Characterization of EEG Morphologies During Drug-Induced Seizures and Peri-Ictal Changes in Non-Clinical Species

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Simon Authien1,2, Mylene Pouliot1, Dominique Paquette1, Michelle Dubuc-Mageau2, Audrey Sanfacon2, Wendy Tan3, Michael Accardi1

1Citoxlab North America, Laval, Canada, 2Faculty of Veterinary Medicine, University of Montreal, St-Hyacinthe, Canada.

INTRODUCTION

Regulatory agencies require that the most sensitive species be used for seizure liability assessment during drug development. A broad range of automated and manual methodologies are available to detect or identify ictal and inter-ictal events in non-clinical EEG obtained by telemetry. The strategy to detect seizure events is often based on EEG morphology and defining those events is essential to ensure appropriate algorithm selection. The current study aimed to analyze EEG morphologies observed during drug induced seizures but also inter-ictal events.

A total of 442 EEG traces from rats, dogs, minipigs and non-human primates were evaluated for spike frequency, amplitude and duration but also premonitory and post-ictal changes.

Most drug-induced seizure events were self-limiting. In all species, post-ictal EEG changes were observed over a period ... only after a seizure episode with resolution prior to clinical signs. Characteristic profiles were noted for individual species (n=106) across non-clinical species.

RESULTS

Most drug-induced seizure events were self-limiting. In all species, post-ictal EEG changes were observed over a period of a few minutes only after a seizure episode with resolution prior to clinical signs. Characteristic profiles were noted for individual animals but also with each drug (i.e. similar patterns noted for a given animal or specific to a drug). Most drug-induced seizures were noted at times of maximal plasma exposure but delayed seizure onset was noted in rare cases. Seizure onsets were associated with stimulation (e.g. handling or lights) in some cases as reported with non-drug related seizures.

CONCLUSION

Overall, this analysis reveals a rich diversity in EEG morphologies associated with drug-induced seizures with implications when selecting detection algorithms, EEG derivations or during manual morphology review.
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