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The corticothalamic loop has long been implicated in a range of neuropsychiatric diseases. The thalamic reticular nucleus (TRN), a part of the corticothalamic loop, plays a key role in selective attention and sleep spindles. Furthermore, sleep spindles are reduced in amplitude and duration in schizophrenia patients, implying clinical relevance of TRN functions. However, while the TRN is topographically organized, it remains unclear whether and how the TRN consists of functionally distinct sub-regions. Combining optogenetic and electrophysiological approaches in mice, we investigated changes in sleep spindles and EEG oscillations caused by optogenetic stimulations in different parts of the TRN. Archaerhodopsin (Arch), a light sensitive proton pump, was expressed specifically in either an anterior or posterior part of the TRN in parvalbumin (PV)-Cre mice using adeno-associated viral vectors. We found restricted expression patterns of Arch in PV-positive neurons of the TRN depending on injection sites. Effects of optical stimulation on cortical EEGs were assessed by delivering green light through chronically implanted optic fibers in up to 1 min periods in freely behaving animals. Tonic stimulations during awake states did not produce any significant change in EEGs whereas stimulations during sleep (mostly slow wave sleep) increased delta power and the number of sleep spindles . Together these data support the notion that activity in the TRN may have different impacts on the modulation of cortical states in a site-dependent manner.
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Poster number: P-T172
Theme: Methods and techniques

A novel microfluidic drug discovery platform for studying communication between synaptically connected neural networks

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Aims: Many in-vitro systems used during pre-clinical trials fail to recreate the biological complexity of the in-vivo neural microenvironment. Taking advantage of recent advances in microfluidic technology, we seek to develop a perfusion based drug discovery platform that is capable of high-throughput pharmacological profiling. This in turn will allow us to better understand how drugs influence the communication between functionally connected neural networks.
Methods: Mixed primary hippocampal networks were grown in microfluidic devices with environmentally separated chambers that allow synaptic connections to be formed with each other via an array of microchannels. The perfusion of multiple compounds in one chamber was achieved using computer controlled fluid actuation connected to the inlets/outlets of the microfluidic device. Responses to perfusates from directly stimulated neurons and those synaptically connected were recorded using calcium imaging.
Results: Following live/dead assays, a flow rate of 4µl min-1 showed the greatest cell viability and was used for subsequent experiments. Subsequently, a glutamate concentration response curve following direct stimulation was obtained which revealed an EC50 = 4µM. Pharmacological manipulation of neuronal activity was also achieved as the neuronal response to glutamate was reversibly reduced in the presence of ionotropic glutamatergic antagonists. Furthermore, repeated glutamate perfusions induced increasing levels of activity in the adjacent, naïve neural network.
Conclusion: The proposed microfluidic system is able to reliably produce pharmacological profiles for drugs in a neurological setting. The novelty of the presented drug discovery platform is its ability to not only determine the properties of a new drug, but how the drug influences communication between neural networks.

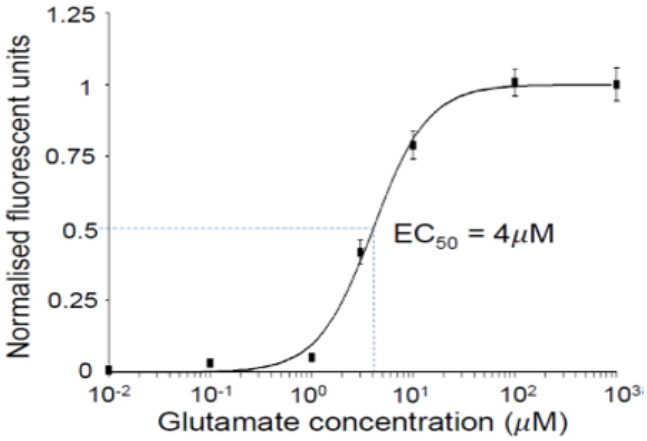

Figure 1: A concentration response curve produced following multiple glutamate perfusions reveals an EC_{50} of 4μM; n = 6 cultures, 14 devices, 184 cells.

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Poster number: P-T173
Theme: Methods and techniques

Neuroimaging assessment of cumulative experience in non-human primates

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Researchers have ethical and legal obligations to optimise the physical and emotional wellbeing of their animals. Furthermore, current European legislation places an emphasis on the animal's lifetime experience. However, current methods for assessing the cumulative experience of animals are poorly validated and suffer from a lack of sensitivity and/or specificity. The general goal of this work was to develop and validate a new method to assess cumulative experience in non-human primates (NHPs).

Recent development in stress biology has shown that in rodents, NHPs and humans, the amount of grey matter in the hippocampus co-varies with the cumulative experience of individuals. These new findings open the possibility to use the amount of hippocampal grey matter as a biomarker of cumulative experience in laboratory animals. The hippocampus is not a homogenous region and its different functions seem to be spatially segregated. In this study, we tried to identify which part of the hippocampus is most sensitive to cumulative experience in NHPs.

As a proxy for cumulative experience, we used artificial weaning age (i.e. definitive separation from the mother forced by human caretakers). Early artificial weaning is a well-established early-life stressor in NHPs. It is also known to have long-lasting detrimental effects on emotionality, social, sexual and maternal behaviours, as well as growth, immune responses and in some cases survival, inducing a poorer life time experience in individuals weaned earlier. Eleven male adult macaques were scanned with a 4.7 T MRI scanner. In each subject, the amount of grey matter of each voxel comprised in the hippocampus was determined using voxel-based morphometry. After controlling for covariates including age and total brain size, a multiple regression analysis revealed a positive correlation between weaning age and the amount of grey matter in the right anterior hippocampus.

We argue that with appropriate strategies to control for potential confounding factors, the amount of grey matter in this specific part of the hippocampus can now be used to measure the cumulative experience of NHPs.

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Poster number: P-T174
Theme: Methods and techniques

Implementing hybrid circuits with StdpC, a flexible, easy-to-use dynamic clamp software