A neuroergonomic study protocol evaluating cannabis' effects on neural and behavioral responses to a public speaking challenge in adults with anxiety

Bridget Kajs[1], Amy Wegener[1], Adrian Curtin[2], Bartu Atabek[2], Kevin L. Ramirez-Chavez[2], Zuhal Ormanoglu[2], Benjamin Cocchiaro[3], David Bennett[1], Carolyn Edwards[4], Hasan Ayaz[2], Wei Du[1,5]

[1]Department of Psychiatry, Drexel University College of Medicine

[2]School of Biomedical Engineering, Science and Health Systems, Drexel University

[3]Dornsife School of Public Health, Drexel University

[4]Division of Infectious Diseases and HIV Medicine, Drexel University College of Medicine

[5]Department of Pharmacology and Physiology, Drexel University College of Medicine

Synopsis

This pilot study uses neuroergonomic methods to evaluate the effects of medical cannabis on anxiety-related responses in a real world context. Adults with anxiety enrolled in the Pennsylvania Medical Marijuana Program will be followed for one month while initiating medical cannabis treatment. At baseline and one-month follow-up, participants will complete a public speaking challenge during which behavioral, physiological, and brain activity measures will be collected. We hypothesize that medical cannabis treatment will be associated with reduced anxiety, attenuated physiological stress responses, and altered prefrontal cortical activity during the task among individuals living with anxiety.

Background

Anxiety is one of the most common conditions for which people seek medical cannabis treatment. Although anecdotal reports suggest cannabis may reduce anxiety symptoms, empirical findings have remained mixed. Prior work on delta-9-tetrahydrocannabinol (THC), the principle psychoactive ingredient of cannabis, suggests dose effects, with lower doses being potentially anxiolytic and higher doses being anxiogenic (Stoner, 2017). In contrast, cannabidiol (CBD), another major cannabinoid, appears to show primarily anxiolytic effects (Berger et al., 2022). Given the rising use of cannabis to treat anxiety and the equivocal state of the literature, further clinically relevant research is needed to clarify its effects on anxiety outcomes.

While clinical research has helped to develop our initial understanding of the relationship between cannabis and anxiety symptoms, most studies have used research metholodogies and paradigms with limited real-world applicability. For example, many studies have examined neurophysiological changes using functional magnetic resonance imaging (fMRI) where individuals are confined within a scanner, limiting natural movement and real-world experiences. In addition, many of these studies have utilized emotional processing tasks to study anxiety instead of real-world scenarios that provoke anxiety such as public speaking. In this study, we seek to fill these gaps in knowledge by utilizing neuroergonomic methods to examine the effects of cannabis on neural, behavioral, and physiological responses to a public speaking challenge in individuals with anxiety.

Methods

Adult patients enrolled in the Pennsylvania Medical Marijuana Program who have at least moderate anxiety and a moderate fear of public speaking and plan to initiate treatment with medical cannabis for anxiety will be eligible to participate. Individuals with significant psychiatric conditions (e.g., schizophrenia, bipolar disorder, etc.), substance use disorders, or other medical conditions that pose risks to subjects or possibly interfere with study completion will be excluded. Participants will be followed over the course of one month post-initation of medical cannabis.

During in-person study visits at baseline and one-month follow-up, participants will undergo a standardized public speaking task (Glassman et al., 2014) during which behavioral, neurobiological, and physiological symptoms of anxiety will be meaured (Figure 1). Participants will be asked to give a four-minute speech in front of a virtual audience that participants will be told is observing them live; the “audience” is actually pre-recorded and will display generally flat affect throughout the participant’s speech, presented to the participant on a monitor.Two different speech topics and audience videos will be used at the baseline and one-month visits and will be presented in a counterbalanced order across participants.

To capture neural responses in a naturalistic setting, functional near-infrared spectroscopy (fNIRS) will be used to assess prefrontal cortical activity while participants remain seated upright and facing forward to view their virtual audience within a conference room. Additional measures will include self-reported measures of anxiety using the Subjective Units of Distress Scale (SUDS), physiological data including skin conductance, heart rate, blood pressure, as well as video-based facial expression analysis.

At the one-month visit, participants will come to the study visit at least one hour after taking their usual dose of medical cannabis and will have their blood drawn to measure circulating levels of THC and THC metabolites. In between the two in-person visits, participants will complete short weekly surveys virtually regarding their anxiety and cannabis use. We will also record adverse events that occur during the course of this study, including unexpected illness or hospitalizations. We plan to enroll 30 participants in this study starting in April of 2026.

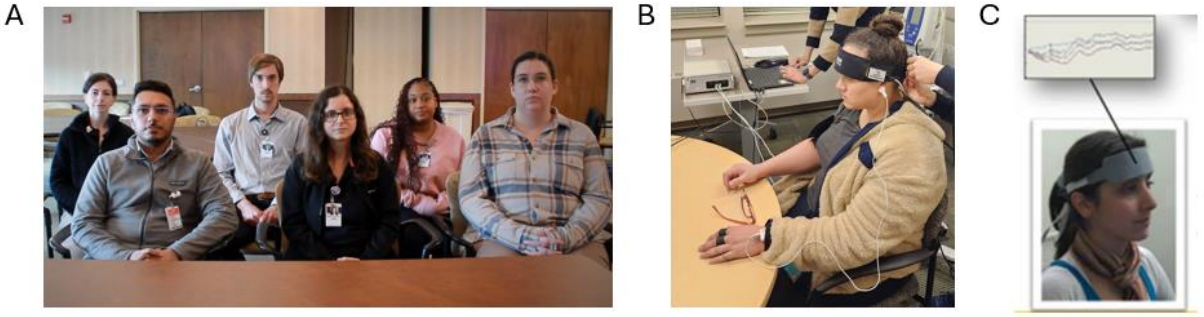

Figure 1. A. An example pre-recorded virtual audience that will be used in this study B. Experimental set-up for the study including placement of equipment for measuring skin conductance (Shimmer3 GSR+ Unit), heart rate (Scosche Rythm24 armband), blood pressure (electronic blood pressure monitor), and neural activity (prefrontal fNIRS headband) C. Functional near-infrared spectroscopy (fNIRS) headband and example neural activity recordings (Ayaz et al., 2013)

Results

The primary endpoints for this study are changes in 1.) neural activity and 2.) state anxiety during the public speaking task at baseline compared to one-month follow-up. Secondary endpoints for this study include changes in generalized and social anxiety symptoms, skin

conductance, heart rate, blood pressure, and facial emotions at baseline compared to one-month follow-up. Planned analyses include paired t-tests or Wilcoxon signed rank tests, as appropriate, and repeated measures analysis of variance for within subject comparisons across time. We hypothesize that one month of medical cannabis treatment will be associated with reduced subjective and physiological stress responses, along with altered neural responses during public speaking in individuals with anxiety.

Discussion

This study's unique design utilizing neuroergonomic methods will allow us to be the first to examine neurobiological changes during a real-world anxiety provoking situation, public speaking, in medical cannabis patients. This study has the ability to greatly increase our understanding of the relationship between cannabis and anxiety by extending the field's current findings to real-world situations. This study will also provide a multimodal measurement model for future studies examining medical cannabis' association with anxiety. Finally, findings from this study may inform patient decision making, provider practice, and evidence-based public policy surrounding the use of medical cannabis for the treatment of anxiety.

Disclosures

This study is funded through financial support from Agronomed Biologics. Dr. Ayaz has equity in fNIR Devices LLC that licensed IP from Drexel University and manufactures optical brain imaging sensors used in the study.

References

Ayaz H., Onaral B., Izzetoglu K., Shewokis P.A., McKendrick R., Parasuraman R. (2013). Continuous monitoring of brain dynamics with functional near infrared spectroscopy as a tool for neuroergonomic research: Empirical examples and a technological development. *Frontiers in Human Neuroscience*, 7, 1-13. doi: 10.3389/fnhum.2013.00871

Berger M., Amminger G.P., McGregor I.S. (2022). Medicinal cannabis for the treatment of anxiety disorders. *Australian Journal of General Practice*, 51(8), 586–592. doi: 10.31128/AJGP-04-21-5936

Glassman L.H., Herbert J.D., Forman E.M., Bradley L.E., Izzetoglu M., Ruocco A.C., Goldstein S.P. (2014). Near-infrared spectroscopic assessment of in vivo prefrontal activation in public speaking anxiety: A preliminary study. *Psychology of Consciousness: Theory, Research, and Practice*, 1(3), 271-283. doi: 10.1037/cns0000009

Stoner, S. (2017). Effects of marijuana on mental health: anxiety disorders. *Alcohol and Drug Abuse Institute*. https://adai.uw.edu/pubs/pdf/2017mjanxiety.pdf