Health Outcomes and Long-Term Care Following Extremity Injury

Nociceptin/Orphanin FQ Peptide Receptor (NOP)-Related Agonists as Analgesics in Primates

Blast injuries invariably result in pain. Opioids, such as morphine, that bind to the mu opioid receptor are the most efficacious agents for the treatment of moderate to severe pain. However, morphine-like drugs have side effects, including respiratory depression, physical dependence, and abuse liability that reduce their usefulness in some situations and for some individuals with pain. Previous studies have shown that NOP-receptor agonists may have morphine-comparable analgesic effects without morphine-associated side effects in primates. However, pharmacological data derived from the NOP agonists in primates are limited, because only one non-peptidic NOP agonist has been studied in the primate models. Initiated with funding from the Peer Reviewed Medical Research Program, and with continued support from the Joint Warfighter Medical Research Program, researchers from Wake Forest University Health Sciences are determining the relative antinociceptive effectiveness, safety, and abuse potential of various NOP-related agonists in different primate pain models. Evidence suggests that in non-human primates, the selected NOP-related agonists produced antinociceptive effects comparable to morphine, with a wider therapeutic window, and without the induction of respiratory depression or itch-scratching behavior, suggesting that these agonists are effective and safe analgesics in primates. Moreover, the selected agonists did not produce reinforcing effects as compared to mu opioid agonists. Thus, these agonists have promising therapeutic profiles as analgesics to be further developed for use in the treatment of blast and other battlefield injuries.

Pain relief is an essential component of CCC. For injured Service Members, analgesia can enhance comfort, allowing them to remain quiet when noise discipline is at a premium, and enhance mobility so that they might either carry on their mission, or remove themselves from dangerous areas. Although NOP agonists, such as morphine and fentanyl, can provide all of these benefits, and could be used effectively by the Service Member in the field for self-medication, these drugs have some limiting side effects. Among the most dangerous are respiratory depression/arrest, the risk that Service Members given access to large quantities of NOP agonists might abuse these drugs, and the risk that Service Members might develop physical dependence following chronic administration. Many combat Service Members were heavy users of widely available and relatively pure heroin

and/or prescription opioids. These young men and women are at a vulnerable age and in high-stress situations that greatly increase the risk of recreational use of opioids if they were made available for emergency pain relief. Research to identify potential analgesics with fewer side effects and more importantly, with reduced abuse liability and physical dependence, is pivotal to advances in healthcare of all individuals, but most critically, military personnel.