Preclinical animal models are essential for successful development of safe and effective commercialized CNS therapies. Objective data from animal models establish proof of concept evidence and provide critical inputs to the design of later phase clinical studies. In medical device development, a large animal with an intact nervous system is preferred because it permits use of human-scaled devices and controlled testing that cannot be replicated with computer modeling or bench-testing. Therefore, we established an in-house sheep platform for early-phase testing of deep brain stimulation (DBS) therapy concepts and devices within the movement disorders space. In twelve animals commercial DBS leads with four active contacts were targeted to the subthalamic nucleus (STN), a common stimulation target in Parkinson disease. Overall, DBS lead implantation was not associated with remarkable neurological or histopathological complications. Assessments of targeting using standard comparisons of pre and post-operative brain images indicated that accuracy was comparable to clinical experience. Methods were developed to quantitatively assess motor behavior of chronically-implanted animals in the awake state. In open and blinded settings, we consistently found that motor behavior responses to STN stimulation significantly depended on the stimulation contact selected and parameters tested, including voltage, pulse width and frequency. Quantitative electromyographic assessments confirmed the motor
behavior findings. This work establishes in-house capabilities for controlled testing of emerging DBS therapy concepts and device prototypes. Further work is ongoing to test prototype devices and develop additional objective physiological monitoring methods and biomarkers.


Keyword(s): PARKINSON
STIMULATION
ANIMAL MODEL