## A. PERSONAL DETAILS

### PERSONALIA

1.	Name:	Frank Julius Meye (m)

- 2. Birth date 19-04-1984
- 3. Born in: Utrecht, The Netherlands

4. Professional address
Department of Translational Neuroscience
Brain Center | UMC Utrecht
Universiteitsweg 100; 3584 CG Utrecht; The Netherlands
Office: Stratenum 4.231



- 5. Contact information
  - a. Phone +31 (0)88 756 1234
  - b. Email <u>f.j.meye-2@umcutrecht.nl</u>
- Language skills
   Dutch Native
   English Fluent (near native) French Fluent (approx. C1 level)
- 7. Formal degrees and training degrees

2005 – 2007: MSc (cum laude) Neuroscience and Cognition	-	Utrecht University, NL
2002 – 2005: BSc (cum laude) Cognitive Neuroscience	-	Utrecht University, NL

8. Doctorate

2007 – 2012: PhD in Neurophysiology – University Medical Center Utrecht.
 PhD obtained on 26<sup>th</sup> of September 2012.
 Promotor: Prof. dr. Dr. Roger Adan
 Copromotor: Dr. Geert Ramakers

### POSITIONS

### **Current position**

- 2023 - Current: Group leader / Associate Prof (Tenured). Department of Translational Neuroscience, UMCU, The Netherlands.

### **Prior positions**

-2018 – 2023: Group leader / Assistant Prof (Tenured) Department of Translational Neuroscience, UMCU, The Netherlands.

-2016 – 2018: Group leader / Assistant Prof Department of Translational Neuroscience, UMCU, The Netherlands.

-2012 – 2016: Postdoc researcher - *Dr. Mameli Lab* Institut du Fer à Moulin INSERM, Paris, France

## B. RESEARCH INTERESTS

### Background:

Throughout my career I have been fascinated by how brains encode motivational drives, and how this process can go awry. After my undergraduate studies in cognitive neuroscience (UU, NL), I became particularly interested in the underlying neurobiological "nuts and bolts" for the cognitive and emotional processes implicated in motivated behavior. I did a PhD on G protein-coupled Receptor (common drug targets) control over synapse neurophysiology in the dopamine system and on motivated feeding behavior in the lab of Dr. Geert Ramakers and Dr. Roger Adan (UMCU/UU; PhD obtained 2012). I subsequently did postdoctoral training in the lab of Dr. Manuel Mameli (INSERM, Paris, France), combining neurophysiological approaches with advanced neural circuit mapping/manipulation techniques (e.g. optogenetics, viral tracing), to explore the role of the habenula in drug addiction. Then in 2017 I founded my own research group (UMC Utrecht, NL).

<u>Research:</u> The research of my lab focuses on the neurobiology underlying the interplay between stressed states (due to environmental stressors) and motivated (reward seeking) behavior. This interaction plays an important role in a variety of psychiatric disorders, particularly in those with a strong cyclical manifestation where stress is a common trigger for relapsed maladaptive coping. Eating disorders are prime examples of such conditions. For those suffering from an eating disorder in which binge eating features heavily, stress is often a potent trigger to engage in such a binge. For others, stress has a strong suppressive effect on food intake, and may instead trigger other kind of (mal)adaptive behaviors (e.g. excessive hyperactivity). Indeed, the interaction between stress and reward is a complex and certainly partly individualized one, though there are of course also evolutionarily very well-conserved interactions between what is stressful, what is rewarding and how those processes and underlying systems interact.

The scientific approach of my lab is to use high-resolution neurophysiological measurement techniques to determine, in preclinical models, how stressors change the strength of specific synapses and circuits in the brain (particularly focusing on those linked to processes of motivation, reward, emotional states, and behavioral control). Furthermore we use brain stimulation techniques (e.g. optogenetics, chemogenetics) to gauge the causal contributions of such stress-driven brain changes for motivated (feeding) behavior. Thus by mapping, monitoring, and then mimicking/preventing/reverting specific effects of stress in these brain systems, we seek to ultimately understand the complex relationship between stress and motivated behavior.

# C. (INTER)NATIONAL ACTIVITIES

### I. Invited lectures at (inter)national meetings

- 2024: SILS, Amsterdam, NL. Mini-symposium "Future of Electrophysiology". Invited speaker.
- 2023: Bordeaux Neurocampus, Seminar series, France. Invited speaker.
- 2023: Brainscapes NL seminar, The Netherlands. Invited speaker.
- 2022: CNCR departmental seminar Free University Amsterdam, Amsterdam, NL. Invited speaker.
- 2022: Neuronus IBRO, Krakow, Poland. Invited session keynote speaker.
- 2022: Central Military Hospital MGGZ Expertise Center, Utrecht, The Netherlands. Invited speaker.
- 2022: Stress-NL Meeting, Utrecht, The Netherlands. Invited speaker.
- 2022: Lowlands Molecular Neuroscience Meeting, Antwerp, Belgium. Invited speaker.
- 2022: International Winter conference, Soelden, Austria. Invited speaker.
- 2022: Dutch Neuroscience Meeting, Tiel, The Netherlands. Invited speaker.
- 2022: Young UMCU Meeting. Invited speaker.
- 2020: Netherlands Institute of Neuroscience, Amsterdam, NL. Invited speaker & masterclass
- 2019: Society for the Study of Ingestive Behavior (SSIB), Utrecht, NL. Invited speaker.
- 2019: Mediterranean Synapse Meeting, Marrakech, Morocco. Invited speaker.
- 2019: Dutch Neuroscience Meeting, Lunteren, The Netherlands. Invited speaker.
- 2018: Utrecht Brain Conference, Utrecht, The Netherlands. Invited speaker.
- 2018: Stress Meeting, Rotterdam, The Netherlands. Invited speaker.
- 2017: European Synapse Meeting, Milan, Italy. Invited speaker.
- 2017: ONWAR Career Event, Amsterdam, The Netherlands. Invited speaker.
- 2017: Cajal Course, Champalimaud, Portugal. Invited lecturer.
- 2017: Nudgelt Meeting, Bristol, 2017. Invited speaker.

### II. Poster presentations at (inter)national meetings

- 2018: FENS Meeting, Berlin, Germany. Poster presenter.
- 2018: Dutch Neuroscience Meeting, Lunteren, The Netherlands. Presentation.
- 2018: Stress Nutrition Meeting, Amsterdam, The Netherlands. Poster presenter.
- 2016: Dopamine Meeting, Vienna, Austria. Poster presenter.
- 2016: Kavli-FENS Annual Meeting, Chicheley, UK. Poster presenter.
- 2015: GRC Meeting on Catecholamines, Newry, Maine, USA. Selected poster presenter.
- 2015: Society for Neuroscience Meeting, Chicago, USA. Poster presenter.
- 2013: Dopamine Meeting, Alghero, Italy. Poster presenter.
- 2010: Society for Neuroscience Meeting, San Diego, USA. Poster presenter.
- 2010: IDARS-NIDA Meeting, San Diego, USA. Selected poster presenter.

### III. Organisation of Scientific Meetings:

- 2022: Organizing member of Dutch Neuroscience Meeting 2023 (international event).
- 2022: Organization of X-talk University Medical Center Utrecht (interdisciplinary event)
- 2021: Organizing member of Dutch Neuroscience Meeting 2022 (international event).
- 2021: Organization of X-talk University Medical Center Utrecht (interdisciplinary event)
- 2019: Organizing member of Dutch Neuroscience Meeting 2020 (international event).
- 2019: Co-chair of session Mediterranean Neuroscience Meeting 2019 in Marrakech, Morocco
- 2015: Organizer of 6<sup>th</sup> IFM colloquium, Paris, France "Basal Ganglia in Health and Disease"
- 2013: Organizer of Young Researcher Symposium, Paris, France.

## IV. Outreach events:

- 2024: Participated on workshop on "how to fund your research", The Netherlands.
- 2023: Participation in *ConnecTED* seminar for UMCU young group leaders, The Netherlands.
- 2022: Participation in a Research career Q&A for biology PhD students of UU.
- 2022: UT Southwestern Masterclass on scientific career.
- 2022: Participation in a Research Funding Q&A for UMCU / UU colleagues.
- 2022: Young UMCU Meeting *Invited lecture*
- 2022: Betweter festival lecture, Utrecht, The Netherlands. (>60k viewings online per March 2023)
- 2021: UT Southwestern Masterclass on scientific career.

### V. Invited journal article reviewing (selection):

- Science

- Cell Reports
- Nature Communications
- Science Advances

Addiction BiologyNeuropharmacology

- Physiology & Behavior

- Nature Reviews Endocrinology

## VI. Invited grant reviewer:

- European Research Council Advanced grant (ERC-ADG)
- European Research Council Consolidator Grant (ERC-COG)
- APC Microbiome Ireland (NSpire)
- Swiss National Science Foundation (SNF)
- French National Research Agency (ANR)
- French Foundation for medical research (FRM)
- Israel Science Foundation (ISF)
- Netherlands Organisation for Scientific Research (NWO)
- Alzheimer NL (NL)

### VII. Committee activities

- Dutch Neuroscience Meeting Organization Committee
- Internationalization committee UMC Utrecht
- ZonMW Open Competition Committee member
- UMCU Young Academy (ended 2022)
- UMCU Brain Advisory Board
- Chair of Translational Approaches horizontal line within UMC Utrecht Brain Focus Area

### VIII. Invited panel member on PhD Thesis committees:

2024:	Wouter van Elzelingen	<ul> <li>University of Amsterdam, The Netherlands</li> </ul>
2024:	Margo Slomp	<ul> <li>University of Amsterdam, The Netherlands</li> </ul>
2022:	Thomas Contesse	<ul> <li>Universite Cote d'Azur, Valbonne, France</li> </ul>
2022:	Jian Liang	<ul> <li>Utrecht University, The Netherlands</li> </ul>
2020:	Huub Terra	<ul> <li>VU Amsterdam, The Netherlands</li> </ul>
2020:	Tamas Dalmay	<ul> <li>Radboud University, The Netherlands</li> </ul>
2020:	Dennis Kruijssen	<ul> <li>Utrecht University, The Netherlands</li> </ul>
2020:	Myrtille Gumbs	- AMC, University of Amsterdam, The Netherlands
2018:	Sara Brignani	<ul> <li>UMCU, Utrecht University; The Netherlands</li> </ul>

#### D. **TEAM DIRECTION AND THESIS ACTIVITIES**

### Postdoc direction:

1.	Dr. Danai Riga	Postdoc
2.	Dr. Rogier Poorthuis	Postdoc

- 3. Ms. Karlijn Kooij Postdoc
- 4. Ms. Janna Smeets Postdoc
- (Ended 2021) 5. Dr. Evelien Schut Postdoc (Ended 2022)

### PhD Thesis direction:

1. Louisa Linders PhD student

- 2. Laura Supiot PhD student
- 3. Ioannis Koutlas PhD student
- 4. Wenjie Du PhD student
- 5. Roberto D'Angelo PhD student

### PhD Thesis co-direction:

1.	Emel Souki	PhD student
2.	Oxana Garritsen	PhD student
3.	Nick Papavoine	PhD student
4.	Laura Pieper	PhD student
5.	Lianne Delwel	PhD student

### Technician direction

- 1. Ms. Inge Wolterink-Donselaar Research technician
- 2. Ms. Lefkothea Patrikiou Research assistant (Ended 2022)

#### Ε. **GRANTS, HONORS AND AWARDS**

### Grants received directly:

- 2023: Co-recipient (/w Drs. Koelemans, Schiffelers & Braun) of Hersenstichting grant
- 2022: Co-recipient (/w Dr. Lesscher) of NWO ENW-M2 grant
- 2022: Center of unusual collaborations UcO grant (3x, between 2020-2022)
- 2020: Recipient of VIDI grant from Netherlands Organisation for Scientific Research
- 2019: Co-Recipient of NWO Gravitation Grant.
- 2019: Recipient of CJ Vaillant Grant.
- 2018: Recipient of European Research Council (ERC) Starting Grant.
- 2017: Recipient of Rudolf Magnus Young Talent grant.
- 2015: Recipient of VENI grant from Netherlands Organisation for Scientific Research
- 2012: Recipient of Fondation Fyssen postdoctoral scholarship.
- 2006: Recipient of Erasmus scholarship for master internship Cambridge, UK.

### Grants where acting as direct Mentor and Host lab

- 2023: Rudolf Magnus Young Talent grant of Drs. Huffels & Van 't Klooster.
- 2021: NWO-XS Grant for Dr. Danai Riga
- 2021: Chinese Research Council fellowship for Ms. Wenjie Du

- 2019: Marie Curie Individual Fellowship for Dr. Rogier Poorthuis
- 2019: NWO Veni Grant for Dr. Danai Riga

## Awards received:

- 2019: Co-Recipient of Young IBRO Connecting Regions Award
- 2017: Recipient of Rudolf Magnus Young Talent award.
- 2016: Recipient of NARSAD Young Investigator award (by BBR Foundation)
- 2012: First prize for PhD oral presentations Figon Dutch Medicine Days.
- 2011: First prize for PhD poster presentations. Top Institute Pharma Forum
- 2011: Thesis support grants Netherlands Brain Foundation & Dutch Society for pharmacology
- 2010: Travel award for the National institute on Drug Abuse symposium. (NIDA).

## F. PUBLICATIONS

### **Output as group leader (including collaborations)**

- Koutlas, I., Patrikiou, L., Van der Starre, S., Danko, D, Wolterink-Donselaar, I., Luijendijk, M., Adan, R. & Meye, F.J. (2024). Distinct ventral tegmental area neuronal ensembles are indispensable for reward-driven approach and stress-driven avoidance behaviors. <u>BioRXiv.</u> doi: https://doi.org/10.1101/2024.05.30.596611.
- Supiot, L.F., Benschop, A., Nicolson, A., Haak, R, Wolterink-Donselaar, I., Luijendijk, M., Adan, R., Poorthuis, R.B\*. & Meye, F.J\*. (2024). A prefrontal cortex-lateral hypothalamus circuit controls stress-driven food intake.
   <u>BioRXiv.</u> doi: https://doi.org/10.1101/2024.05.02.592146
- Ducrocq, F., Brouwer, E., Kooij, K., Wolterink-Donselaar, I., Drost, L., Hak, J., Veendijk, M., Luijendijk, M., Meye, F.J. & Adan, R.. (2024). Reduced GABA transmission onto ventral tegmental area dopamine neurons underlies vulnerability for hyperactivity in a mouse model for Anorexia Nervosa. *BioRXiv*. doi: https://doi.org/10.1101/2024.03.14.585038.
- Riga, D., Rademakers, K., Wolterink-Donselaar, I. G., Meye, F.J. Neuropeptide Y neurons of the locus coeruleus inhibit noradrenergic system activity to reduce anxiety. *BioRXiv.* doi: https://doi.org/10.1101/2023.10.16.562534
- Damstra, H.G.J.<sup>#</sup>, Passmore, J.B.<sup>#</sup> #, Serweta, A.K., Koutlas I., Burute M., Meye, F.J., Akhmanova, A., Kapitein, L.C.. GelMap: Intrinsic calibration and deformation mapping for expansion microscopy. <u>Nature Methods</u>, 2023. #Equal contribution.
- Linders, L. E., Patrikiou, L., Soiza-Reilly, M., Schut, E. H. S., Van Schaffelaar, B. F., Böger, L., Wolterink-Donselaar, I. G., Luijendijk, M. C. M., Adan, R. A. H. & Meye, F. J. (2022). Stressdriven potentiation of lateral hypothalamic synapses onto ventral tegmental area dopamine neurons causes increased consumption of palatable food. *Nature Communications*. 13(1):6898. doi: 10.1038/s41467-022-34625-7.

- Linders, L. E<sup>#</sup>., Supiot, L. F<sup>#</sup>., Du, W., D'Angelo, R., Adan, R. A. H., Riga, D.\*, & Meye, F. J.\* (2022). Studying synaptic connectivity and strength with optogenetics and patch-clamp electrophysiology. *International Journal of Molecular Sciences*. 23(19):11612. doi: 10.3390/ijms231911612.
- Koutlas, I., Linders, L.E., Van der Starre, S.E., Wolterink-Donselaar, I.G., Adan, R.A.H., Meye,
   F.J. (2022). Characterizing and TRAPing a social stress-activated neuronal ensemble in the ventral tegmental area. *Frontiers in Behavioral neuroscience*. eCollection 2022. doi: 10.3389/fnbeh.2022.936087.
- Huffels, C. F. M., Van Dijk, R. E., Karst, H., **Meye, F. J.**, Hol, E. M., & Middeldorp, J. J. (2022). Systemic injection of Aged Blood Plasma in Adult C57BL/6 Mice Induces Neurophysiological Impairments in the Hippocampal CA1. *Journal of Alzheimer's Disease*, 89(1):283-297.
- Van de Haar, L., Riga, D., Boer, E.J., Adolfs, Y., Sieburgh, T.E., Van Dijk, R.E., Watanabe, K., Van Kronenburg, N.C.H., Broekhoven, M.H., Posthuma, D., Meye, F.J., Basak, O., & Pasterkamp, R.J. (2022). Molecular signatures and cellular diversity during mouse habenula development. <u>Cell Reports.</u> 40(1):111029. doi: 10.1016/j.celrep.2022.111029.
- Montalban E, Giralt A, [......] Meye F.J., Gambardella N, Roussarie JP, Girault JA. (2022). Translational profiling of mouse dopaminoceptive neurons reveals region-specific gene expression, exon usage, and striatal prostaglandin E2 modulatory effects. <u>Molecular</u> <u>Psychiatry</u>. Apr;27(4):2068-2079. doi: 10.1038/s41380-022-01439-4. Epub 2022 Feb 18.
- Kallo, I., Omrani, A., **Meye, F.J.**, De Jong, H., Liposits, Z. & Adan, R.A.H. (2022). Identification of novel neurocircuitry through which leptin targets multiple inputs to the dopamine system to reduce food reward seeking. *Brain Structure and Function*, 227(3):1083-1098.
- Omrani A, de Vrind VAJ, Lodder B, [......], Dickson SL, Meye FJ, Adan RAH (2021). Identification of Novel Neurocircuitry Through Which Leptin Targets Multiple Inputs to the Dopamine System to Reduce Food Reward Seeking. <u>Biological Psychiatry</u>. 90(12):843-852. doi: 10.1016/j.biopsych.2021.02.017. Epub 2021.
- Homberg, J. R. et al. [......], Genzel, L. (2021). The continued need for animals to advance brain research. <u>Neuron</u>. 109(15):2374-2379.
- Willems J, de Jong APH, Scheefhals N, Mertens E, Catsburg LAE, Poorthuis RB, de Winter F, Verhaagen J, Meye FJ, MacGillavry HD. (2020). ORANGE: A CRISPR/Cas9-based genome editing toolbox for epitope tagging of endogenous proteins in neurons. <u>PLoS Biology</u>. 18(4):e3000665.
- Genzel et al., [......], Homberg, J.R. (2020). How the COVID-19 pandemic highlights the necessity of animal research. *Current Biology*, 30(21):4328.

 Tan, D., Nuno-Perez, Mameli, M. & Meye, F.J. (2019). Cocaine withdrawal reduces GABAB R transmission at entopeduncular nucleus - lateral habenula synapses. *European Journal of* <u>Neuroscience</u>, 50(3):2124-2133.

## **Output as postdoctoral fellow**

- Soiza-Reilly, M., Meye, F.J., Olusakin, J., Telley, L., Petit, E., Chen, X., Mameli, M., Jabaudon, D., Sze, J.Y. & Gaspar, P. (2018). SSRIs target prefrontal to raphe circuits during development modulating synaptic connectivity and emotional behavior. <u>Molecular Psychiatry, doi:</u> <u>10.1038/s41380-018-0260-9.</u>
- **Meye, F.J.,** Trusel, M., Soiza-Reilly, M. & Mameli, M. (2017). Neural circuit adaptations during drug withdrawal Spotlight on the lateral habenula. <u>*Pharmacology Biochemistry and Behavior*</u>, doi.org/10.1016/j.pbb.2017.08.007.
- Doly, S., Quentin E, Eddine R, Tolu S, Fernandez SP, Bertran-Gonzalez J, Valjent E, Belmer A, Viñals X, Callebert J, Faure P, Meye FJ, Hervé D, Robledo P, Mameli M, Launay JM, Maldonado R, Maroteaux L (2017). Serotonin 2B receptors in mesoaccumbens dopamine pathway regulate cocaine responses. *Journal of Neuroscience*, pii: 1354-17.
- Lecca, S., Meye, F. J., Trusel, M., Tchenio, A., Harris, J., Schwarz, M.K., Georges, F. & Mameli, M. (2017). Aversive stimuli drive hypothalamus-to-habenula excitation to promote escape behavior. *eLife*, 6, pii: e30697. doi: 10.7554/eLife.30697.
- Morel, C., Fernandez, S.P., Pantouli, F., Meye, F. J., Marti F., Tolu, S., Parnaudeau, S., Marie, H., Tronche, F., Maskos, U., Moretti, M., Gotti, C., Han, M-H., Bailey, A., Mameli, M., Barik, J. & Faure, P. (2017). Nicotinic receptors mediate stress-nicotine detrimental interplay via dopamine cells' activity. <u>Molecular Psychiatry</u>, doi: 10.1038/mp.2017.145
- Meye, F. J., Soiza-Reilly, M., Smit, T., Diana, M. A., Schwarz, M. K. & Mameli, M. (2016). Shifted pallidal co-release of GABA and glutamate in habenula drives cocaine withdrawal and relapse. <u>Nature Neuroscience</u>, 19(8):1019-24.
- Doly, S., Shirvani, H., Gata, G., Meye, F. J., Emerit, MB., Enslen, H., Achour, L., Pardo-Lopez, L., Yang, SK., Armand, V., Gardette, R., Giros, B., Gassmann, M., Bettler, B., Mameli, M., Darmon, M., & Marullo, S. (2016). GABAB receptor cell-surface export is controlled by an endoplasmic reticulum gatekeeper. *Molecular Psychiatry*, doi: 10.1038/mp.2015.72.
- Meye, F. J\*., Valentinova\*, K., Lecca, S\*., Marion-Poll, L., Maroteaux, M. J., Musardo, S., Moutkine, I., Gardoni, F., Huganir, R., Georges, F. & Mameli, M (2015). Cocaine-evoked negative symptoms require AMPA receptor trafficking in the lateral habenula. <u>Nature Neuroscience</u>, 18(3),376-8. [\*=equal contribution].

- Glangetas C., Fois G.R., Jalabert M., Lecca S., Valentinova K., Meye F. J., Diana M., Faure P., Mameli M., Caille S. & Georges F. (2015). Ventral Subiculum Stimulation Promotes Persistent Hyperactivity of Dopamine Neurons and Facilitates Behavioral Effects of Cocaine. <u>*Cell*</u> <u>*Reports*</u>, 13(10):2287-96.
- Lecca, S., **Meye, F. J.** & Mameli, M. 2014. The lateral habenula in addiction and depression: an anatomical, synaptic and behavioral overview. *European J. of Neurosci*, *39(7)*, 1170-1180.
- **Meye, F. J.,** Lecca, S., Valentinova, K., & Mameli, M. (2013). Synaptic and cellular profile of neurons in the lateral habenula. *Frontiers in human neuroscience*, *16(7):* 860.

## Output as PhD student

- **Meye, F. J.**, Ramakers, G. M. J. & Adan, R. A. H. (2014). The vital role of constitutive GPCR activity in the mesolimbic dopamine system. *Translational Psychiatry*, *11(4)*, e361.
- **Meye, F. J**. & Adan, R. A. H. 2013. Feelings about food: the ventral tegmental area in food reward and emotional eating. *Trends in Pharmacological Sciences*, *35(1)*, 31-40.
- Meye, F. J., Trezza, V., Vanderschuren, L. J. M. J., Ramakers, G. M. J. & Adan, R. A. H. (2013). Neutral antagonism for the cannabinoid 1 receptor is a safe tool to treat obesity. <u>Molecular</u> <u>Psychiatry</u>, 18(12), 1294-1301.
- **Meye, F. J.**, Van Zessen, R., Smidt, M. P., Adan, R. A. H. & Ramakers, G. M. J. (2012). Morphine withdrawal enhances constitutive mu-opioid receptor activity in the ventral tegmental area. *Journal of Neuroscience*, *32(46)*, 16120-8.
- De Rover, M., **Meye, F.J.**, & Ramakers, G.M. 2008. Presynaptic metabotropic glutamate receptors regulate glutamatergic input to dopamine neurons in the ventral tegmental area. *Neuroscience*, 154(4)1318-23

# Narrative contributions to Science (examples)

<u>Category 1:</u> G protein-coupled receptors (GPCRs) play an important role in regulating synaptic activity in many neural circuits, including those encoding motivation, hunger and aversion. GPCRs, like the cannabinoid 1 and mu-opioid receptors are typically activated by agonists, but tentative evidence suggested they can also spontaneously switch to an active state (constitutive activity). During my doctoral training I have shown that constitutive GPCR activity indeed plays an important role in regulating synaptic activity in neural populations involved in emotions and motivation. We showed that constitutive GPCR activity levels are dynamic, and that abolishing them due to improperly chosen drug treatment can cause unnecessary psychiatric side effects. This work resulted in various publications, including in Molecular Psychiatry (Meye et al., 2013) and Journal of Neuroscience (Meye et al., 2012). <u>Category 2:</u> Withdrawal from addictive drug intake leads to an aversive state, with physical and persistent psychological symptoms that can promote resumed drug use to alleviate them. These drug-induced aversive states therefore play a critical role in drug addiction, and it is vital to unravel their neural substrates. During my postdoctoral training with Dr. Mameli in the Institut du Fer à Moulin in Paris, I showed how synaptic plasticity in the lateral habenula plays an important role in the occurrence of these aversive withdrawal symptoms. This work resulted in multiple papers, including two first author papers in Nature Neuroscience, (Meye et al., 2015; Meye et al., 2016) and a last-author paper in European Journal of Neuroscience (Tan et al., 2018).

<u>Category 3:</u> Stress can drive food reward seeking, including binge eating behavior. My current work focuses on unraveling the neural circuit changes that take place after stressful events that ultimately drive aberrant feeding patterns. My focus in this regard is on the interaction between hypothalamic, midbrain and prefrontocortical circuits. This ongoing work is in part inspired by our review in Trends in Pharmacological Sciences paper (Meye & Adan, 2014) and also exemplified by our paper in Nature Communications (Linders et al., 2022).