Project proposal

Project title:	Neural networks of susceptibility to post-traumatic stress disorder
On-site supervisor:	Dr. Marloes Henckens (jPI)
Donders Theme:	Plasticity and memory
Research centre:	DCMN
Department:	Cognitive Neuroscience
Duration internship:	6-12 months

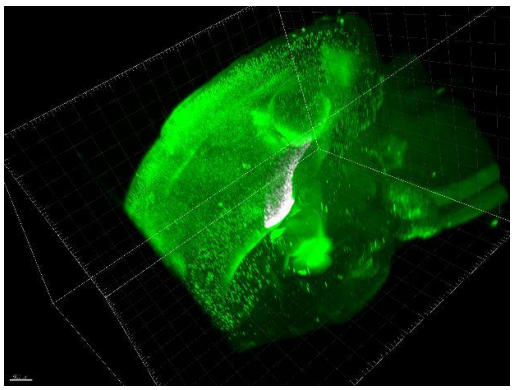
Background

Post-traumatic stress disorder (PTSD) is a debilitating disorder that develops after an individual is exposed to a traumatic event and which affects ~8% of the general population. Symptoms include hypervigilance and hyperarousal, as well as flashbacks of the event, insomnia, irritability and difficulty concentrating. Interestingly, only 15-20% of those individuals exposed to a traumatic event develop the disorder, while over 80% is resilient, recovers adequately and stays healthy. We believe that investigating the differences between the PTSD-vulnerable and -resilient brain might provide new insights into treatment.

Experimentally, we use an established mouse model of PTSD[1,2], in which mice are first exposed to a severe stressor, followed by a mild stressor the next day in a different context. This protocol has been shown to reliably induce PTSD-like symptomatology in a subset of mice, whereas others are resilient. Previously, we have employed the transgenic ArcTRAP mouse line[3] to fluorescently label all activated (i.e., *Arc*-expressing) neurons either before, during or following trauma to assess potential differences in brain activity patterns between PTSD-like and resilient mice. We focussed on brain regions critically involved in the processing of emotional memories, i.e. the amygdala and hippocampus, and observed differential activity between PTSD-like vs. resilient animals, both during trauma and basally after trauma, while the pre-trauma data is still being processed.

Project description

While differences in brain activity between the resilient and PTSD-like animals were found in these specific region-of-interest approaches, neuroscientists increasingly appreciate that the brain is functioning as a set of interconnected networks. Therefore, we want to follow up the initial brain slice immunohistochemistry experiments with the novel iDISCO+ technique[4], in which intact brain hemispheres can be used to immunolabel and image whole 3D tissue. During this project you will learn this brain-clearing technique, image the tissue using our novel light-sheet microscope, and analyse the results implementing network approaches. Programming experience in Matlab or Python is a pre. Furthermore, you will be able to familiarize yourself with several other laboratory techniques, including DNA isolation, PCR and gel electrophoresis, or, if wanted, animal behaviour.



Fluorescently marked neurons that were active prior, during or post-trauma exposure (green) will be identified (white marker indicates neurons in hippocampus) and compared between groups

More information

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Relevant literature

1. Lebow M, Neufeld-Cohen A, Kuperman Y, Tsoory M, Gil S, Chen A (2012). Susceptibility to PTSD-like behavior is mediated by corticotropin-releasing factor receptor type 2 levels in the bed nucleus of the stria terminalis. *J Neurosci* 32(20): 6906-6916.
2. Henckens MJAG, Printz Y, Shamgar U, Dine J, Lebow M, Drori Y, Kuehne C, Kolarz A, Eder M, Deussing JM, Justice NJ, Yizhar O, Chen A (2017). CRF receptor type 2 neurons in the posterior bed nucleus of the stria terminalis critically contribute to stress recovery. *Mol Psychiatry* 22(12):1691-1700.
3. Guenthner CJ, Miyamichi K, Yang HH, Heller HC, Luo L (2013). Permanent genetic access to transiently active neurons via TRAP: targeted recombination in active populations. *Neuron* 78(5):773-84.
4. Renier N, Wu Z, Simon DJ, Yang J, Ariel P, Tessier-Lavigne M (2014). iDISCO: a simple, rapid method to immunolabel large tissue samples for volume imaging. *Cell* 159(4):896-910.