A novel microfluidic drug discovery platform for studying communication between independent 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, the flow rate that showed the greatest cell viability was used for subsequent experiments. Subsequently, a glutamate concentration response curve following direct stimulation was obtained which revealed an EC_{50} = 1μM. Furthermore, increasing glutamate concentrations resulted in concomitant increases in neuronal activation in adjacent networks. Pharmacological manipulation of neuronal activity was also achieved as the neuronal response to glutamate was reversibly reduced in the presence of ionotropic glutamatergic antagonists.

Conclusion: The proposed microfluidic system is able to reliably produce pharmacological profiles for drugs in a neurological setting. The ability to not only determine the properties of a new drug, but how the drug influences communication between neural networks makes this model a novel drug discovery platform.