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Scientific Abstract

Cigarette smoking is the most common preventable cause of death and disease in the US. Approximately 20% of Americans smoke cigarettes and a growing number of users, especially adolescents, have tried or are using alternative tobacco products (e.g. e-cigarettes). Nicotine addiction remains poorly treated with recidivism rates exceeding 90%; less is known for alternative tobacco product users. Nicotine addiction is the primary health outcome that leads to the distal developments of cancers, cardiovascular and respiratory disease. Emerging genetic and neuroimaging evidence, including from our group, has provided initial evidence of the biological basis of nicotine addiction, although no consensus biomarkers exist that can quantitatively measure addiction severity, follow dependence trajectory or predict outcome for either traditional or alternative tobacco users. Absent sound clinically relevant biomarkers, objective efficacy assessment is virtually impossible and continues to hinder scientifically based regulatory policies.

Thus, the goal of this project is to develop a quantitative, genetically informed, evidence based nicotine addiction 'sphygmomanometer'. This biomarker will be created using neuroimaging and genotyping and epigenetic data with multivariate feature selection techniques including support vector machine learning and neuronal network/graph theory matrix to classify and differentiate: traditional cigarette smokers by addiction severity; traditional smokers from alternative tobacco users; brain circuits that follow dependence severity and predict outcome success or failure.

To fully capture the biological correlates of dependence, smokers will be followed up to a year after smoking cessation. E-cigarettes will substitute for tobacco cigarettes during a 12-week monitored cessation phase. Anatomical and functional measures will be taken before a quit attempt, and post quit at days 2 and 7, and again at 3, 6 and 12 months. Neurobiological data acquired will include DTI (white matter integrity), T1 (gray matter density and cortical thickness morphometry), resting state BOLD (functional connectivity) along with genotyping and methylation epigenetic analysis.

The novelty of this approach is the combination of cutting edge multimodal measures to enhance discriminability and precision of the classifier. This information services both of our aims: to quantify abuse severity and create a biomarker that can reflect the abuse potential of alternative tobacco products. Our proposal targets specific FDA CTP research priorities by developing a quantitative biomarker that predicts smoking and smokeless tobacco adverse health outcomes.

Members of our multidisciplinary team are experts in fields spanning nicotine addiction neurobiology, clinical medicine, human genetics, imaging biophysics

and signal processing. We maintain an ongoing successful collaboration; one project recently identified part of a genetically driven, cortical-stria