Project proposal

Project title:	Neural activity associated with 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:	3-6 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 during trauma exposure to assess potential differences in neural responding between PTSD-like and resilient mice. We found differential activity in brain regions critically involved in the processing of emotional memories, i.e. the amygdala and hippocampus.

Project description

In this project, you will analyse whether these differences in brain activity between resilient and PTSD-like animals remain present following trauma recovery, and whether these relate to the observed behavioural abnormalities. Moreover, you will test whether brain differences are related to the memory of the traumatic event. You will do so by implementing immunohistochemical stainings in brain slices, which you will image using a fluorescence microscope. Furthermore, you will be able to familiarize yourself with several other laboratory techniques, including DNA isolation, PCR and gel electrophoresis, or, if wanted, mouse behaviour.

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.

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