INTRODUCTION

Currently, the evaluation of EEG may be assessed through the use of 2 primary platforms: restrained subdural model or surgically implanted telemetry. Restrained subdural evaluations are most beneficial for prescreening applications (to eliminate animals with underlying predispositions to lowered seizure threshold) or for investigation of compounds with a known window of convulsive risk. Surgical implants offer continuous assessment of EEG with greater signal reliability for chronic evaluations when the potential period of risk is unknown or not repeatable among all subjects.

The intent of this study was to evaluate a new device to bridge the gap between acute and chronic evaluations to assess seizure potential when the time of insult is unknown. The EMKA eegPACK was evaluated for potential use in acute assessments or for moderate durations of ambulatory evaluation, without the need for surgical implantation. In the restrained state, the animals are susceptible to noise in the EEG waveform from excessive struggling due to agitation from restraint. In the ambulatory state, the animals are able to freely move about their home cages without the additional stresses associated with the restraint system.

In a prior internal investigative study, the use of needle electrodes vs. pediatric, adhesive button electrodes were evaluated. Both electrodes provided equivalent signal quality. As the pediatric button electrodes allowed for potential use in an ambulatory environment, this electrode was utilized in this study.

RESULTS AND DISCUSSION

PTZ effects were initially investigated in detail using implanted telemetry and NeuroSense (DSI). Administration of PTZ produced seizures in two animals at 19 and 21 minutes postdose, respectively. Prostructural behavioral observations correlated with EEG abnormalities indicative of increased risk of seizure were noted and included salivation, increased swallowing, agitation, tremors, tonic contractions and stereotypy (chewing). Prostructural EEG abnormalities indicative of increased risk of seizure consisted of isolated sharp waves (ISW) or organized sharp waves (OSW) and repetitive bursts of high frequency EEG (low gamma). Stereotypy and tonic contractions were noted mostly during high frequency discharges, while OSWs and ISWs were generally associated with mild myoclonus. Diastem was administered shortly after the onset of each contraction, effectively interrupting the tonic-clonic events. Prostructural attenuation with residual epileptiform activity was noted for ~30 sec after the end of each frank seizure, followed by EEG slowing.

The EEG channel 1 of the EMKA eegPACK external system retained sufficient EEG for analyses of prodromal EEG such as sharp waves and/or slowing during periods of excessive excitation/movement (Figure 1). EMKA eegPACK data were sampled at 1000 hz (in opposition to DSI data sampled at 500 hz) in an effort to minimize potential of missing a ISW due to sample rate limitations. The difference in sampling rate may however have introduced greater high frequency noise, thus impeding detection of these biomarkers. In absence of significant motion artifact, the system demonstrated sensitivity to capture biomarkers of lowered seizure threshold (ISW/OSW) (Figure 2).

Synchronization of video with RAW data traces and display issues were identified with the EMKA eegPACK external system and were communicated to the vendor for suggestions of future improvements.

MATERIALS AND METHODS

- 2 male Bougie dogs approximately 10 months old and weighting approximately 9.2 kg were used as the test subjects.
- Animals were previously implanted with DSI D70-EEE transmitters.
- 2 bipolar EEG leads were placed equidistant to bregma; 1 lead was placed in the neck muscle for evaluation of EMG
- Animals were sufficiently accustomed to sleep restraint.
- Baseline data were collected for approximately 10 minutes prior to dosing.
- Pentylenetetrazol (PTZ) was infused at 1.5 mg/kg/min using calibrated infusion pumps.
- The animals were monitored continuously during the infusion. At the sign of first sign of clear paroxysmal activity or convulsive phenomena were observed, PTZ infusion was stopped and Diazepam (1 mg/kg) was injected and administered to effect by a staff veterinarian.
- Telemetry data were delayed from the EEG device using a single RMC-1 transmitter connected to a data exchange matrix using the DSI Paramec Physiology Platform (PT) data acquisition software (v5.2).
- All EEG and EMG signals were collected at 500 Hz.
- Time matched video data were acquired using Axis 211 network cameras (resolution setting of 480x380 at 30 frames per second) interfaced with the video module within P3.

External Telemetry System:
- Telemetry data were transmitted via Bluetooth using the EMKA eegPACK v3 transmitter encased in a filled ambulatory cap atop the subjects head (Schematic 1).
- Signals were collected using disposable pediatric adhesive electrodes with 2 lead set-ups (placement mimicked the implanted EEG configuration).
- Data were collected using JO2 (v 2.14.4) sampled at 100Hz.
- Video data were acquired using 1 FOSCAM camera and an EDS14 NAS (for video storage and synchronization).