Project Information

4R01DK093924-04

Project Number: 4R01DK093924-04 **Former Number:** 5R01DK093924-04

Contact PI / Project Leader: TEK, CENK

Title: NALTREXONE FOR ANTIPSYCHOTIC-INDUCED WEIGHT GAIN

Awardee Organization: YALE UNIVERSITY

Abstract Text:

DESCRIPTION (provided by applicant): People with severe mental illness (SMI) die 25 years earlier, mostly due to cardiovascular disease and diabetes, which are directly related to obesity. Obesity is a leading cause of preventable death in the US, second only to smoking. There is an urgent need for the development of interventions for the growing problem of obesity as well as related morbidity and mortality in this vulnerable population. Poor knowledge about nutrition, lack of access to healthy foods, and the increased costs of healthy foods contribute to increased prevalence of obesity among SMI patients. Regardless, the most important contributor to the obesity epidemic in this population is antipsychotic-induced weight gain. Behavioral interventions are necessary to fight obesity, but are insufficient, as patients continue to need their psychiatric medications, which in turn increase their appetite and make the task of losing weight extremely difficult. We have developed a working model of antipsychotic-induced weight gain. We hypothesized that antipsychotic medications attenuate the rewarding effects of food, thus causing SMI patients to eat more to get the same level of reward. To prove the concept, we completed a pilot study using naltrexone, a medication which blocks the effects of endorphins, the brain proteins which mediate the reward. If the additional reward is not gained with eating more, patients should stop doing so. Indeed, the pilot study showed that naltrexone stopped the weight gain trend in a group of patients taking antipsychotics and, in fact, produced significant weight loss for non- diabetic patients, while the placebo group continued to gain weight during the trial. This is an indirect evidence to support our hypothesis, as naltrexone does not produce weight loss in standard obesity treatment. Based on this evidence, naltrexone may be a useful, easy to use and cost effective medication to counteract antipsychotic-induced weight gain. In this application, we propose a large double blind, randomized clinical trial utilizing two doses of naltrexone compared to placebo over a period of one year (52 weeks) to counteract antipsychotic induced weight gain and obesity among a group of patients with SMI.

Public Health Relevance Statement:

PUBLIC HEALTH RELEVANCE: In order to prevent the resulting morbidity and mortality, there is an urgent need for the development of interventions for the growing problem of obesity in the severely mentally ill (SMI) population. Behavioral interventions are useful to fight obesity, but are insufficient, as patients continue to need their psychiatric medications which often increase their appetite. One explanation for the increase in appetite that these medications trigger is the subsequent disruption of the food reward system in the brain. In this application, we propose a large double-blind, placebo-controlled, randomized clinical trial utilizing two doses of the opioid antagonist medication naltrexone to block the reward received from overeating for the treatment of obesity among a group of patients with SMI.

Project Terms:

Accounting; Affect; Affinity; Antipsychotic Agents; arm; Attenuated; bariatric surgery; base; Behavior Therapy; Body mass index; Body Weight decreased; Brain; Cardiovascular Diseases; Cardiovascular system; Cessation of life; clinically significant; Communities; cost; cost effective; Desire for food; Development; Diabetes Mellitus; diabetic; diabetic patient; Dietary Intervention; Dopamine D2 Receptor; Dose; Double-Blind Method; Eating; Eating Behavior; Economics; effective intervention; Endorphins; Epidemic; fasting glucose; fighting; Food; Funding; General Population; Generations; Glycosylated Hemoglobin; Glycosylated hemoglobin A; Guidelines; Haloperidol; Health; health disparity; Health Food; Health Insurance; Histamine H1 Receptors; Hyperphagia; improved; increased appetite; Individual; Intervention; Knowledge; Life Style; Lipids; Mediating; Mentally Ill Persons; Modeling; Morbidity - disease rate; mortality; Naltrexone; Narcotic Antagonists; non-diabetic; nutrition; Obesity; obesity treatment; Opioid Receptor; Patients; Pharmaceutical Preparations; Physical activity; physical conditioning; Pilot Projects; Placebo Control; Placebos; Population; Prevalence; prevent; programs; Proteins; Psychiatric therapeutic procedure; Public Health; Randomized; Randomized Clinical Trials; receptor; Request for Applications; Rest; Rewards; Risk Marker; Risk Reduction; Running; Scheme; Schizophrenia; Serum; severe mental illness; Smoking; Symptoms; System; therapy development; trend; United States; Vulnerable Populations; waist circumference; Weight; Weight Gain; Work