OVPR
University of Pennsylvania

Last updated: 10/29/2019

PI Name: First Last
Academic Rank: Assistant Professor
School: Perelman School of Medicine

Amount Requested: $50000

Project Title: Ketamine in the treatment of cortical spreading depolarization in a swine TBI model

Select Your Score Below:

Your score for this application based upon significance, Investigator(s), Innovation, Approach, and Environment.*

N/R - Not Reviewed
1-2 Truly outstanding
3-4 Excellent
5-6 Average
7-8 Poor
9 Not acceptable

6

Reviewer Type: Primary

Summary & Critique:

Comments will be shared with panel members. They will NOT be shared with the applicant.

The applicant is interested in traumatic Brain Injury (TBI) and the secondary injuries that further devastate the brain. The applicants team studies TBI in swine using a closed head model of rotational acceleration. Use of pigs to study TBI is common and faithfully duplicates much of the pathology seen in humans. A recently described secondary injury is the phenomenon of cortical spreading depolarization (CSD) that is strongly correlated with poor outcomes. These are waves of extreme cortical depolarization that come from the injury site in severe TBI, subarachnoid hemorrhage, and ischemic stroke. Ketamine has been identified as a therapeutic agent to counteract hypothesis for aim 1 is simply that the porcine model will show the development of post-traumatic CSDs. The applicant includes references that show that a similar porcine model of CSD has been published by a group from Heidelberg, Germany.

The second aim is to test the effect of ketamine in the swine model. This was also already done by the group in Germany. It is not obvious what this group is looking for that is unique or will give additional insights. Maybe the neuromonitoring techniques is the new contribution but that was not made clear. What is the innovation? Another weakness is that the proposal focuses on treating the CSD phenomenon without any attempts to link that treatment to more relevant clinical outcomes such as lower mortality, less disability, fewer seizures, *etc*. The swine are to be sacrificed after TBI and ketamine or control treatments and measurement of CSD but without measuring clinical outcomes. A potential weakness is the lack of a true control group - shouldn't some of the animals be treated with vehicle? Or some kind of cross-over design be used for ketamine and a placebo? The applicant is a new (2018) assistant professor in Neurosurgery at Penn. He has research experience clinically in neurotrauma and a porcine model of peripheral nerve injury. Thus, he has worked with porcine models before but it is not clear that he has worked with TBI models. His only current support is a substantial start-up package (600K). The budget is all for supplies including the pigs, which are expensive, monitoring equipment, and scanning time. He has assembled a strong group to support him.

Concerns. In view of the $0.6 M startup package it is difficult to approve pilot funding under this grant mechanism.

- **https://grants.nih.gov/grants/peer/guidelines_general/scoring_system_and_procedure.pdf**