SUBSTANCE ABUSE RESEARCH TRAINING PROGRAM

SART

PRESENTED BY:

RAVEN BEAN, MPH

CLINICAL RESEARCHER COORDINATOR I

INTERNAL MEDICINE

SUBSTANCE **A**BUSE **R**ESEARCH **T**RAINING (**SART**)

TEAM

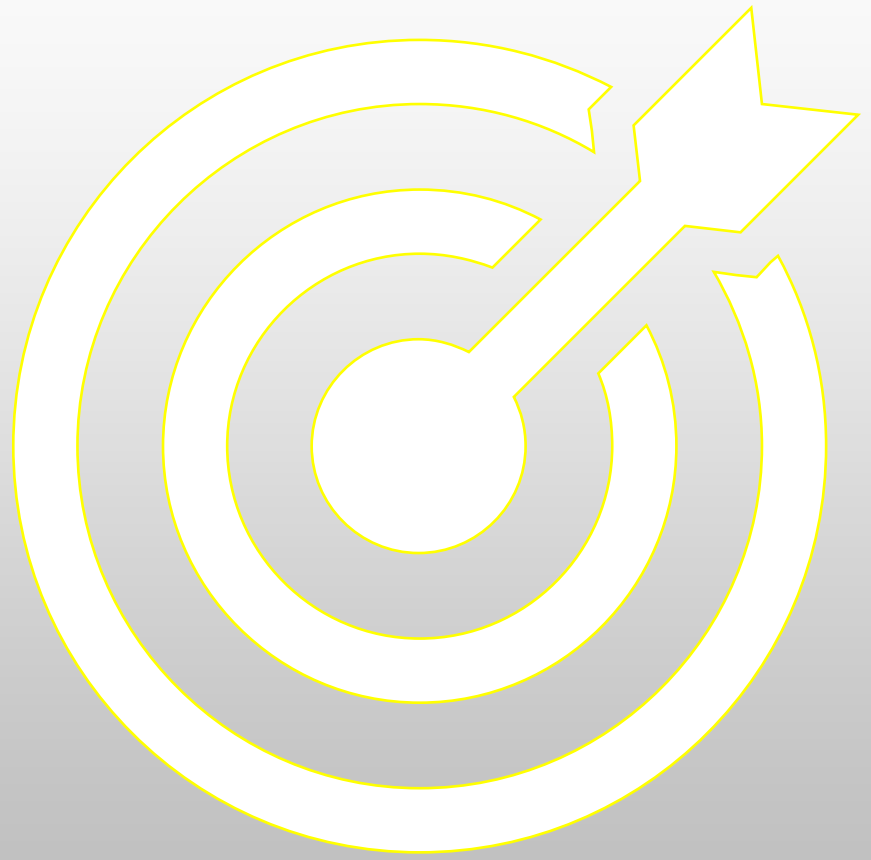
- THEODORE C. FRIEDMAN, MD, PH.D. (CDU)
- AMIYA SINHA-HIKIM, PH.D. (CDU)
- CHRISTINE GRELLA, PH.D. (UCLA)
- JUANITA BOOKER-VAUGHNS, PH.D. (CDU)
- MOHSEN BAZARGAN, PH.D. (CDU)

OVERVIEW

- What is SART
- Goals
- Objectives
- SART Program
- Events
- Poster Presentation

WHAT IS (SART)

THE CURRENT **N**EXT **G**ENERATION **S**UBSTANCE **A**BUSE **R**ESEARCH **T**RAINING 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. **S**UBSTANCE **A**BUSE **R**ESEARCH **T**RAINING (**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 HEATH 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

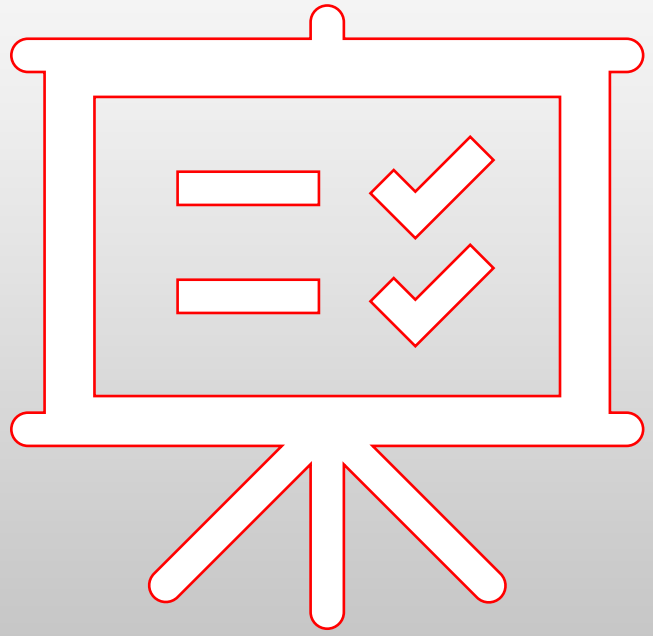
RECENTLY COMPLETED Ph.D OR FIRST POST-DOCTORAL FELLOWSHIP WITH PRIOR EXPERIENCE OR INTEREST IN SUBSTANCE USE RESEARCH AND HAVE OTHER SIMILAR SKILLS SUCH AS NEUROBIOLOGY OR MOLECULAR BIOLOGY.

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 1YEAR 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

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 SCIENCE AND MORE

- **RESPONSIBLE CONDUCT OF RESEARCH TRAINING (RCR)** [MANDATORY]
- **RETREAT** [VOLUNTEER]

SUBSTANCE ABUSE RESEARCH TRAINING (SART) RETREAT

UCLA David Geffen School of Medicine Integrated Substance Abuse Programs
UCLA Brain Research Institute SART UCI

2nd Annual Southern California Substance Addiction Research Training Retrea
CDU SART/ UCLA T32/ UCI T32/USC 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/632755888897
Time: 8:30am-4:30pm
Virtual via Zoom, register at https://www.eventbrite.com/e/634969850917
https://us02web.zoom.us/j/88157712788
Meeting ID: 881 5771 2788

AGENDA

7:30-8:15 Registration and Breakfast
8:15-8:30 Introduction to Southern California Substance Addiction Research Training Retreat
Theodore C. Friedman M.D., Ph.D.

8:30-9:30: Highlights of Basic Neuroscience/ Drug Addiction Research:
Juan Carlos Rivera, Ph.D.
David Sanchez, Ph.D.
Emily Marie Castro, Ph.D.
Lindsay Lueptow, Ph.D.

9:30-10:30 Highlights of Clinical/Translational Neuroscience/ Drug Addiction Research:
Elisa Pabon, Ph.D.
Alexandra Donovan, Ph.D.
Alyssa Harlow, Ph.D.
Dylan Kirsch, Ph.D.

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

11:30-12:30 Lunch and Networking

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

1:35-2:35 Breakout Sessions A
Emerging Pharmaceutical Targets for Substance Use Disorder https://us02web.zoom.us/j/88157
Liana Asatryan, Ph.D.
Steven Shoptaw Ph.D.
Larissa Mooney, M.D.

Or

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

2:40-3:40 Breakout Sessions B https://us02web.zoom.us/j/88157712788
Health Disparities of Substance Use Disorders
Angie Otiniano Verissimo, Ph.D.
Shervin Assari, M.D., MPH
Andrew Subica, Ph.D.

Or

Detrimental and beneficial effect of Cannabis: https://us02web.zoom.us/j/4209687343
Linda Richter, Ph.D.
Daniele Piomelli, Ph.D.
Scott Hunter, M.D.
Elisa Pabon, Ph.D.

3:40-4:00 Synopsis of Breakout/ Wrap-up/ Evaluation

This years event will include five training and research programs in Southern California: *UCLA T32 Program in the Trans
Drug Abuse *UC Irvine T32 Training Program in Substance Use and Use Disorders *Charles Drew Medical University *U
Institute for Addiction Science *CA State Univ. San Bernardino Smoke and Tobacco Outreach and Prevention Scholar (ST

CME/CE Keynote speakers designated by # will be CME/CE talks.

UCLA Integrated Substance Abuse Programs (ISAP) is accredited by the California Medical Association (CMA) to provid
education for physicians.

UCLA Integrated Substance Abuse Programs (ISAP) designates this live in-person/live virtual training course for a maxim
PRA Category 1 Credits™. Physicians should claim only the credit commensurate with the extent of their participation in t

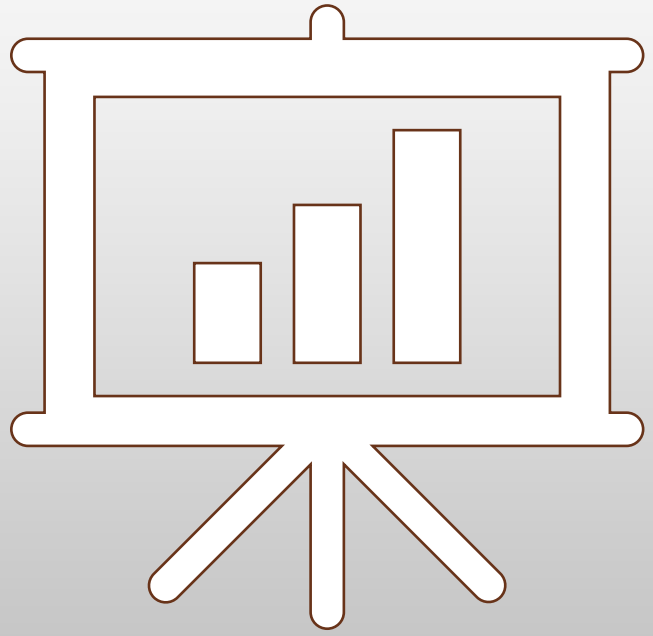
The California Board of Registered Nursing recognizes that Continuing Medical Education (CME) is acceptable for meetin
education requirements as long as the course is certified for *AMA PRA Category 1 Credits™* (rn.ca.gov). Nurses will receiv
Participation following this activity that may be used for license renewal.

Continuing medical education will be awarded within 6-8 weeks following completion of the training.

APA APPROVED SPONSOR

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

Diminished Protective Effects of School Performance on Black Youth Substance Use

John Ashley Pallera[1] , Arash Rahmani [2], Shervin Assari[3,4,5]

[1]Department of Biomedical Sciences, Charles R. Drew University of Medicine and Science, Los Angeles, CA [2] Marginalization-related Diminished Returns, Los Angeles, CA, USA
[3]Department of Family Medicine, Charles R. Drew University of Medicine and Science, Los Angeles, CA, USA [4] Department of Internal Medicine, Charles R. Drew University of Medicine and Science, Los Angeles, CA, USA[5] Department of Urban Public Health, Charles R. Drew University of Medicine and Science, Los Angeles, CA, USA

Background

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 inequalities 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

To examine the connection between school performance and substance use in White and Black youth in the United States:

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
- *Outcome*: Substance use score
- *Moderator*: *Race/Ethnicity*
- *Covariates*: Age, sex, parental education

*Please refer to QR code for information regarding how variables were assigned values for statistical analysis, supplemental results, and figures.

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

B, 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

	B	Std. Error	Beta	Lower Bound	Upper Bound	p
Model 1						
Race (Black)	-0.101	0.011	-0.093	-0.122	-0.080	0.000
Gender (Male)	-0.031	0.008	-0.037	-0.047	-0.015	0.000
Age	0.184	0.008	0.216	0.168	0.200	0.000
Parents Married	-0.013	0.009	-0.014	-0.030	0.004	0.142
Parental Education (1-5)	0.008	0.003	0.024	0.002	0.015	0.015
School Grades (Good)	-0.028	0.003	-0.108	-0.033	-0.023	0.000
Model 2						
Race (Black)	-0.278	0.044	-0.256	-0.365	-0.191	0.000
Gender (Male)	-0.031	0.008	-0.036	-0.047	-0.015	0.000
Age	0.184	0.008	0.216	0.168	0.199	0.000
Parents Married	-0.013	0.009	-0.014	-0.030	0.004	0.147
Parental Education (1-5)	0.009	0.003	0.026	0.002	0.016	0.008
School Grades (Good)	-0.033	0.003	-0.127	-0.038	-0.027	0.000
School Grades (Good) x Black	0.026	0.006	0.166	0.013	0.038	0.000

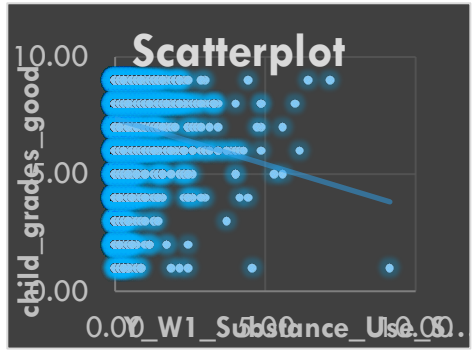


Figure 1. Scatter plot of linear regression line in the pooled sample

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 and associated segregation on the differential return of academic achievement for Black and White students.

Acknowledgements

Funded by NIH under SART (R25DA050723-04) and TRDRP (T32IR5355). Support also received from CZI *(CZIF2022-007044),* Hologic, and Kaiser Permanente *(#138285).*

References

*Please refer to QR code for information regarding references used for this study.

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 tool for cigarette cessation or a safer alternative to traditional cigarettes. E-cigs do not burn tobacco; they generally use a chemical like nicotine and various flavors that appeal to a younger audience.

Lipolysis is a significant component in adipose tissue metabolism to maintain the cells. Nicotine can induce lipolysis in adipose tissue, increasing serum-free fatty acids (FFAs). Increased levels of FFAs are one of the key elements in generating a proinflammatory response and lead to lipotoxicity.

We aim to study the differentially expressed genes in adipose tissue of mice treated with saline, e-cigarette (2.4%) acipimox (a lipolysis inhibitor). IPA showed canonical pathways affected across e-cig with acipimox, e-cig (2.4%), and saline. Phagosome formation is an autophagy pathway that changes during exposure to e-cig. Additionally, there are disturbances in the Fc receptor-mediated phagocytosis in macrophages and monocytes related to e-cig exposure. Additionally, we observe an increase in Leukocyte extravasation signaling, CLEAR signaling pathway, and circadian 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-cigs 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 20.8% 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 FFA, 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, acipimox 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, unfiltered read counts were also used for gene set enrichment analysis (GSEA) using GSEA version 4.1.0. The gene sets that our RNA-seq data was analyzed against are all available from the Molecular Signatures Database.

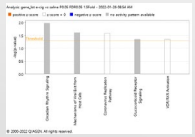
P-values (P) and fold change (FC) filters were applied for differentially expressed gene lists. The filter was $P < 0.01$ and FC > 2-fold for all differential gene expression results. Ingenuity Pathway Analysis software (IPA) was used to predict changes in canonical pathways.

The two phenotypes selected for comparison were the e-cigarette group versus the rest of the groups, which consisted of saline and e-cigarette plus acipimox. Default GSEA parameters were used in our study. This study used the conventional cut-offs for statistical significance: nominal P value ≤ 5% and false discovery rate (FDR) Q value ≤ 25%.

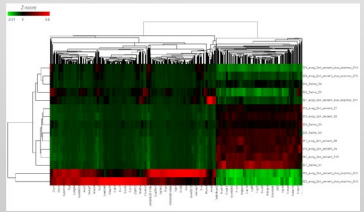
We matched multiple data sets using the Raw Read count to understand which genes were over-represented in the tissue and which pathways they related to.

https://handijovan2485l.blogspot.com/2021/04/juul-pods-cop-color-and-flavor-new.html

Results



The Canonical Pathways show the z-score with the most significant upregulation, relating to phagosome formation and keeping a proper metabolic system within the adipose tissue. As we see in the acipimox rescue, which halts the lipolysis process, the genes responsible for allowing the cell to get rid of foreign substances increase stress on the system affecting cell migration, growth, metabolism, and autophagy.



Specific Genes being expressed in a similar pattern, we see the downward expression of Fcgr3, which in the mouse model enables IgG binding—acts upstream of several processes: antibody-dependent cellular cytotoxicity and phagocytosis.

SnX20 and Atf3 are both genes involved in modulating metabolism and immunity. It can act as a transcriptional factor and repressor, being downregulated in the e-cig samples.

Conclusions

Exposure to e-cigarettes shows signs of disruption in specific pathways such as phagosome formation, Leukocyte Extravasation signaling, and CLEAR Signaling pathway, all related to metabolism in adipose tissue. With the downregulation of specific genes, we can see the disruption of the metabolic process in adipose tissue. The CLEAR signaling pathway was rescued by acipimox and showed upregulation, reducing the amount of FFA in the stressed metabolism in adipose tissue.

Future Directions

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

References

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Acknowledgments

This work was supported by was supported by the 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

Non-Alcoholic 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, obesity, and insulin resistance. Smoking has been shown to influence the development of NAFLD by causing lipolysis. When combined with a high-fat diet (HFD), nicotine triggers oxidative stress and hepatocyte apoptosis, leading to hepatic steatosis, non-alcoholic steatohepatitis, and hepato-carcinoma. NAFLD differs in prevalence and severity within genders—the biological differences impact its pathogenesis. Factors include DNA, sex hormones, age, and metabolism. Men are at higher risk of developing NAFLD at fertile age, but women have an increased prevalence at post-menopause. This study examines whether there are gender differences in NAFLD in mice when smoking and HFD are combined. We used Apolipoprotein E null (ApoE -/-) mice, a standard model of obesity and NAFLD. Male and female mice feeding on normal chow diet (NCD) and Western diet (WD) were exposed to conventional tobacco cigarettes (cCig) for 12 weeks. The control group consisted of mice that were given only NCD and WD. Livers and serum were collected for downstream analysis: western blotting (WB), quantitative RT-PCR, triglyceride assay, free fatty acid assay, and immunohistochemistry. We found that cCig exposures caused significant weight loss in males on NCD and WD. However, minimum differences were found in females. Additionally, males exposed to cCig ate less than the control, but no differences were found in females. H&E-stained liver sections revealed that fat accumulation in female mice exposed to both stressors is higher compared to males. WB analysis of metabolic genes showed that the expression of pAMPK, pACC, and Sirt1 in females treated with both was lower than in males. Intriguingly, the expression of BMAL1, a circadian gene regulating hepatic steatosis, was decreased in females than in males. These results suggest that the combined effect of cCig and WD could profoundly perturb the hepatic circadian system. The level of Sirt1, a positive regulator of BMAL1, was lower in females exposed to both. Our study concluded that cCig and WD combination could exacerbate NAFLD in females more than in males. The differential effect on Sirt1 and BMAL1 expression exerted by cCig and WD could be a causal factor for gender differences in NAFLD.

Background

- If more than 5% of the liver weight 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 fibrosis, which can progress to cirrhosis
- Males use tobacco products more and are 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
- Males and females distribute energy differently due to the deposit of fat in certain areas and the level of sex hormones.

However, gender differences in the combined effect of obesity and smoking on NAFLD is unknown

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 -/-)
- 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

Downstream analysis:

- Livers and Serum were collected for:
  - Western Blotting
  - Triglyceride (TG) Assay
  - Free Fatty Acid (FFA) Assay
  - Immunohistochemistry (IHC)

Results

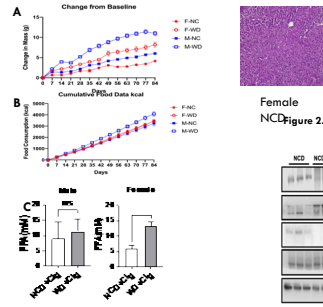

Figure 1: Body weight gain(A), food consumption (B) and serum FFA level (C) in different groups of mice

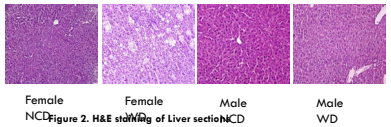

Figure 2. H&E staining of Liver sections

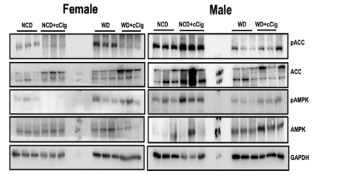

Figure 3: Western Blot Analysis for pACC, ACC, pAMPK and AMPK in the livers of different groups of mice

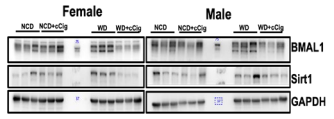

Figure 4: Western Blot Analysis of SIRT1 and BMAL1 Expression in Female Groups

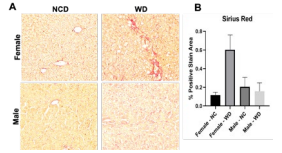

Figure 5: Sirius Red staining (A) and Intensity of fibrosis

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. Bmal1, a circadian gene regulating lipid metabolism, and NAFLD were much reduced in female livers than in males, causing higher fat accumulation.
5. Sirt1, a positive regulator of Bmal1, was significantly decreased in response to the combined effect of tobacco smoking and WD.
6. Our results further showed that NAFLD triggered pronounce fibrosis in female mice than male mice.
7. Altogether, our data suggest neither stressor has a short-term detrimental effect on male and female mice. However, these two factors, in combination, exacerbate NAFLD in female mice more 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)

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