**Application and Characterization of Neural Probes**

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**Introduction:** Brain probes constitute the only available tool for examining the link between the electrical activity of single neurons and subject behavior. Because the electrodes contained in the neural probes need to be positioned within tens of micrometers of the neurons of interest, these are necessarily invasive devices. As such they incur the damage of neural tissue, therefore unleashing the chain of events that characterizes inflammation. As it happens with any foreign material that is implanted in the body, the process starts with the unspecific adsorption of proteins and the recruitment of defense cells that attempt to clean up the site and eliminate the threat of the invader. If the threat persists, a chronic inflammatory process ensues, with the attempt to shield the affected area from the surrounding tissue. The common perception is that this shielding, which in the brain consists of a capsule formed predominantly by astrocytes, gradually decreases the quality of the recorded neuronal signals. This project will focus on the application and characterization of neural probes already designed and fabricated by the BRAINN research groups. Furthermore, this project will also have the objective of producing new probe configurations and materials for the improvement of neural recordings in experimental animal models.

**Materials and Methods:** Stereotaxic surgery for implantation of recording neural probes will be performed in Fischer 344 male rats (aged 12 weeks) acquired from Cemib, State University of Campinas (Unicamp). Rats will either receive recording neural probes developed previously in Brainn projects, or commercial silicon probes (Neuronexus), or stainless steel micro wires. Recording probes will be implanted into the dentate gyrus of the hippocampus (AP -3.0; L ±2.0; V -3.5) and bipolar stimulating electrodes will be implanted into the perforant pathway (AP -8.0; L ±4.5; V -3.0). After a period of 7 or 28 days, neural electrical activity will be recorded. Subsequently, rats will be euthanized and the nervous tissue of rats that received chronic probe implants will be analyzed with immunofluorescence labeling for markers for foreign body reaction such as the astrogliosis markers GFAP and microglia activation marker CD68. Gene expression analysis of tissue reactivity markers will also be performed in laser microdissected regions proximal to probe implantation and will be subjected to transcriptome analysis by RNA-seq. All procedures were approved by the Ethics Committee for Animal Research at the Unicamp (protocol 4438-1).

**Results:** In this project, we will explore the use of neural probes developed in previous Brainn projects for nervous tissue electrical activity recording. Furthermore, we will explore and characterize tissue reaction to different neural probe materials and design.

**Discussion:** Recent evidence suggests the neurotoxic effect of the signaling cytokines that are released by nervous tissue in contact with implanted probes. It is noteworthy that such inflammatory process may result in the loss of the ability to record single action potentials. Consequentially, exploring tissue reaction is crucial for the development of more efficient implantable neural probes.

**Conclusion:** The present work will permit to evaluate the biocompatibility and efficacy of the neural probes designed and developed by BRAINN team researchers for application in animal models researches and with potential for application in humans.

**References:** [1] Kozai TDY. et al; ACS Chem Neurosc. 6, 48-67, 2015.