J Neurol Neurosci ©
14 (2) 2023 : 001-05 • RESEARCH ARTICLE

SCL6A4 gene variants moderate associations between childhood food insecurity and adolescent mental health

Stefanie Pilkay[1]*, Meagon Nolasco[1], Sarah Nunes[1], Andie Riffer[2], Danielle Femia[1], Devorah Halevy[3], Tara Veerman[4], Stephanie Heiland[1], Nikki Trexler[1]

[1]Syracuse University, School of Social Work, 900 South Crouse Avenue, Syracuse, NY. 13244, USA

[2]Univeristy of Illinois Chicago, Jane Addams College of Social Work, 1040 W Harrison St, Chicago, IL. 60607, USA

[3]Yeshiva University, Wurzweiler School of Social Work, 2495 Amsterdam Ave, New York, NY. 10033, USA

[4]Centenary University, School of Social Work, 400 Jefferson St. Hackettstown, NJ. 07840, USA

SUMMARY

Background: Food insecurity is a persistent concern in the U.S. and has been shown to affect child mental health and behavior. The SCL6A4 gene has been indicated as a moderator of the effects of chronic stress on anxiety in adolescents aged 14-21. However, it is unclear if SCL6A4 may also play a role in the effects of childhood food insecurity, a form of chronic stress, on adolescent mental health. This study aimed to identify effects of food insecurity on adolescents' mental health and delinquent behavior when both mom and child go hungry in the child's early years, and the potential interaction with SCL6A4 variants (SS/LL). Methods: The data and sample for this research are from The Future of Families and Child Wellbeing Study. The cohort consists of 4,898 children (age 1-15 years, male=47%, African American=50%) and their respective caregivers sampled from large cities in the U.S. from 1998 to 2000. Results: The SCL6A4 serotonin transporter short/short allele emerged statistically significant as a moderator of childhood food insecurity and adolescent mental health. Specifically, the presence of the short/short allele increased anxiety symptoms in adolescents with exposure to food insecurity in childhood. Conclusion: The SCL6A4 short/short allele amplifies risk of anxiety related mental illness when children experience food insecurity. The gene environment interaction provides insight into the mechanistic pathway of the effects of poverty related adversity, such as food insecurity, on developmental trajectories of mental health.

Keywords: SCL6A4; Gene environment; Anxiety; Adolescence; Food insecurity

Address for correspondence:

Dr. Stefanie Pilkay
Syracuse University, School of Social Work, 900 South Crouse Avenue, Syracuse, NY. 13244, USA
Tel: (865) 454-1112
E-mail: srpilkay@syr.edu

Word count: 3015 **Tables:** 00 **Figures:** 03 **References:** 22

Received: 06.03.2023, Manuscript No. ipjnn-23-13540; **Editor assigned:** 08.03.2023, PreQC No. P-13540; **Reviewed:** 22.03.2023, QC No. Q-13540; **Revised:** 28.03.2023, Manuscript No. R-13540; **Published:** 05.04.2023

INTRODUCTION

Food insecurity is a persistent concern in the U.S. and has been shown to affect child development and well-being as examined by mental and behavioral health research [1,2]. Food insecurity is defined by the United States Department of Agriculture (USDA) as the inability to acquire adequate food due to lack of money or other resource deficiencies USDA [3]. Food insecurity is defined broadly to include being unable to live a healthy life and feeling unsatisfied as it relates to the amount and variety of diet [4]. According to the USDA's 2020 Food Security Survey, food insecurity is prevalent in U.S. households as evidenced by the 10.5% or 13.1 million U.S. households who reported food insecurity at some point in 2020 USDA [3].

Food insecurity is measured at two levels: low food security and very low food security. Low food security is characterized by reducing quality of diet and lack of diet variety. Food insecurity has also been measured based on satisfaction with food consumption and the ability to know food will be available [4]. Very low food security is characterized by disrupted frequency of meals and lack of food intake due to household inability to obtain food USDA [3]. Moreover, households with children were more likely to be food insecure than those without children, 14.8% and 8.8% respectively USDA [3]. Of these 13.1 million households, 6.1 million children lived in food insecure households with over 580,000 living in low food security households USDA [3]. Since the global COVID-19 pandemic, households with children have tripled in reports of food insecurity [5].

Food insecurity has been shown to affect a child's mental health and behavior. Canadian youth who live in households that are food insecure *vs.* secure are more likely to report mood disorders, anxiety disorders and emotional distress [2]. Risk of suicidal thoughts increased, up to 6.49 times higher, for children experiencing food insecurity [1,2] identified that childhood material hardship, especially at the ages of 9 and/or 15, showed an association with adolescence experiencing anxiety and depression symptoms at age 15. Edmunds C and Alcaraz M [1] measured material hardship by the lack of basic needs, adequate food in the household being a basic need, amongst other poverty factors related to material hardship. Food insecurity in children and adolescents also shows heightened risk for behavior problems [6], internalization of these behavior problems

[7] and higher risk of alcohol and other substance use [8]. Children go through various milestones of development from birth to 5 years of age, many milestones can be influenced by the stressors stemming from food insecurity as well as food insecurity as a sole stressor [9].

Early childhood development is sensitive to food insecurity in other ways such as gene-environment interactions. For example, the SCL6A4 gene was found to moderate the effects of chronic stress on anxiety in adolescents aged 14-21 [10]. The SCL6A4 gene has many aliases, such as HTTPLR, HTTP, and SERT, and regulates the serotonergic system. Serotonin has been linked to emotionality [11] and behavior [12] The SCL6A4 gene has been shown in multiple studies to interact with experiences that cause stress and thereby increase risk for mental and behavioral health issues [10]. The theory of risk is that certain variants (carriers of the short or long allele) of SCL6A4 affect an individual's biological response to psychological stress [13] making it an important consideration for examining the effects of food insecurity on children and adolescents. The present study aimed to determine if the SCL6A4 gene moderates associations between food insecurity, mental health, and delinquent behavior in children and adolescents.

METHODS

Sample: The data and sample for this research are from The Future of Families and Child Wellbeing Study. The cohort consists of 4,898 children and their respective caregivers sampled from large cities in the U.S. from 1998 to 2000. Initial data was collected from the mothers shortly after the birth of the child and follow-up data was collected when the children were of subsequent ages (1, 3, 5, 9, 15, and 22 years). The child cohort is almost equally divided by sex (Male 47.8%), mostly African American (n=1800) followed by Latin X (n=817), Caucasian (n=780), Asian American (n=102), and Indigenous (n=52) with 27% of the cohort not reporting on race. More than half of the sample were living in households with an annual income below the federal poverty line (68.7%) and the mothers' were a mean age of 25.27 years (SD=6.03) at the time of child's birth.

Variables: Food insecurity was measured with the Household Food Security questionnaire. The variables included in this study consisted of the mother missing meals (0=no, 1=yes), child missing meals (0=no, 1=yes), and receiving food resources (0=no, 1=yes) at years one and five. Adolescent mental health focused on anxiety related items from the BSI 18 with a likert scale option (1=strongly disagree, 2=somewhat disagree, 3=somewhat agree, 4=strongly agree) for the following statements: "I feel nervous or shaky inside", "I feel fearful", "I feel so restless I can't sit still", "I have spells of terror or panic", "I feel tense or keyed up", and "I get suddenly scared for no reason". Adolescent delinquent behavior was measured at age 15 with the Delinquent Behavior Scale that indicates the frequency with which an action has been done (1=never, 2=1 or 2 times, 3=3 or 4 times, 4=5 or more times). The following items represent adolescent delinquent behavior: "Taken from a store without paying for it", "Gotten into a serious physical fight", "Driven a car without its owner's permission", "Hurt someone badly enough to need bandages or medical care", "Use or threaten to use a weapon to get something", "Sold marijuana or other drugs", and "Gone into a house or building to steal something". The SCL6A4 gene variant variable included the short/short and long/long alleles.

Statistical analyses: Cohort demographics were examined with descriptive statistics. All predictor and outcome variables were assessed with a correlation matrix to identify initial associations for further multiple regression analyses. Multiple regression tests included possible covariates identified in the correlation matrix and bootstrap confidence intervals to reduce type I error from spurious associations, possible non-normality of data, and multiple comparisons. Gene-environment interactions were examined with a computed interaction variable for each of the SCL6A4 variants and the predictor variable of interest. Any statistically significant interactions were then graphed for visual representation.

RESULTS

Food insecurity: Mothers who reported receiving food resources during the child's first year were more likely to report receiving food resources at year 5 (r=.324, p=.036), and year 9 (r=.534, p < .001). However, even with the food resources the mothers still reported skipping meals due to food insecurity during the child's first, 5th, and 9th year of life as shown in Figure.1. Children reported to have gone hungry in year 1 were more likely to be reported going hungry in year 5 (r=.468, p=.002), and to have their mothers report going hungry in year 5 (r=.334, p=.031). Maternal reports of mom going hungry in child's first year were more likely to report their child going hungry in year 5 (r=.313, p=.044). Mothers going hungry during child's 5th year was moderately positively associated with children going hungry during their 5th year (r=.465, p=.002) **Fig. 1.** The initial correlation matrix identified that maternal food insecurity showed a moderate positive association with adolescent anxiety symptoms at year 15. Mothers who reported going without food when hungry during their child's first year had adolescents who reported more unexpected panic spells (r=.424, p=.005). Moreover, panic spells at age 15 were positively correlated with the adolescent reporting they have used a weapon to threaten a person to steal from them (r=.361, p=.019). A multiple regression analysis with an interaction term of maternal hunger and child sex as a predictor revealed that child sex moderates the influence of maternal food insecurity on the development of panic spells in adolescence (B=.299, t=2.569, p=.01, bootstrap CI [.071, .527]). Specifically, females are more likely to develop panic spells in adolescence compared to males, and the occurrence of panic spells increases for females if their mother went hungry in the first year of the adolescent's life (see Figure. 2). Maternal reports of mom going hungry in first year of child's life positively associated with adolescents receiving a diagnosis of depression or

anxiety at 15 years of age (r=.382, p=.013). Primary caregiver reports of going hungry during child's 9th year positively associated with 15-year-old reported frequency of intentionally hurting another person and causing serious injury (r=.345, p=.025), and adolescent reported frequency of feeling restless and anxious (r =.353, p=.022) **Fig. 2.**

Gene-environment interactions: The SCL6A4 serotonin transporter short/short allele emerged statistically significant as a moderator of food insecurity and child mental health shown in Figure.3. Multiple regression indicated that adolescents with the short/short allele who had mothers who experienced going hungry in the adolescents first year of life were more likely to report a greater frequency of feeling fearful at 15 years (B=.413, t=1.972, p=.049, bootstrap CI [.002, .823]). Adolescents with short/short allele who reportedly went hungry during their 5th year were more likely to report a greater frequency of unexpectedly suddenly feeling scared (b=.718, t=2.033, p=.042, bootstrap CI [.026, 1.409]). Multinomial logistic regression revealed adolescents without the short/short allele and without going hungry during their 5th year were 478% less likely to be diagnosed with depression or anxiety at 15 years of age (B=1.754, Odds ratio=5.78, p=.047, bootstrap CI [1.026, 32.548]). The short/short allele did not associate with delinquent behaviors (p > .05). The SCL6A4 serotonin transporter long/long allele emerged statistically significant as a moderator of food insecurity and adolescent delinquent behavior. Multiple regression indicated that mothers who reported going hungry in the child's first year of life had adolescents who reported a greater frequency of using or threatening to use a weapon to steal from a person at 15 years if they had the long/long allele (B=.090, t=2.744, p=.006, bootstrap CI [.026, .154]). The long/long allele was not a statistically significant moderator of food insecurity for the child and adolescent mental health or other delinquent behaviors (p > .05), or of food insecurity for the mother or primary caregiver and adolescent mental health or other delinquent behaviors (p >.05) **Fig. 3.**

DISCUSSION

These study findings highlight that if both mom and child are going hungry in early years of life that mom and child will continue to go hungry, even if they receive food resources. Moreover, food insecurity in the first year of a child's life is likely to still be present over the next decade. Children whose mothers went hungry were more likely to become adolescents with poor psychological development. These adolescents experienced more frequent panic spells, especially in females. Females were also more likely to develop anxiety disorders in relation to food insecurity. The conversation of proper food security must continue

Fig. 1. Bar graph of mother and child food insecurity with food resources.

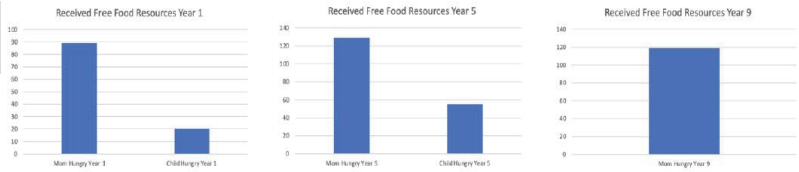


Fig. 2. Line graph of maternal food insecurity and child sex moderation of adolescent panic spells.

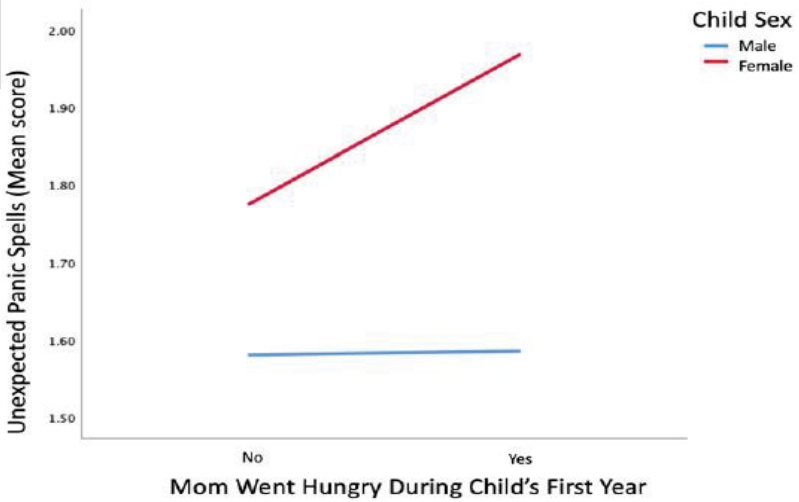
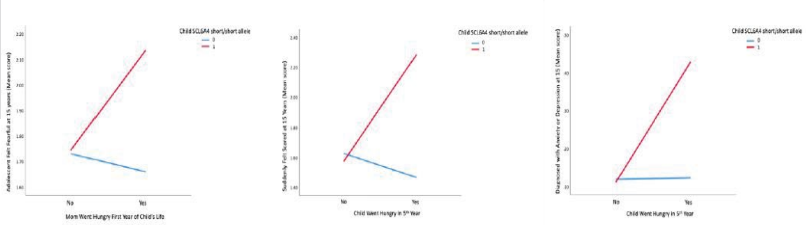


Fig. 3. Gene X environment interaction with scl6a4 short/short allele and food insecurity with adolescent anxiety features.



forward even when social policy changes create resources for this social problem. The United States of America was ranked lowest among 10 developed Western nations overall in 2014, ranking 5th in poverty and 8th in economic mobility (Corak). In terms of social mobility, defined as the ability for children to have better lives than their parents, the United States ranks 27th [14]. America falls behind 26 other nations in terms of the ability for individuals to move upwards in their socio-economic status [14]. Individuals who live in poverty in the United States have a grim chance of moving out of poverty within their lifetime, as do their children. Policies need to reflect equitable access to food resources so that those who are in extreme poverty are able to meet the basic needs of survival without worrying about having enough food to properly feed their families. Interestingly, the SCL6A4 serotonin transporter short/short allele does moderate the association between food insecurity and adolescent mental health. Adolescents with the short/short allele whose mothers went hungry in their first year were more likely to report feeling afraid. If the adolescent went hungry in their 5th year they were more likely to report feeling terrified unexpectedly. Evidence of resilience emerged, showing adolescents without the short/short allele and without going hungry in their 5th year were 478% less likely to have depression or anxiety. Our findings are consistent with previous research indicating the long/long allele as promoting resilience in children and adolescents in the face of adversity [15]. However, recent findings indicated adolescents with the long/long allele were more likely to experience mental health issues from stress unless they were indicated as having high resilience as measured by the Connor-Davidson Resilience scale which could be evidence of a gene environment interaction [10]. The multifaceted SCL6A4 variant mechanisms of effects of stress inducing experiences on mental health and delinquent behavior could also be influenced by an individual's psychological resilience to stress which we did not measure [16]. This speaks to the complexity of the model for gene-environment interactions and likely suggests that there are other factors to be considered that influence an individual's psychological resilience, such as the family shared environment and emotion-oriented coping [17]. Moreover, it remains unclear how gene variants, such as the short/short allele of SCL6A4, affect emotionality and behavior. Research investigating serotonin would be limited to measuring the neurotransmitter in proxy tissues (blood, saliva, etc.) and would not have opportunity to observe the varying actions of serotonin at distinct receptors. We know from psychosis focused research that specific dopamine receptors have varying effects on psychotic symptoms, emotionality, and behavior [18]. It is imperative that in future research we consider the complete serotonergic system and the potential for gene variants to affect serotonin regulation *via* specific serotonin receptors. Food insecurity can be caused by, and cause, factors of parental mental health that affect the family shared environment and the development of emotion regulation in children and adolescents. Future research on food insecurity effects would benefit from including measures of psychological resilience, family shared environment, and child/adolescent emotion regulation to clarify the pathways of influence for gene-environment interactions with SCL6A4 gene variants [19-22].

CONCLUSION

These findings should be considered within the limitations of this study. First, while we modeled food insecurity as a stressor, it can also have nutritional consequences that affect human development and overall health. We were not able to include nutritional factors in our study which could have contributed to our findings. Second, we were unable to assess the potential effects of psychological resilience to stress in our overall model. Psychological resilience has been suggested to play a role in the pathway mechanisms of stress effects on mental health and behavior as previously noted. However, this initial investigation provides novel insight into food insecurity and the harmful effects on adolescent mental health and behavior that can be used to inform future research and strengthen the theoretical model posited. To address the limitations, we applied the advanced statistical approach of bootstrapping to reduce our type I error and generate population parameters for each tested model. This would reduce the likelihood of spurious relationships and further support that the addition of suggested variables could enhance, but not replace, the food insecurity variable in the model.

ACKNOWLEDGEMENTS

The authors would like to acknowledge and thank The Future of Families and Child Wellbeing Study researchers and participants for their contribution to the data included in this study.

DECLARATIONS

No funding was received for conducting this study and the authors have no competing interests to declare.

REFERENCES

1. **Edmunds C, Alcaraz M.** Childhood material hardship and adolescent mental health. *Youth Soc*. 2021;53(7):1231-1254.
2. **Men F, Elgar FJ, Tarasuk V.** Food insecurity is associated with mental health problems among Canadian youth. *J Epidemiol Community Health*. 2021;75(8):741-748.
3. USDA ERS - Definitions of Food Security. (n.d.). https://www.ers.usda.gov/topics/food nutrition-assistance/food-security-in-the-u-s/definitions-of-food-security/
4. **Schroeder K, Smaldone A.** Food insecurity: A concept analysis. *Nurs forum*. 2015;50(4): 274-284.
5. **Schanzenbach D, Pitts A.** How much has food insecurity risen? Evidence from the Census household pulse survey. Institute for Policy Research Rapid Research Report. 2020:1-10.
6. **Greder KA, Peng C, Doudna KD, et al.** Role of family stressors on rural low-income children's behaviors. *Child Youth Care Forum.* 2017; 46 (4): 703-720.
7. **Burke MP, Martini LH, Çayır E, et al.** Severity of household food insecurity is positively associated with mental disorders among children and adolescents in the United States. *J Food Nutr*. 2016;146(10):2019-2026.
8. **Turner VE, Demissie Z, Sliwa SA, et al.** Food insecurity and its association with alcohol and other substance use among high school students in the United States. *J Sch Health.* 2022;92(2):177-184.
9. What is a Developmental Milestone? (2022, December 29). Centers for Disease Control and Prevention. https://www.cdc.gov/ncbddd/actearly/milestones/index.html
10. **Ollmann TM, Voss C, Venz J, et al.** The interaction of 5-HTT variation, recent stress, and resilience on current anxiety levels in adolescents and young adults from the general population. *Depress Anxiety*. 2021;38(3):318-327.
11. **Meneses A, Liy-Salmeron G.** Serotonin and emotion, learning and memory. *Rev Neurosci*. 2012;23(5-6):543-553.
12. **Crockett MJ, Clark L, Tabibnia G, et al.** Serotonin modulates behavioral reactions to unfairness. *Sci*. 2008 Jun 27;320(5884):1739.
13. **Mueller A, Strahler J, Armbruster D et al.** Genetic contributions to acute autonomic stress responsiveness in children. *Int J Psychophysiol*. 2012;83(3):302-308.
14. World Economic Forum. (2020). The global social mobility report 2020. *World Economic Forum*. Retrieved February 6, 2023.
15. **Niitsu K, Rice MJ, Houfek JF, et al.** A systematic review of genetic influence on psychological resilience. *Biol Res Nurs*. 2019;21(1):61-71.
16. **Sharpley CF, Christie DR, Bitsika V, et al.** Does psychological resilience buffer against the link between the 5-HTTLPR polymorphism and depression following stress. *Physiol Behav*. 2017;180:53-59.
17. **Navrady LB, Zeng Y, Clarke TK et al.** Genetic and environmental contributions to psychological resilience and coping. *Wellcome Open Res.* 2018;3(12):12.
18. **Richtand NM, Woods SC, Berger SP, et al.** D3 dopamine receptor, behavioral sensitization, and psychosis. *Neurosci Biobehav Rev*. 2001;25(5):427-443.
19. **Olivier B.** Serotonin and aggression. Annals of the New York Academy of Sciences. 2004 Dec;1036(1):382-392.
20. **Seeman P, Schwarz J, Chen JF, et al.** Psychosis pathways converge *via* D2high dopamine receptors. *Synapse*. 2006;60(4):319-346.
21. Stanford Center on Poverty and Inequality. (2016, August). Pathways: A Magazine on Poverty, Inequality, and Social Policy. Stanford Center on Poverty and Inequality.
22. **Sweet RA, Nimgaonkar VL, Kamboh MI, et al.** Dopamine receptor genetic variation, psychosis, and aggression in Alzheimer disease. *Arch Neurol* 1998;55(10):1335-1340.