

## **TITLE; Role of the endogenous opioid system underlying modulation of experimental pain**

### **ABSTRACT**

The goal this proposal is to develop additional preliminary data and demonstrate feasibility for a R01 grant submission by Dr. Joseph Riley III. The aims of the planned R01 will be to test for age differences in pain modulation across a battery of laboratory pain testing protocols that are dynamic and involve pain inhibition. We are requesting funding to demonstrate the role of endogenous opioids in one of our experimental protocols using naltrexone, an opioid antagonist, and to identify other biological markers that may serve as mechanistic mediators of impaired pain modulation (inhibition or facilitation) that we expect to observe in older adults. Funding from this proposal will allow us to test the hypothesis that younger adults will demonstrate greater endogenous pain inhibition than older adults and this difference will be attenuated by naltrexone (opioid antagonist) in experiment #1 and examine biomarkers as mediators of age differences in pain modulation as part of experiment #2. For this project we will recruit 30 subjects divided equally into two age cohorts; subjects ages 18-49 and subjects 50-65 to bracket the ages of peak pain complaints. Our experimental model is described as 'diffuse noxious inhibitory controls' (DNIC) which implicates the existence of an endogenous pain modulation system in human studies. The basic principle of DNIC is "pain-inhibition-by-pain" where a pain stimulus in a local area (experimental stimulus) is inhibited by a second painful stimulus (conditioning stimulus) at another body site. Our chosen methodology uses emerging the foot in a cold water bath as the conditioning stimulus and focal heat at the palm as the experimental stimulus. Experiment 1 will consist of five testing sessions including calibration and training sessions. The final three sessions constitute the experimental sessions and are a control session without a water bath, a DNIC cold water bath session with naltrexone, and a DNIC cold water bath session with naltrexone. They will be presented in random order across subjects. Each experimental session will consist of five thermal trials of 60-second duration with experimental stimulus (contact heat) with a 3-minute rest period between trials. Subjects will receive heat stimuli to the dominant palm using the heat previously determined to produce a maximum pain rating in the 40-50 range (0-100 scale). Experimenters will be blinded concerning the constitution of the pill. Experiment #2 will characterize physiological response to the cold water bath as measured by immune markers, beta-endorphin, and cortisol and will consist of a single session. Following a baseline blood draw and collection of a saliva sample, respondents will be exposed to the cold water bath which is the conditioning stimulus from experiment 1. A second and third blood draw/saliva sample will occur at 30 and 60 minutes after the cessation of the last cold water trial. This experiment will also allow us to determine if markers found in saliva will be sufficiently sensitive to changes induced by our pain stimulus.

### **PROJECT NARRATIVE**

It is unknown why older adults develop a range of chronic pain conditions in greater numbers than younger persons. This proposal will allow this research team to use a specific narcotic antagonist drug, i.e. naltrexone, to test whether age differences seen in their earlier studies are the result of reduced activity of the endogenous narcotic, i.e. endorphin system in older subjects.