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Optimization and validation of the NeuroLux wireless optoelectronics system for optogenetics

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EXECUTIVE SUMMARY

This preliminary study sought to optimize and validate the novel NeuroLux wireless optoelectronics system for optogenetics, which is a technique that permits the activation or deactivation of a cell through the utilization of light-activated microbial opsins (Deisseroth et al., 2006; Scanziani and Hausser, 2009; Deisseroth 2010, 2011). Classical optogenetics relies on wires connecting light sources to light outputs via traditional fiberoptics, thereby resulting in the tethering of experimental subjects, which poses significant translational concerns, and the exposure of the subjects to the visible light source, which poses translational concerns in addition to the potential for confounds during experimentation. Given its applications in social memory, among other areas (Williams Avram et al., 2019; Smith et al. 2016), translational applications of optogenetics are of great interest. Though other wireless optogenetics systems have been utilized, the NeuroLux wireless optoelectronics system for optogenetics provides a steppingstone in the translation of optogenetics, as the system withstands potential interference that affects the performance of other wireless systems, and the implants are robust, working efficiently up to three months post-implantation (Shin et al., 2016).

In the setup of the NeuroLux system, variables including relative placement of each element of the system, wrapping of the copper antenna wire around the antennaed enclosure, and placement of jumpers located in the Antenna Tuner Box were optimized to permit adequate signaling to the wireless implants. The optimized setup of the system was verified by visual analysis, which consisted of implant light-emitting diodes (LEDs) emitting similar brightness throughout the enclosure, and numerical analysis, which yielded a Standing Wave Ratio (SWR) of 2.7, an absolute impedance (|Z|) of 50.6 Ω, and a reactance (X) of -38.4 Ω (Fig 1a, 1b, 1c).

This study found that the NeuroLux system effectively stimulated the dorsal cornu ammonis 2 (dCA2) region of the hippocampus in transgenic mice that express Cre recombinase from the arginine vasopressin (Avp) 1b receptor promoter (Avpr1b-Cre). Effective stimulation caused by the NeuroLux system was confirmed by the visual analysis (Fig 4a, 4b) of cFos expression in the dCA2 region of Avpr1b-Cre mice. Additionally, cFos expression, quantified using Mean Grey Value, in the dCA2 of Avpr1b-Cre mice was determined to be significantly different than wild-type (WT) mice using both Binary Image Analysis ($P = 0.0034$, Fig 5b) and Fluorescence Intensity Analysis ($P = 0.0024$, Fig 5d).

The optimization and validation of the NeuroLux wireless optoelectronics system for optogenetics permits a more translational form of optogenetics in comparison with classical optogenetics. Though obstacles pertaining to genetic engineering exist with the system, the NeuroLux system acts a steppingstone in the usage of optogenetics in a clinical setting, which may lead to advancements in the understanding of areas such as social memory, which corresponds with the optogenetic work conducted with the dCA2, in humans.

With this study, the authors obtained a greater understanding of experimental design and optimization, microscopy, electrical engineering and circuitry, genetic engineering and virology, and visual and statistical analysis. Furthermore, the authors engaged in critical thinking, technical writing, and literature review.

Recommendations for future work include the usage of the novel NeuroLux wireless optoelectronics system for optogenetics in place of classical optogenetics. In addition, the authors recommend conducting analysis of the system's efficacy several months after implantation, inspecting possible corrosive properties of the implants, and investigating the effects of interference at radio frequency.

Body of report intentionally omitted.

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