

NRSA Proposal Topic – Part III Comprehensive Exam 2019

Many of the 50 million Americans with chronic pain are prescribed opioid medications to manage their pain, yet there is limited evidence to suggest that long-term use of opioids is effective for managing pain in these patients. Long-term use of opioids can lead to addiction and uncontrollable drug craving. New, safer and less addictive treatment options for pain management are needed to improve quality of life and reduce the number of people exposed to the risks of opioids. Toward this goal, NIH is currently supporting research across the development spectrum. This encompasses efforts to understand the biological underpinnings of chronic pain, accelerate the discovery, preclinical development and testing of non-addictive alternatives to opioids, multipronged approaches to understand and treat specific pain conditions, comparative effectiveness research and tailored approaches to acute and chronic pain conditions, as well as pragmatic and implementation studies for the management of pain focused on patient outcomes and real-world results. The first step toward useful pharmacological alternatives to opioids is a fundamental understanding of opioid addiction in terms of the biochemical and neurogenic changes in the brain that are caused by opioid use, the opioid receptors that are involved and the mechanisms by which drugs such as methadone work to lessen opioid craving (so called opioid replacement therapy).

Prepare an NRSA style research proposal that addresses the following three questions. Make sure to select and justify an appropriate animal model for the studies.

1. What biochemical and neuroanatomical changes occur in the brain because of opioid overuse?
2. What receptors are responsible for mediating the effects of opioids?
3. How does methadone or other replacement drugs function to lessen opioid craving?

Make sure to state any hypotheses that will be tested in your proposal and provide a clear experimental approach, with expected findings, for each of these questions.

Here are a few review articles to use as a starting point in developing your proposal.

Volkow ND, McLellan AT. Opioid Abuse in Chronic Pain--Misconceptions and Mitigation Strategies. *N. Engl J Med.* 374 (2016) 1253-63

Salsitz EA. Chronic Pain, Chronic Opioid Addiction: A Complex Nexus. *J. Med. Toxicol.* 12 (2016) 54-57.

Dugosh K, Abraham A, Seymour B, McLoyd K, Chalk M, Festinger D. A Systematic Review on the Use of Psychosocial Interventions in Conjunction With Medications for the Treatment of Opioid Addiction. *J Addict Med.* 10 (2016) 93-103.

Finan PH, Remeniuk B, Dunn KE. The risk for problematic opioid use in chronic pain: What can we learn from studies of pain and reward? *Prog Neuropsychopharmacol Biol Psychiatry* 87 (2018) 255-262.

Additional Direction:

In writing your proposal, you can consult the tips provided by the NIH for writing proposals (http://grants.nih.gov/grants/writing_application.htm). For this exam you only need to consider specific aims, significance, innovation and approach. Remember that the reviewers need to be convinced that you have a grasp of the topic and that you convey your research plan clearly. Even though the research may involve complex relationships you still need to express your ideas as simply as possible. Your answer, not including references, should be no longer than 7 single-spaced printed pages using a font size of 11 points or larger. The first page should contain the Specific Aims; this will be an overview of the problem and your approach. Your research strategy should have the components listed below, with an emphasis on the approach, significance and innovation in that order of priority. In other words, the reviewers are more interested in how you would approach the problem than lots of “hand-waving” about significance and innovation.

Specific Aims

State concisely the goals of the proposed research and summarize the expected outcome(s), including the impact that the results of the proposed research will have on the research field(s) involved. List succinctly the specific objectives of the research proposed, e.g., to test a stated hypothesis, create a novel design, solve a specific problem, challenge an existing paradigm or clinical practice, address a critical barrier to progress in the field, or develop new technology.

Research Strategy

Organize the Research Strategy in the specified order and using the instructions provided below. Start each section with the appropriate section heading—Significance, Innovation, Approach. Cite published experimental details in the Research Strategy section and provide the full list of references in the Bibliography and References Cited section.