PALADINS: PROTECTIVE APPROACHES LEVERAGING AD-APTIVE AND IN-NATE SYSTEMS

Effect Of Viral Challenge Dose On Electroencephalogram (eeg) Patterns From Nonhuman Primates Aerosol Exposed To Venezuelan Equine Encephalitis Virus (veev)

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A positive-strand RNA virus of the Alphavirus genus, VEEV causes a severe, but for the most part non-lethal disease in humans and nonhuman primates (NHPs). Despite previous development as a biological weapon, currently there are no medical countermeasures to prevent or treat VEE disease. VEE disease typically manifests initially as fever, headache, photophobia, myalgia, malaise but can progress to encephalitis in some cases. The NHP model of VEEV recapitulates the three measurable hallmarks of VEE disease in humans: fever, viremia, and lymphopenia; however, quantifying the neurological effects in NHPs has been challenging. Recently, advances in radiotelemetry have facilitated the ability to continuously measure EEG signals in NHPs. A study by Ma et al. monitoring EEG after VEEV exposure identified no consistently significant change in wavebands until after day 3 post exposure (PMID: 35696423). The authors also noted significant individual variation between NHPs. Despite this, a generalized EEG slowing, consistent with EEG observations from VEEV infected patients, was observed. Here, we examined the EEG patterns from NHPs aerosol exposed to either 1E8 (n=5) or 1E6 (n=4) PFU of VEEV Trinidad donkey strain in order to confirm these findings at a secondary test site and determine if dose of challenge agent altered the EEG spectrum. Analysis of EEG data did not identify any epileptiform, ictal activity or other types of EEG abnormalities likely due to the low incidence of these complications after VEEV exposure. EEG slowing was observed in 66% of the NHPs in this study (3 of 5 from 1E8 PFU; 3 of 4 from 1E6 PFU). No appreciable difference was present between the two challenge dose groups do to the variability observed between individual NHPs. An increase in low frequency activity was present but variable for each NHP, particularly in its intensity (i.e. 0-1000%), duration and/or the individual frequencies involved. Increases in frequencies between 8-16 Hz (delta, theta, and alpha) were predominantly observed during the light hours while increases in beta (16-24 Hz) and gamma (>24 Hz) were noted during the dark hours. These results indicate a disruption in the circadian rhythm that occurred as early as 12 hours after exposure but on average started on day 2 after exposure and, in general, returned to baseline by day 15. The general slowing of the EEG spectrum observed in this study is consistent with results reported in the Ma et al. study and is the most common finding during spectral analysis in patients with diffuse viral encephalopathies. Taken together, these data establish a correlation between general slowing of the EEG spectrum and VEE disease progression in NHPs. Given the difficulty of evaluating neurological manifestations of VEE disease in NHPs, EEG monitoring may provide a measurement of the effectiveness of medical countermeasure protection of the central nervous system.

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