwardly rectifying potassium current in dorsal raphe neurons of knock-out mice devoid of the 5-hydroxytryptamine transporter. *J Neurobiol* 66 (13): 1475-88.
14. Charlat S, **Bonnavion P**, Merçot H (2003) Wolbachia segregation dynamics and levels of cytoplasmic incompatibility in *Drosophila sechellia*. *Heredity* 90(2): 157-61.

#### • Book Chapters

Fabre V, Krystal A & **Bonnavion P** (in press) Serotonin and Sleep. Principles and Practice of Sleep Medicine, 7<sup>th</sup> edition. Dement, W.C., Kryger M.H., Roth T. (Eds). Elsevier.

Varin C, **Bonnavion P** (2019) Pharmacosynthetic deconstruction of sleep-wake circuits in the brain. "Sleep-Wake Neurobiology and Pharmacology" series vol 253 of "Handbook of Experimental Pharmacology", H.P. Landolt; D.J. Dijk. (Eds). Springer International Publishing.

#### • Lectures & Invitations

**2021** A reassessment of how the striatum processes motor control, from normal to pathological conditions in mice models. **14th meeting of the Belgium Society for Neuroscience, Brussels.**

**2020** Imaging and control of neuronal activity in animals. Invitation for **Neuropsychology Master courses at ULB.**

**2019** Cracking the neural code of arousal homeostasis: significance of parallel brain networks. **IRIBHM Seminars, ULB, Brussels, Belgium.**

**2017** Opto- and chemo-genetic control of vigilance states. **Neuroconferences, Lyon, France.**

**2017** A critical review on the new genetic methods applied to the study of sleep networks. **First ESRS School, Frejus.**

**2017** Diversity of TMN histamine neurons and their role in arousal stability. **12th meeting of the Belgium Society for Neuroscience, Gent.**

**2017** Ontogenetic dissection of hypothalamic sleep-wake networks. **Lecture invitation by Pr Helmut Haas, University of Düsseldorf (UKD), Germany.**

**2016** Optogenetic deconstruction of hypothalamic networks linking stress, sleep and food intake. **Neuroconferences, Lyon, France.**

**2016** Optogenetic control of histamine neurons in HDC::Cre mutant mice. **23<sup>rd</sup> congress of the European Sleep Research Society, Bologna, Italy** (Chair of the symposium).

**2016** Understanding how the brain regulates behavior through optogenetics. **Workshop & Symposium on electrophysiology organized by IUAP - P7/10 consortium, Brussels, Belgium.**

**2016** Hypocretin and leptin modulate stress. **International Regulatory Peptides Society, Rouen, France.**

**2014** Dissecting the neural circuits of hyperarousal and neuropsychiatric diseases with optogenetics in the behaving mouse. **Annual Conference of the ULB-UNI, Ittre, Belgium.**

**2013** The lateral hypothalamus: Gatekeeper of the stress neuroendocrine response. **Département de Neurobiologie, invited by Dr Thierry Gallopin, ESPCI, Paris, France.**

**2012** A neural circuit in the lateral hypothalamus translates signals about energy balance into glucocorticoid secretion. **Annual meeting of the Hilda & Preston Davis Foundation, NYC, USA. San Diego, USA.**

#### Peer-Reviewing activities

**Editorial board member:** Frontiers in Neuroanatomy, Frontiers in Sleep and Circadian Rhythms.

**Reviewer** on an Ad-hoc basis for Sleep, CNS Neuroscience & Therapeutics, European Journal of Neuroscience, Frontiers in Systems Neuroscience, Neuroscience, Frontiers in Neural Circuits.