Study Protocol

Examination of Psychological and Physiological Pathways Linking Gratitude and Pain

Dr. Nathan T. Deichert

NCT Number: NCT06317844

Approved by BHSU IRB on 04/24/24

Study Protocol

Experimental Design: This one-year randomized controlled trial will begin in September 2024 and conclude by August 2025. Participants will be recruited through flyers and word of mouth. Flyers will be posted electronically on the BHSU campus and through weekly email updates. Interested participants will contact Dr. Deichert's research lab to enroll in the study. Given that the study will be collecting data from human subjects, the study protocol will be reviewed and approved by the Black Hills State University institutional review board as well as the National Institutes of Health prior to participant recruitment. The study will seek to enroll a convenience sample of 150 pain-free healthy individuals who are 18 years of age or older. Exclusionary criteria includes: 1) cardiovascular disease, 2) Raynaud's disease, 3) epilepsy, 4) being pregnant, 5) having a current injury to or open cut or sore on one's non-dominant hand, 6) history of fainting or seizures, 7) history of frostbite, 8) diagnosed with a chronic pain conditions, 9) diabetes, 10) malignant tumor, 11) chronic lung disease, 12) liver disease, 13) kidney disease, 14) gastrointestinal diseases, and 15) individuals currently taking opioids. There will be no restrictions based on race or gender.

This intervention will consist of a single visit to the PI's research laboratory (see Figure 1). During this visit, participants will be screened for eligibility and informed of the study procedures. After giving consent, participants will complete a series of questionnaires. First, participants will complete a brief demographic questionnaire measuring age, sex, body mass index (BMI), current smoking status, subjective socioeconomic status (SES), and experience with gratitude journaling. Participants will then complete a series of questionnaires assessing psychological functioning including depression (Patient Health Questionnaire-9), anxiety (Generalized Anxiety Disorder-7), and perceived stress (Perceived Stress Scale-10) followed by measures assessing baseline levels of pain severity (PROMIS Scale 2.0 – Pain Intensity 3a), pain interference (PROMIS Short Form v1.1 – Pain Interference 8a) and pain cognitions (Coping Strategies Questionnaire). Trait and state levels of gratitude will be assessed using both the Gratitude Questionnaire 6-item form and the Gratitude Adjective Checklist. Following completion of the baseline questionnaires, participants will be randomly assigned to one of two intervention writing conditions. In the gratitude writing condition, participants will write continuously for 5 minutes about someone they are grateful for. Participants in the neutral writing condition will write continuously for 5 minutes about how they got to the research laboratory. After the writing task is completed, participants will report on their state levels of gratitude and be given instructions regarding the cold pressor test and be asked to submerge their non-dominant hand into the cold pressor apparatus for up to 1.5 minutes, reporting their current level of pain every 15 seconds (participants may withdraw their hand at any point during the CPT). Cognitive reactions to pain will be assessed immediately following the cold pressor test using the Rumination and Reappraisal subscales of the Pain-Related Cognitive Processes Questionnaire.

To test the effectiveness of gratitude writing interventions to buffer individuals' physiological responses to stress, saliva samples will be sampled at 4 time points: 1) immediately following completion of baseline demographic and psychological measures, 2) immediately following the experimental writing task, 3) 2-minutes post-CPT, and 4) 10-minutes post-CPT. Samples will be collected using the passive drool method and will be labelled and stored in a -20°C freezer.

To test the hypothesis that COMT genotype will moderate the effects of a brief gratitude writing intervention to influence pain-related outcomes, buccal cells will be collected via cheek swab from all participants at the completion of the experimental procedure. Cells will be collected by

scraping the inside of each cheek for 15 to 20 seconds. Following the conclusion of the experimental procedure, cell samples will be stored in a -20 $^{\circ}$C freezer until DNA extraction and genotype analysis. DNA will be extracted from the buccal cell samples and participants will be genotyped on the *val158met* single nucleotide polymorphism (SNP).

Figure 1. Experimental Protocol Overview