Abstract

Electroencephalography is a useful neurological biomarker with recognized translational applications. Video-EEG interpretation often includes sleep scoring and power spectral analysis. Sleep scoring and spectral parameters were used to quantify caffeine (10 mg/kg, IM, cross-over design) induced pharmacological effects in conscious cynomolgus monkeys (n=10) with continuous video-EEG monitoring using telemetry. Circadian changes in EEG spectral band power (delta 0.5-4 Hz, theta 4-8 Hz, alpha 8-12 Hz, sigma 12-16 Hz and beta 16-24 Hz) were correlated with the sleep cycle in all animals. When compared with saline, caffeine significantly increased total and relative power of beta frequencies (16-24 Hz) which correlated with a decrease in sleep time. The effects of caffeine on absolute and relative power at frequencies ranging from 1 to 127 Hz (1 Hz increments) were evaluated to identify the most sensitive range to caffeine induced effects. A decreased power in lower frequencies (1 to 13 Hz) was noted with progressively shorter effects for higher frequencies in this range and peak effect (relative and absolute) at 2 Hz. An increase of all frequencies above 15 Hz was also observed as expected for a CNS stimulant drug.

Materials and methods

Cynomolgus monkeys (n=10) were implanted with EEG telemetry transmitters (Data Science International, TL11M2-D70-EEETM) and three bipolar derivations (C3-O1, Cz-Oz and C4-O2) at least 2 weeks prior to dosing. Video-EEG monitoring was initiated at least 24 hours prior to dosing and continued for at least 24 hours post-dose. Spectral analysis on the central EEG (Cz-Oz) derivation was performed for power bands and individual frequencies (from 1 to 127 Hz). Sleep was quantified for a 12 hour period post-dosing (Data Science International, Sleep Staging Module, NeuroScore).

Results

Caffeine induced changes in power bands at 3 hours post-administration (IM, 10 mg/kg) p<0.05

Effects of Caffeine (10 mg/kg, IM) on Normalized EEG Beta Frequency (16-24 Hz) Power in Cynomolgus Monkeys (n=8)

Sleep Time in Cynomolgus Monkeys following Caffeine Administration (10 mg/kg, IM) p<0.05 Overall treatment different (ANOVA for repeated measures)

Conclusion

As illustrated by our results, expected stimulatory CNS effects were observed after caffeine administration in cynomolgus monkeys. When non human primates are justified, video-EEG monitoring in this species appears to be a useful methodology to assess pharmacological effects on sleep and arousal.