

Mechanically-flexible, graphene-based, microelectrodes for simultaneous recording and electrical stimulation of deep brain microstructures: an acute *in vivo* study

A. Eladly¹

N. Ria², E. Masvidal^{2,5}, X. Illa^{4,5}, A. Guimerà-Brunet^{4,5}, J.A Garrido^{2,6}, K. Kostarelos^{1,2}, R.C. Wykes^{1,3}.

¹ Nanomedicine Lab, University of Manchester, United Kingdom. ² Catalan Institute of Nanoscience and Nanotechnology (ICN2), CSIC and The Barcelona Institute of Science and Technology (BIST), Campus UAB, Bellaterra, Barcelona, Spain. ³ Department of Clinical & Experimental Epilepsy, UCL Queen Square Institute of Neurology, United Kingdom. ⁴ Institut de Microelectrònica de Barcelona, IMB-CNM (CSIC), Esfera UAB, Bellaterra, Spain. ⁵ Centro de Investigación Biomédica en Red en Bioingeniería, Biomateriales y Nanomedicina (CIBER-BBN), Madrid, Spain. ⁶ ICREA, Barcelona, Spain.

Ahmed.eladly@manchetsr.ac.uk

ABSTRACT:

Parkinson's disease (PD) is a neurological motor disorder that negatively impacts the quality of life of its patients. Deep brain stimulation (DBS) is a well-established therapy used to alleviate PD symptoms. However, standard DBS systems consist of stimulating electrodes also known in the field as 'leads' that are mechanically rigid since metal is used in their construction. The rigid nature of these electrodes can result in excessive glial scarring, lead displacement, or fracture, limiting the longevity of the DBS system. In addition, standard stimulating leads are bulky ($\varnothing > 1$ mm, larger than the brain structures they target) which not only lead to significant tissue damage, but also precludes capturing single unit activity. The ability to record from single units can help surgeons quickly localize deep brain structures and achieve accurate electrode placement required for efficacious DBS. Thus, to overcome the above limitations of current DBS systems, we have developed a mechanically-flexible, 8-channel, graphene-based microelectrode ($\varnothing < 1$ mm) called Egnite where each channel can either be used for stimulating or recording. Sprague Dawley rats received an intracranial injection of either 6-hydroxydopamine (30 $\mu\text{g}/4\mu\text{l}$) or vehicle into their right Medial Forebrain Bundle. Four weeks post-surgery, the rats were anesthetized with an i.p. injection of urethane (1.2 g/kg) and subsequently underwent a burr hole procedure over the subthalamic nucleus (STN). The Egnite was lowered into STN using a microdriver at an insertion speed of 3 $\mu\text{m}/\text{s}$. The Egnite was able to electrographically map the STN i.e. channels within the STN recorded fast spiking activity (10-30 spikes/s) while those outside showed a few number of spikes. Once the STN was reached, a DBS protocol consisting of 75 μA biphasic pulses with duration of 100 $\mu\text{s}/\text{phase}$ was applied at 100 Hz for 1 min. This was preceded and ensued by a 2 min period of recording to capture STN activity pre and post-stimulation respectively. The Egnite was able to reliably localize the STN and delivered DBS that suppressed the excessive firing of the STN neurons which is thought to underlie the motor symptoms of PD. In conclusion, we demonstrate that the Egnite reliably localized and delivered modulatory DBS to the STN.

References

[1] Zhuang, Qian-Xing, et al. The Journal of Clinical Investigation 128.12 (2018): 5413-5427.

[2] Pan, Ming-Kai, et al. The Journal of clinical investigation 126.12 (2016): 4516-4526.
