SUBSTANCE ABUSE RESEARCH TRAINING PROGRAM
SART

PRESENTED BY:
RAVEN BEAN, MPH
CLINICAL RESEARCHER COORDINATOR I
INTERNAL MEDICINE

UCLA
SUBSTANCE ABUSE RESEARCH TRAINING (SART) TEAM

- THEODORE C. FRIEDMAN, MD, PH.D. (CDU)
- AMIYA SINHA-HIKIM, PH.D. (CDU)
- CHRISTINE GRELLA, PH.D. (UCLA)
- JUANITA BOOKER-VAUGHNS, PH.D. (CDU)
- MOHSEN BAZARGAN, PH.D. (CDU)
OVERVIEW

What is SART

Goals

Objectives

SART Program

Events

Poster Presentation
WHAT IS (SART)

The current Next Generation Substance Abuse Research Training at Charles Drew University (CDU) and UCLA (NGSART-CU) program, funded by the National Institutes of Drug Abuse (Grant No. 1R25DA050723-01A). SART stress the importance of educating researchers at all stages of their career in substance use disorder research, responsible conduct of research, and career advancement with a novel emphasis on community engagement and dissemination. Designed to advance research skills and reduce health disparities in substance use disorders. Substance Abuse Research Training (SART), provides in-person and online training in research methods, biostatistics, grant writing, professional development and more.
SUBSTANCE ABUSE RESEARCH TRAINING (SART)

GOAL

PROVIDING TRAINING TO INCREASE DIVERSITY BY IMPROVING THE QUALITY OF THE RESEARCHERS FROM A HEALTH RESEARCHER – IN THIS CASE, RELATED TO ADDICTION.
SUBSTANCE ABUSE RESEARCH TRAINING (SART)

WHO CAN APPLY

PRE-PROFESSIONAL TRAINEES
- UNDERGRADUATES
- MASTER’S STUDENTS
- POST- BACCALAUREATE

POST-DOCTORAL FELLOWS
- RECENTLY COMPLETED Ph.D OR FIRST POST-DOCTORAL FELLOWSHIP WITH PRIOR EXPERIENCE OR INTEREST IN SUBSTANCE USE RESEARCH AND HAVE OTHER SIMILAR SKILLS SUCH AS NEUROBIOLOGY OR MOLECULAR BIOLOGY.

CANDIDATES FROM UNDERREPRESENTED GROUPS IN SCIENCE
- BLACK OR AFRICAN AMERICAN
- HISPANIC OR LATINX
- AMERICAN INDIAN OR ALASKA NATIVE
- NATIVE HAWAIIAN OR PACIFIC ISLANDER
SUBSTANCE ABUSE RESEARCH TRAINING (SART) OBJECTIVE

• SART OBJECTIVE IS TO RECOGNIZE THAT MOST FUTURE ADVANCES TARGETING DIFFICULT DISEASES (SUCH AS SUBSTANCE USE DISORDERS) WILL BE BASED ON RESEARCH TEAMS THAT ARE BOTH MULTIDISCIPLINARY AND INTERDISCIPLINARY AND STRESS TEAM SCIENCE.

• SART OVERALL OBJECTIVE IS TO TRAIN THE FUTURE PI OF A GRANT (SUCH AS MD AND PHD WHO PURSUE A CAREER AS FULL-TIME SUBSTANCE USE RESEARCHERS). TO EDUCATE, MENTOR AND INSPIRE A WIDE VARIETY OF PROFESSIONALS IN THE TRAINING PIPELINE THAT WOULD BE PART OF A TEAM THAT RESEARCHER SUBSTANCE USE AND RELATED DISORDERS.
SUBSTANCE ABUSE RESEARCH TRAINING (SART) PROGRAM

PRE-PROFESSIONAL TRAINEES

- 5-10 HOURS/WEEK FOR 1 YEAR WORKING ON A RESEARCH PROJECT WITH A MENTOR
- MENTOR MEETING WEEKLY WITH RESEARCH MENTOR, MONTHLY WITH COMMUNITY MENTOR.

APPLICATION

- CV & RESUME
- LETTER OF RECOMMENDATION
- PERSONAL STATEMENT
- LETTER OF INTEREST

POST-DOCTORAL FELLOW

- FULL TIME FOR 2.5 YEARS
- MENTOR JUNIOR TRAINEE
- PUBLISH AT LEAST 3 PAPERS
- SUBMIT 1 OR MORE GRANTS

APPLICATION

- CV & RESUME
- LETTER OF RECOMMENDATION
- PERSONAL STATEMENT
- LETTER OF INTEREST

BENEFITS

- PREPARES TRAINEES IN FIELDS OF SUBSTANCE ABUSE RESEARCH
- BE MENTORED BY DIVERSE CDU & UCLA FACULTY WHO HAVE A TRACK RECORD OF ASSISTING TRAINEES AT ALL LEVELS
- ACCESS TO HIGHLY SKILLED AND REPUTABLE FACULTY WITH EXPERIENCE IN NIDA, NIH, AND/OR OTHER FUNDING IN SUBSTANCE ABUSE RESEARCH
- STIPEND 4K, WITH 2K IN THE MIDDLE (MARCH) OF THE YEAR AND 2K AT THE END (JULY)
SUBSTANCE ABUSE RESEARCH TRAINING (SART) EVENTS

• MENTOR AND MENTEES MEETING [MANDATORY]
• INSTITUTES [MANDATORY]
  1) METHODOLOGICAL SKILL DEVELOPMENT
  2) DIVERSE POPULATION WORKING WITH RACIAL, ETHNIC, SEXUAL AND GENDER MINORITIES
  3) BASIC SCIENCE RESEARCH SKILLS DEVELOPMENT
  4) CLINICAL EPIDEMIOLOGICAL AND BEHAVIORAL SKILL DEVELOPMENT
  5) GRANT WRITING SKILL DEVELOPMENT
• FRIDAY EVENTS [MANDATORY]
  1) WOMEN IN SCIENCE
  2) HOW TO BE A GREAT MENTOR AND MENTEE
  3) OPIOID EPIDEMIC
  4) VOICE FROM LIVED EXPERIENCE, TREATMENT SERVICES, TRANSITION, AND POLICY IN ADDITION TO SCIENCE AND MORE
• RESPONSIBLE CONDUCT OF RESEARCH TRAINING (RCR) [MANDATORY]
• RETREAT [VOLUNTEER]
SUBSTANCE ABUSE RESEARCH TRAINING (SART) RETREAT

2nd Annual Southern California Substance Addiction Research Training Retreat
CDU SART/ UCLA T32/ UCI T32/ Rising Stars/ CSUSB STOPs
June 9, 2023 (Hybrid)
Live at the California Endowment, 1000 North Alameda St, Los Angeles, CA 90012
Register at https://www.eventbrite.com/e/63275588897
Time: 8:30am-4:30pm
Virtual via Zoom, register at https://www.eventbrite.com/e/83496983917
https://us02web.zoom.us/j/98137712768
Meeting ID: 981 3771 2768

AGENDA

8:15 Registration and Breakfast

8:30-9:30 Introduction to Southern California Substance Addiction Research Training Retreat
Theodore C. Friedman M.D., Ph.D.

9:30-9:30: Highlights of Basic Neuroscience/ Drug Addiction Research:
Jean Carlos Rivero, Ph.D.
David Sanchez, Ph.D.
Jinny Marie Castro, Ph.D.
jayson Aposhtoli, Ph.D.

9:30-10:30 Highlights of Clinical/Translational Neuroscience/ Drug Addiction Research:
Elisa Palomar, Ph.D.
Alexandra Donovan, Ph.D.
Dyana Harlow, Ph.D.
Yaron Kirsch, Ph.D.

10:30-11:30 Keynote Speaker: William Compton, M.D.
Drug Addiction Science and the U.S. Overdose Epidemic

11:30 Lunch and Networking

12:30-1:30 Keynote Speaker: Adam Levintrot, Ph.D.
Addiction Science: More Substance Than You Might Think

1:30-2:30 Breakout Sessions A
Emerging Pharmaceutical Targets for Substance Use Disorder
https://us02web.zoom.us/j/881915
Jama Asnafy, Ph.D.
Nicole Shoptaw, Ph.D.
Laurisa Moshinsky, M.D.

2:40-3:40 Breakout Sessions B
Health Disparities of Substance Use Disorders
Angie Ortez-Castellanos, Ph.D.
Shervin Assari, M.D., MPh
Andrew Sufka, Ph.D.

3:40-4:40 Synopsos of Breakout: Wrap-up/ Evaluation

Medical use of Psychedelics https://us02web.zoom.us/j/4209687343
Brad Grayson, Ph.D.
Harriet De Wa, Ph.D.
Conor Murray, Ph.D.

Detrimental and beneficial effect of Cannabis https://us02web.zoom.us/j/4209687343
Lisa Edley, Ph.D.
Daniel Pietrulli, Ph.D.
Scott Hunter, M.D.
Elisa Palomar, Ph.D.

Continuing medical education will be awarded within 6-8 weeks following completion of the training.
SUBSTANCE ABUSE RESEARCH TRAINING (SART)  
POSTER PRESENTATION

Trainee’s poster presentation. End of the year event when trainees present their research projects along side their mentors. This event is held in-person at Charles Drew University Medicine and Science and Partners University’s, trainees:

- California State University, San Bernardino
- California State University, Dominguez Hills
- University of Southern California
Built on Minorities’ Diminished Returns (MDRs) Theory (Assari 2018), the purpose of this study is to explore whether the protective health advantage of high school performance in terms of lower substance use is influenced by race, given persistent health inequities despite efforts to address disparities in key social determinants of health (SDHs).

While it's widely acknowledged that school performance can lead to lower health risks and risk behaviors, the benefits of high school performance may not be as strong for Black youth as they are for White youth.

Objectives

1. To test the association between high school performance and substance use in youth
2. To determine if there is a racial variation in the association between them

Methods

PATH Study: The Population Assessment of Tobacco and Health (PATH) study is a nationally representative longitudinal study in the US focused on understanding tobacco use in youth and adults and its effects on health.

PATH Subsample Collection: Participants aged 12-17 and who self-identified as White or Black were selected from the PATH youth subsample.

Study Variables*:
- Predictor: School performance
- Outcomes: Substance use score
- Moderator: Race/Ethnicity
- Covariates: Age, sex, parental education

Data Analysis: Data was analyzed using SPSS 24:
- Univariate: Descriptive analysis
- Multivariable: Two models were utilized in the pooled sample
  - Model 1 – No interaction term between race and school performance
  - Model 2 – Interaction term applied between race and school performance

R, SE, 95% CI, and p-value (p<0.05) were reported from each model.

Results

Overall, 11557 participants included 9471 White and 2086 Black adolescents. Table 1 shows that while age, gender, parental education, and family structure are controlled, higher educational performance was associated with less substance use. However, Model 2 showed an interaction, suggesting weaker protection for Black than White participants. Figure 1 shows the regression line overall.

Table 1. Summary of Linear regressions

<table>
<thead>
<tr>
<th></th>
<th>Model 1</th>
<th>Model 2</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>B</td>
<td>Std. Error</td>
</tr>
<tr>
<td><strong>Race (Black)</strong></td>
<td>-0.101</td>
<td>0.011</td>
</tr>
<tr>
<td><strong>Gender (Male)</strong></td>
<td>-0.021</td>
<td>0.008</td>
</tr>
<tr>
<td><strong>Parental Marital</strong></td>
<td>0.184</td>
<td>0.008</td>
</tr>
<tr>
<td><strong>Parental Education</strong></td>
<td>0.008</td>
<td>0.003</td>
</tr>
<tr>
<td><strong>School Grades (Good)</strong></td>
<td>-0.028</td>
<td>0.010</td>
</tr>
<tr>
<td><strong>Race x Black</strong></td>
<td>-0.278</td>
<td>0.014</td>
</tr>
<tr>
<td><strong>Gender (Male)</strong></td>
<td>-0.031</td>
<td>0.008</td>
</tr>
<tr>
<td><strong>Age</strong></td>
<td>0.184</td>
<td>0.008</td>
</tr>
<tr>
<td><strong>Parental Marital</strong></td>
<td>-0.013</td>
<td>0.009</td>
</tr>
<tr>
<td><strong>Parental Education</strong></td>
<td>0.029</td>
<td>0.003</td>
</tr>
<tr>
<td><strong>School Grades (Good)</strong></td>
<td>-0.033</td>
<td>0.003</td>
</tr>
<tr>
<td><strong>Race x Black</strong></td>
<td>0.026</td>
<td>0.006</td>
</tr>
</tbody>
</table>

Conclusions

Based on our analysis of data collected from the PATH study, we found:

- An inverse association between high school performance and substance use
- The inverse association between high school performance and substance use was weaker for Black adolescents compared to White adolescents, which aligns with the broader literature of MDRs theory
- We attribute these diminished returns to social stratification and racism.

Study Limitations

- The PATH study was not originally designed to investigate substance use among youth and important factors related to substance use may not have been collected.
- Included only White and Black youth participants, limiting the generalizability of the results to other racial groups.
- Age was treated as a dichotomous variable, potentially oversimplifying the relationship between age and substance use.
- Self-reported data was used, which may be subject to bias and underreporting of substance use.
- Statistical analysis used in the study may not have fully accounted for all relevant confounding variables that could impact the relationship between school performance and substance use.

Despite these limitations, the study provides valuable insights into the relationship between school performance and substance use among Black and White youth, highlighting the need for targeted interventions to address substance use in this population.

Future Research

Future research should explore why the protective effects of high school performance against substance use is much weaker for Black adolescents compared to White adolescents, including the roles of high-risk school environments, neighborhood risk, peer risk, and other contextual conditions.

It’s also important to investigate the impact of structural and systemic racism and discrimination associated segregation on the differential return of academic achievement for Black and White students.

Acknowledgements

Funded by NIMH under SART (R25DA050723-04) and TRDRP (T32IR5355). Support also received from CZI (CZIF2022-007044), Hologic, and Kaiser Permanente ($119285).
Adipose Tissue Transcriptomic Analysis of the Role of Lipolysis in E-cigarettes Treated Mice.

Waleed Janjua, Jorge Espinoza-Derout.

Charles R. Drew University of Medicine and Science, Los Angeles, CA

Abstract

Electronic cigarettes were introduced to the market as a safe alternative for cigarette cessation or as a safer alternative to traditional cigarettes. E-cigarettes do not burn tobacco; they generally use a chemical like nicotine and various flavors that appeal to the younger generations. Lipolysis is a significant component in adipose tissue metabolism to maintain the cell. Lipases can reduce lipoprotein in adipose tissue increasing serum-free fatty acids (FFA). Increased levels of FFAs are one of the key elements in generating a proinflammatory response and lead to obesity. We aim to study the differentially expressed genes in adipose tissue of mice treated with saline, e-cigarette (2.5%) acipimox is lipolysis inhibitor. IPA showed canonical pathways affected across e-cig with acipimox, e-cig 2.5%, and saline. Phagosome formation is an autophagy pathway that changes during exposure to e-cig. Additionally, there are disturbances in the Fx receptor-mediated phagolysosome in macrophages and monocytes related to e-cig exposure. Additionally, we observe an increase in Leukocyte Extravasation signaling, CLEAIR signaling pathway, and cardiac rhythm signaling, all about metabolic adaptations during stress, such as fasting and starvation, and maintaining plasma glucose levels.

Introduction

Despite health warnings from multiple public health authorities, the products are gaining popularity, especially among adolescents, with sales hitting $10 billion in 2017. E-cigarettes do not burn tobacco; they generally use a chemical like nicotine and various flavors that appeal to the younger generations. Nicotine is a dangerous substance because of its biochemical pathways, within which it binds to acetylcholine receptors (nAChRs), which are involved in the mesolimbic pathway. In the US, past 30-day vaping among high school students rose from 1.5% in 2011 to 11.7% in 2017 to 20.0% in 2018. Adipose Tissue stores and releases free fatty acids and synthesizes many compounds involved with plasma FFA, used as energy. With the increase in FFAs, there is an increase in insulin resistance and induced inflammation in multiple cell types. IL-6 is a signaling molecule that influences inflammation and cardiac dysfunction, released by adipocytes and macrophages in adipose tissue.

Hypothesis Objectives

If lipolysis is necessary for e-cigarette changes in the adipose tissue, adipocytes should normalize the effect of e-cigarettes. In the RNA-seq analysis, we expect the dysregulated genes indicating an inflammatory phenotype will be normalized by acipimox.

Experimental Design and Methods

Two analyses were done in parallel: differential gene expression and Ingenuity Pathway analysis of the normalized and filtered gene list and gene set enrichment analysis of the entire list of normalized gene counts. The normalized, filtered read counts were also used for gene set enrichment analysis (GSEA) using GSEA version 4.1.0. Two additional sets were analyzed against all available from the Molecular Signatures Database. Phases (P) and fold change (FC) filters were applied for all differential gene expression results. Ingenuity Pathway Analysis (IPA) was used to predict changes in canonical pathways.

Results

The Canonical Pathways show the z-score with the most significant responsible for allowing the cell to get rid of foreign substances phagocytosis. In modulating metabolism and immunity. It acts upstream of several processes antibody-dependent cellular cytotoxicity and phagocytosis. Specific genes being expressed in a similar pattern, we see the downward expression of Fgfr1, which in the mouse model enables IgG binding—such upsurge of several processes antibody-dependent cellular cytotoxicity and phagocytosis. Specific genes are both genes involved in modulating inflammation and longevity. It can set as a transcriptional indicator and represent, being downregulated in the e-cig samples.

Conclusions

With the downregulation of specific genes, we can see the disruption of the repressor, being downregulated in the e-cigarette group versus the rest of the phenotype selected for comparison were the e-cigarette group versus the rest of the ingenuity pathway analysis (IPA) showed canonical pathways affected across e-cig with acipimox, e-cig 2.5%, and saline. Exposure to e-cigarettes shows signs of disruption in specific pathways such as phagosome formation, Leukocyte Extravasation signaling, and CLEAIR signaling pathway, all related to metabolism in adipose tissue.

Future Directions

Validation of the findings needs to be made with qPCR. A study needs to be validated of the immune pathways activated in adipose tissue to understand further the ability to maintain proper metabolic systems.

References

7. Hologic, and Kaiser Permanente (# 138285)

Acknowledgments

This work was supported by NIH grants: NIGMS (SC2GM135127) and NIDA (R25DA050723).
Gender Differences in NAFLD: Impact of Smoking and High-Fat Diet in Mice

Charles R. Drew University of Medicine and Science, Los Angeles, CA
Erica Martinez, Theodore Friedman, Kenneth Roos, and Kamrul Hasan

Abstract
Nonalcoholic fatty liver disease (NAFLD) is characterized by fat accumulation in the liver unrelated to alcohol consumption. It has been associated with metabolic syndromes that can lead to cardiovascular disease, diabetes, and liver disease. Smoking has been shown to influence the development of NAFLD by varying factors. When combined with a high-fat diet (HFD), cigarette smoking triggers oxidative stress and hepatic inflammation, leading to hepatic fibrosis, non-alcoholic steatohepatitis, and hepatic carcinoma. NAFLD differs in prevalence and severity within genders—the biological differences impact its pathogenesis. Factors include sex hormones, age, and metabolism. Our study examines whether there are gender differences in NAFLD when smoking and HFD are combined. We used hyperglycemic HFD (Apoe(-/-) mice, ApoE-/- mice, a standard model of obesity and NAFLD). Male and female mice were exposed to conventional cigarette smoke (cCig) and Western diet (WD) to examine the impact of smoking on liver fat accumulation.

Background
• If more than 5% of the liverweight is fat, it is considered a fatty liver (steatosis).
• There are two different types:
  1. Simple fatty liver: fat in the liver but little or no inflammation or damage to liver cells
  2. Nonalcoholic steatohepatitis (NASH): - Severe form of NAFLD - development of hepatitis - Causes inflammation, liver damage, fat accumulation - Can lead to the development of cirrhosis, which can progress to cancer
• Makes use of tobacco products more in males and more susceptible to developing NAFLD than women in fertile age. Women are more susceptible to menopause age.
• Metabolic gene SIRT1, an essential positive regulator of BMAL1, has been closely affiliated with the regulation of metabolism along with pAMPK and pACC
• Makes and females distribute energy differently due to the deposit of fat in certain areas and the level of sex hormones.

Hypothesis Objectives
This study investigated gender differences in non-alcoholic fatty liver disease (NAFLD) in mice when smoking and a high-fat diet (HFD) were combined.

Experimental Design and Methods
Animals:
• 8-week-old Female and Male Apolipoprotein (ApoE -/-) mice
• Control Group: mice were only given a normal chow diet (NCD) and Western diet (WD) only
• Experimental Group: mice were given NCD and WD and were exposed to conventional cigarette smoke (cCig) for 12 weeks

Body weight and food consumption recorded weekly.

Results
• Livers and Serum were collected for:
  • Western Blotting
  • Trycystine (TC) Assay
  • Free Fatty Acid (FFA) Assay
  • Immunohistochemistry (HC)

Sirt1, a positive regulator of Bmal1, was significantly decreased in females exposed to both. Our study concluded that the combined effect of cCig and WD could profoundly perturb the hepatic circadian system. Significant weight loss in males on NCD and WD. However, minimum differences were found in females.

Conclusions
• 1. Smoking could trigger more profound NAFLD in obese female mice than male obese mice.
• 2. Higher serum FFA indicates that lipolysis in female mice is higher than in male mice.
• 3. Mechanistically, WD and smoking in combination increase the expression of the lipogenic gene in female mice.
• 4. Both, a circadian gene regulating lipid metabolism, and NAFLD were much reduced in female mice than in males, causing higher fat accumulation.
• 5. Sirt1, a positive regulator of Bmal1, was significantly decreased in females exposed to both.
• 6. Our results further showed that NAFLD triggered pronounced fibrosis in female mice than male mice.

Future Directions
Further studies should be conducted to validate the impact of differential gene expressions and their downstream regulation. Additionally, investigations should be undertaken to assess the effects of DNA methylation and histone modifications to understand better their role in non-alcoholic fatty liver disease (NAFLD)

References
2. Theodore C. Friedman and others, Additive Effects of Nicotine and High-Fat Diet on Hepatic Steatosis in Male Mice, International journal of biological sciences, Volume 159, Issue 2, 10.5005/jp -journals-10018-1370
3. Mohammad Kamrul Hasan and others, Hepatic Steatosis in Male Mice by Inhibiting Oxidative Stress and Stimulating AMPK Signaling, Volume 159, Issue 2
4. 7-Nicotinic Acetylcholine Receptor Agonist Ameliorates Nicotine Plus High-Fat Diet–Induced Hepatic Steatosis in Female Mice, Volume 159, Issue 2
5. Sirt1, a positive regulator of Bmal1, was significantly decreased in females exposed to both.

Acknowledgments
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