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Family Socioeconomic Status and Children's Nucleus Accumbens Response to Loss Anticipation: Racial Differences

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Abstract

Objective: Socioeconomic Status (SES) and race (as a proxy of racism) may have overlapping effects on substance use and related brain mechanisms such as nucleus accumbens function. Therefore, we hypothesized that nucleus accumbens function might be jointly affected by race and SES.

Materials and Methods: The Adolescent Brain Cognitive Development (ABCD) study baseline data was used for this cross-sectional study. The study included 7791 children between the ages of 9 and 10. The independent variable was parental education as our SES indicator of interest. The moderator was race as a social factor rather than a biological factor. The confounders included sex, age, ethnicity, and family structure. The outcome variable was nucleus accumbens function measured using functional MRI (fMRI). We used mixed-effects regression models with and without race by SES interactions to analyze the data.

Results: Children with higher parental education had lower nucleus accumbens function during loss anticipation (conceptualized as a risk factor of substance use). However, this effect was larger for White children than it was for Black children. Thus, the effects of race and SES on nucleus accumbens function were multiplicative rather than additive.

Conclusion: Children's race and SES have implications for nucleus accumbens function. The results are important because nucleus accumbens function may correlate with future substance use. However, SES effects on nucleus accumbens function may differ by race, explaining why the risk of substance use remains high in high SES Black youth.

Keywords: Socioeconomic Status; Adolescent Brain Cognitive Development; functional MRI

Background

Substance use is disproportionately more consequential among racial minorities, particularly Black individuals [1]. Inequalities by socioeconomic status (SES) and race may exist in high-risk behaviors, such as early substance use in childhood, which increases the risk of addiction later in life [2]. Although the separate effects of each social determinant on children's health risk are well known, the underlying mechanism of the joint effects of multiple social determinants such as race and SES on children's substance use risk are not well understood. This study focused on the underlying mechanism of the joint and interrelated effects of race (as a proxy of racism) and SES on a correlate of children's substance use risk, namely nucleus accumbens function.

A health disparity is one of the ways that social inequality projects its shadow on people's lives. According to Healthy People 2030, health disparities are linked to social, economic, and environmental inequality. Race and SES are among social characteristics that correlate with societal barriers of population groups to secure health [3]. Race and SES are two social determinants of health because they are proxies of the individual's social environment and living experiences.

However, SES does not directly and independently impact health outcomes but rather through biological mechanisms (e.g., brain development) and through interaction with other social determinants such as race. Both race and SES are proxies of socioeconomic conditions, and such a disadvantaged environment may lead to worse health [4]. In addition, these social determinants show effects in adults and children [5-7].

Additionally, racial minorities partly show health disparities because of an overlap between race and SES [8,9]. Sociodemographic factors [10] and racism [11] are among the causes of racial health disparities. Under-resourced and under-served communities in the United States are predominantly populated by racial minorities [12]. Understanding the underlying cause of health disparity is crucial in creating a longitudinal solution to reduce health disparities and promoting equality for all.

According to the World Health Organization, social determinants of health are the conditions where the person is born in, grows in, works in, and lives in [13]. Social determinants of health may explain up to

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50% of people's health [13]. These conditions include race and SES that shape financial, food, and housing security, access to education and health care, early childhood development, and other social exposures. According to the American Psychological Association, SES is the social class of an individual, and it is often associated with education, income, and occupation [14]. A vast number of studies have confirmed the impact of SES on a person's health condition. High SES is also associated with a lifestyle that shows a significant positive effect on individuals' physical and psychological health [15]. Furthermore, almost all SES markers are associated with a wide range of physical health outcomes, including cardiovascular disease [16], obesity and diabetes [17], and breast cancer [18]. High SES is also linked to low stress [19]. Yet, how multiple social determinants such as race and SES jointly affect individual health is still an ongoing question.

Several studies have proposed environmental effects as partial contributing factors to individual's health. A study by Schultz and colleagues showed a correlation between socioeconomic disparities and adverse health outcomes, which is partially explained by lower-quality care received and lack of healthy food options in the neighborhood [16]. Moreover, the stressors from low SES and racial discrimination take a toll on children's development early on and affect individual health later in adulthood. Parental SES is repeatedly shown to significantly impact children's physical and mental well-being [20].

Low levels of parental education had adverse outcomes on youth inhibitory control, which prevents high-risk behaviors such as impulsivity, aggression, obesity, poor school performance, and substance use [21]. In addition, the adverse effects on children's emotional and behavioral problems are observed in correlation with low parental education [22], low family income [23], and poverty [24]. Partial explanations of the adverse effects of low SES on children's development are stress, food insecurity, environmental toxins, and parenting [25]. Low socioeconomic status has negative effects on children's health and brain development.

WHO categorizes minority status as a major social determinant of health [13]. Minority groups include sexual minorities [26], racial and ethnic minorities [27], and those living with a disability [28]. There is increasing interest in minority health disparities, particularly on racial and ethnic minorities, due to the increasing trend of non-White populations in the United States [29]. The health disparities among racial minority results in the high prevalence of chronic disease, lower quality of life, and premature death [30].

Racial minorities are treated worse than non-Hispanic Whites in American society [31]. In addition, multiple studies show the correlation between racial minority and low SES with low childhood brain development [32]. This is partially due to chronic stress from racial discrimination [33] and stressful experiences [32]. As a result, racial minorities with low SES are at risk of low academic achievement [34], depression [35], suicide [36], binge eating [37], and smoking [38]. They are also at an increased risk of substance use later in their adulthood [39]. The potential environmental factors that explain the increased risk behaviors of low SES and racial minorities include a disadvantaged socioeconomic situation such as unsafe neighborhood, low-quality school, stress in daily living, and, as a result, limited children development [40].

Family SES (e.g., parental education) is among the strongest child's social determinants of health overall [41,42]. However, recent studies have documented unequal effects of SES between Black and White individuals [43]. Minorities' Diminished Return (MDRs) theory refers to the weaker protective effects of SES indicators, such as parental education, for Black people than White people [44]. As a result of MDRs, children from racial minorities show worse school performance [45], higher depression and suicidal attempts [46], higher body mass [47], higher youth impulsivity and other emotional and behavioral problems [22,48], and higher substance use [25,49] in comparison to White counterparts with the same family SES. The MDRs theory explains these results by structural racism and social stratification as well as discrimination in the daily lives of racial minorities as early as when kids begin attending school [43,45]. This underlying and often overlooked outcome is critical in understanding health disparities among racial minorities.

Social determinants of health such as SES and race have a significant impact on the brain development of children, which shapes future decision-making and judgment via alternation of brain processes such as reward processing [50-52]. High SES may alter the brain reward process that protects youth against substance use [53]. Substance use and addiction are mediated by reward responsiveness [54]. Reward responsiveness is responsible for the ability to experience pleasure from reward-related stimuli [54]. This includes behaviors that stimulate the sense of high risk with high rewards like such as aggressive behaviors, early sexual exposure, and early use of alcohol, substances, and tobacco [55]. Racial minority and low SES children may have high reward responsiveness [56]. Furthermore, alterations to brain development, such as the amygdala, which regulates emotions, behaviors, and social relations [50], as well as frontal lobe activity that controls emotion and stress [24] showed significant alteration in volume and activity.

Social determinants also reflect the environment that surrounds the child development. For example, previous studies have shown that low socioeconomic status in racial minorities was associated with a higher frequency of alcohol consumption [57], cigarette smoking habits [58], marijuana use [59], and other substance use [60]. This is due to increased availability of alcohol in the low SES neighborhood, decreased parental monitoring, and inadequate education. As a result, the constraint of external resources and discrimination in racial minorities with low SES results in the altered neurological pathways that leads to the jeopardized reasoning ability and behavior later in life.

Social determinants have significant effects during childhood. The difference in SES creates conditions that limit children's brain development. A few of the conditions are unsafe neighborhoods, inadequate schools, and more stress in daily life. These environmental conditions jeopardize the harm avoidance and engagement in low-risk behaviors so they may be involved in high-risk behaviors such as dropping out of school, aggressive behaviors, impulsivity, binge drinking, alcohol consumption, early smoking, and other substance use. However, the effects of SES on individuals' health are unequal across all racial groups. The protective effects of SES may be weaker for Black and other racial minorities than White families.

While critical development occurs in the adolescent years, human brain is not fully mature until the age of 25 [61]. During this period, brain development is highly dependent on the external stimuli in which environmental enrichment stimulates the early maturation of synapses and more efficient signaling of the brain [62]. Environmental and social determinants, as a result, have a notable impact on the youth brain developmental processes. In contrast, the negative stimuli may result in alteration of synaptic connectivity and brain function [63]. However, intellectual exercise, physical activity, hormones, heredity, and environment are key elements of proper brain maturation [61].

According to the Centers for Disease Control and Prevention (CDC), health disparities due to social determinants occur due to unequal social, political, economic, and environmental resources [64]. Poverty, environmental threats, inadequate access to health care, individual and behavioral factors, and educational inequalities are the major factors in creating adolescent health disparities [64]. Social determinants can stimulate or inhibit normal adolescent development in various parts of the brain, such as the prefrontal cortex [65,66] and their connectivity [67]. The alteration of children's brain development can jeopardize children's physical and mental well-being and in their adulthoods [7]. Furthermore, according to the Minorities' Diminished Returns theory, the effects of social determinants on health are unequal for racialized and White individuals [44]. Although the effects of social determinants on children's brain development are well established, the mechanisms for such effects are still not known. Therefore, understanding how social determinants such as race and SES operate and how SES operates across racial groups is crucial in creating solutions that can minimize SES and racial health disparities.

SES effects on human brain development may impact mental abilities in humans that cause them to avoid risk, make decisions, learn, think, reason, memorize, solve problems, and pay attention [68]. These cognitive abilities are essential to develop adaptive behaviors to best survive in a particular environment. Factors that can shape human survival skills are the ability to learn from experience, memory, and utilize these for future decision-making [69].

The dopamine-signaling pathway or reward system is involved with the response to risk and reward by providing a learned signal to cues [70]. This serves as a guide to future behavior via goal-oriented and motivated behavior and associated reinforcement [71]. The reward system is one of the major neurological pathways with major implications for human adaptive behaviors, thoughts, feelings, and behaviors [72]. The American Psychological Association defines reward as the reinforcement or intent to repeatedly receive the consequence of behavior rather than focusing on the significance of the consequence of the behavior [73]. A change in the reward system has implications in high-risk behaviors such as binge eating, obesity, substance use, or addiction [74]. This brain network is also implicated in social comparison and self-validation [75], depression [76], alcohol consumption [77], and substance use [78]. Substance use is, as a result, derived from the brain reward system [54].

There are multiple dopamine pathways: the mesolimbic, mesocortical, nigrostriatal [79], and tuberoinfundibular, which is less understood [80]. The mesolimbic dopaminergic system has been extensively studied due to its function in seeking pleasure and reward [70]. This pathway allows the organism to engage in instinctual emotional seeking by searching for life-promoting stimuli and to avoid harm [71]. The mesolimbic dopamine pathway, also known as the brain reward system, begins in the Ventral Tegmental Area (VTA) in the midbrain, where dopamine is generated [81]. The dopamine is then projected into the nucleus accumbens, which its function correlates with reward-seeking behaviors [82].

Previous studies have shown that psychostimulants or natural rewards such as food can alter the mesolimbic signaling pathway via nucleus accumbens, which triggers addictive behaviors [83-85]. In addition, impulsivity [86], stress, and depression [87,88] are all associated with modified nucleus accumbens function and size. The alteration in nucleus accumbens function predicts subsequent substance use and addiction later in life [89].

Multiple social risk factors early in life interfere with normal cognitive development [90]. The early childhood cumulative risks are more common in social determinants of health such as race and SES. These social influences include family income, single-parent households, low parental education, high-risk family environment, and stressful life events [90]. Studies have shown socioeconomic and racial inequalities in children's brain development and function. For instance, low SES Black and Latino children had smaller amygdala sizes in comparison to high SES, non-Latino, White children [50], while small amygdala development is correlated with over-reaction to ambiguous stimuli [91]. In addition, early childhood cumulative risk is associated with reducing the children's brain's gray matter volume, cortex volume, right superior parietal, and inferior parietal thickness resulting in a reduction of attention, learning, memory, and inhibitory control [90]. Thus brain development can mediate the effects of early childhood cumulative risks on adulthood problems [92] such as binge drinking, heavy drinking, risky sexual behavior, obesity, diabetes, depression [93], higher body mass index [94], aggression [95], obsessive-compulsive disorder [96], school dropout, smoking, and substance use [97-99].

Nucleus accumbens plays a major role in decision making via action selection toward motivational stimuli, which is critical in determining children's high-risk behaviors later in life [100,101]. Children from higher SES families showed a positive relationship with dopaminergic connectivity, while early childhood stress altered the development of this pathway [102]. An alteration in the size or function of the nucleus accumbens might predict high-risk behaviors that lead to substance use, binge eating, or obesity in low SES, Black, and Latino children [103]. Other studies have suggested similar findings of altered nucleus accumbens connectivity in adolescents may influence the reward system's role in vulnerability to substance use [104,105].

Children's brain development is a predictive factor for adulthood behaviors. Nucleus accumbens is a part of the dopamine-signaling pathway in the midbrain that is associated with decision-making, motivation, and reward. Nucleus accumbens was shown to be susceptible to alteration an early age via external and environmental social determinants such as SES and race. Similarly, nucleus accumbens was shown to be altered by substances and awards, leading to substance-seeking behaviors. As a proxy of the brain reward

system, the result is that studying correlates of nucleus accumbens has implications for the prevention of substance use.

Purpose

This analysis was performed under the Substance Abuse Disorders Research Training (SART) Program funded by the National Institute on Drug Abuse (NIH) to underlying the effects of social determinants of health on the children brain development of brain reward system in the nucleus accumbens using the Adolescent Brain Cognitive Development (ABCD) Study, a longitudinal study on brain development and child health, to reduce health disparities due to socioeconomic and racial inequalities related to substance use disorders and addiction.

The study utilized functional MRI images from the ABCD study to understand the joint effects of SES and race on brain reward system regulation in children. The results will help us better understand the social patterning of substance use trajectories in adolescents. As most children in the ABCD study are 9-10 years old and have not started to use the substance, substance use was not included in this study. Nucleus accumbens function is a predictor of substance use.

We hypothesized that high SES is associated with increased regulation of the brain reward system (reduced nucleus accumbens function during MID in response to loss). Still, a weaker effect is expected in the marginalized communities, including racial minorities.

Materials and Methods

This is a secondary analysis of the Adolescent Brain Cognitive Development (ABCD) data. Our analysis was exempt from a full review. The ABCD study protocol, however, was approved by the University of California, San Diego (UCSD) Institutional Review Board (IRB) [106]. The primary aim of the Adolescent Brain Cognitive Development (ABCD) study is to track human brain development from childhood through adolescence. This enables us to study environmental factors that impact brain development trajectories [107]. The data collection of the ABCD study was launched in September 2016 and will continue for ten years. The study details can be found at www. abcdstudy.org. ABCD is a national, state-of-the-art brain imaging study of childhood brain development [106,108]. The advantages of the ABCD study include a national sample, a large sample size, a large sample of minorities such as Blacks, Latinos, Asians, and Other/Mixed race, available data, robust measures of brain development, and considerable socioeconomic factors [108-112]. This cross-sectional analysis only applied data from the baseline ABCD study.

Participants of the waive one of the ABCD study were children ages between 9 and 10 years old. Children were recruited into the study from 21 sites from multiple cities across US states. The primary method of sampling children into the ABCD study was through the school system (school selection) informed by race, ethnicity, sex, SES, and urbanicity. More details of ABCD sampling are published elsewhere [113]. Inclusion criteria were being a White, Black, Asian, and other/mixed-race child between ages 9 and 10 and having valid data on nucleus accumbens function during the MID task. Baseline data collection was performed between 2016 and 2018. Eligibility for this analysis included high-quality data for the MID task and complete data for all our variables. All racial and ethnic groups were included. Only baseline data were used (n = 7791),

Functional Magnetic Resonance Imaging (fMRI) data were used to measure nucleus accumbens function during the MID task. As described in detail by Casey et al. [109], participants completed high-resolution T1 and T2 weighted fMRI scan (1mm isotropic voxels) using scanners from Philips Healthcare (Philips, Andover, Massachusetts, USA), GE Healthcare (General Electrics, Waukesha, WI, USA), or Siemens Healthcare (Siemens, Erlangen, Germany) [109]. All the MRI data were processed using FreeSurfer version 5.3.0, available at http://surfer.nmr.mgh.harvard.edu/ [114,115], according to standard processing pipelines [109]. Processing included removal of non-brain tissue, segmentation of gray and white matter structures [116], and cortical parcellation [117]. All scan sessions underwent radiological review, whereby scans with incidental findings were identified. Quality control for the structural images comprised visual inspection of T1 images and FreeSurfer outputs for quality [107]. Imaging quality checks were conducted by the ABCD team. Subjects whose scans failed inspection (due to severe artifacts or irregularities) were excluded. Regions of interest included right Nucleus accumbens. In this analysis, we used the nucleus accumbens function during MID task data in subcortical (ASEG) regions of interest (ROIs) provided by the ABCD data.

Variables

The study variables included demographic factors, family SES indicators, and right nucleus accumbens function during anticipation of loss during the MID task. A detailed explanation of the procedures and harmonization of the MRI devices in the ABCD study is available here [109].

Right nucleus accumbens function during MID (loss anticipation in contrast to neutral). The primary outcome was total nucleus accumbens function during MID (loss anticipation), measured by functional MRI. In addition, nucleus accumbens function is shown to be under the influence of SES [102,103].

Race: Identified by the parent, race was a nominal variable. Black, Asian, Other/mixed race, and White (reference).

Parental educational attainment: Participants reported their schooling as a five-level categorical variable: Less than high school (reference group), high school degree, some college, college completion, and graduate study.

Age: Age was a continuous variable in months. Parents reported the age of the children.

Sex: Sex was 1 for males and 0 for females.

Ethnicity: Parents were asked if they were of Latino ethnic background. This variable was coded as Latino = 1 and non-Latino = 0.

Parental marital status: Parental marital status was 1 for married and 0 for any other condition.

Data analysis

Data analysis was performed using the Data Analysis and Exploration Portal (DEAP), which operates based on the R statistical package. The DEAP is available at the NIH NDA. Mean (standard

deviation; SD) and frequency (relative frequency; %) of all variables were described overall and by race and family income. We also used the ANOVA and chi-square tests for bivariate analysis to compare the study variables across racial and income groups. For multivariable modeling, we ran mixed-effects regression models. In our model, the right nucleus accumbens function during loss anticipation during the MID task was the outcome. Parental education was the predictor. Ethnicity, family structure, age, and sex were the covariates. Race was the moderator. All models were performed in the pooled sample (n = 7791). Our 1st model was conducted in the absence of any interaction terms; our 2nd model was performed with interaction terms between race and parental education. Before we performed our models, we ruled out multi-collinearity between study variables. We also explored the distribution of our predictor, outcome, residuals, and quantiles. Regression coefficients (b), SE, and p-value were reported for our model. A p-value of equal or less 0.05 was significant.

Results

A total number of 7791 aged 9-10 years old participants entered our analysis. In this study, 5299 (68.0%) children were White, 1023 children (13.1%) were Black, 176 individuals (2.3%) were Asian, and the remaining 1293 children (16.6%) were other/mixed race. Table 1 illustrates the summary statistics of the overall pooled sample and by race.

Table 2 shows the results of mixed-effects regression models in the total sample with the right nucleus accumbens function during MID (in response to loss anticipation) as the outcome. High parental education was inversely associated with nucleus accumbens function, net of confounders. This effect was significantly larger for White Americans than Black American children, documented by a significant interaction between race and parental education on the right nucleus accumbens function (Figure 1).

Discussion

Our goal was to identify the joint effects of two major interrelated social determinants, namely race and SES, on children's nucleus accumbens function. This study found that family SES is associated with the right nucleus accumbens function in 9-10 years old American children. However, this effect was stronger for White children than Black children.

Multiple studies have documented the role of brain structures involved in the brain reward system, including but not limited to nucleus accumbens for substance use [103]. Many brain structures are under the influence of social determinants such as SES indicators (parental education) and race. This impact is through a wide range of mechanisms including, parenting, nutrition, school quality, familial home environment, and stressful life events. As a result of racism, the benefits of SES may be smaller for racial minority populations [90].

High SES has an impact on nucleus accumbens through a wide range of mechanisms such as parental engagement, parenting, diet, and stress, but all these effects are weaker among racial minorities due to structural racism, which reduces the return of education in altering daily experiences of non-White people. The brain's influence on substance use risk is in part through the reward system, the mesocorticolimbic circuit, both prior and following exposure to substances and related cues. The nucleus accumbens, a component of

Table 1: Descriptive Statistics.

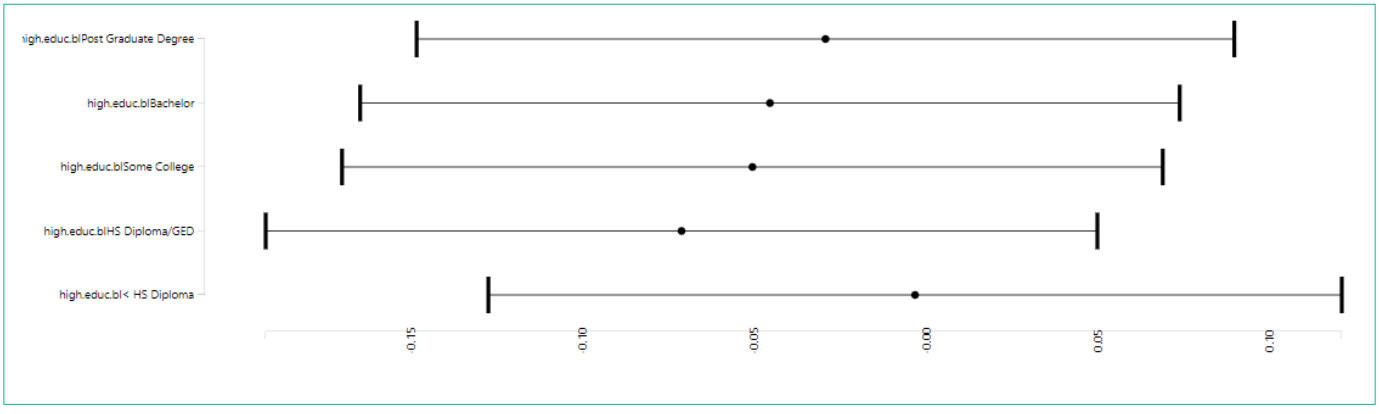
Level	All	White	Black	Asian	Other/Mixed	P*
N	7791	5299	1023	176	1293	
	Mean (SD)	**Mean (SD)**	**Mean (SD)**	**Mean (SD)**	**Mean (SD)**	
Age (Month)	119.27 (7.51)	119.28 (7.52)	119.42 (7.37)	119.80 (8.09)	119.01 (7.52)	0.41
Right Nucleus accumbens Function	0.00 (0.33)	0.00 (0.33)	0.02 (0.33)	0.00 (0.22)	0.00 (0.35)	0.54
	n (%)	**n (%)**	**n (%)**	**n (%)**	**n (%)**	
Parental Education						
< HS Diploma	306 (3.9)	131 (2.5)	86 (8.4)	4 (2.3)	85 (6.6)	< 0.001
HS Diploma/GED	628 (8.1)	250 (4.7)	240 (23.5)	2 (1.1)	136 (10.5)	
Some College	1931 (24.8)	1093 (20.6)	391 (38.2)	13 (7.4)	434 (33.6)	
Bachelor	2079 (26.7)	-30	145 (14.2)	47 (26.7)	297 (23.0)	
Post Graduate Degree	2847 (36.5)	-42.2	161 (15.7)	110 (62.5)	341 (26.4)	
Sex						
Female	3877 (49.8)	2583 (48.7)	541 (52.9)	100 (56.8)	653 (50.5)	0.019
Male	3914 (50.2)	2716 (51.3)	482 (47.1)	76 (43.2)	640 (49.5)	
Married Family						
No	2270 (29.1)	1074 (20.3)	706 (69.0)	26 (14.8)	464 (35.9)	< 0.001
Yes	5521 (70.9)	4225 (79.7)	317 (31.0)	150 (85.2)	829 (64.1)	
Latino						
No	6222 (79.9)	4349 (82.1)	971 (94.9)	162 (92.0)	740 (57.2)	< 0.001
Yes	1569 (20.1)	950 (17.9)	52 (5.1)	14 (8.0)	553 (42.8)	

*Comparison of racial groups

Table 2: Regressions in the overall sample with the right nucleus acumens function as the outcome (n=7791).

	B	SE	p	Sig	B	SE	p	Sig
	Model 1				Model 1 + Interactions			
Parental Education								
HS Diploma/GED	-0.068	0.023	0.004	**	-0.092	0.036	-0.092	*
Some College	-0.047	0.021	0.023	*	-0.065	0.031	-0.065	*
Bachelor	-0.042	0.021	0.049	*	-0.071	0.031	-0.071	*
Post Graduate Degree	-0.026	0.021	0.223		-0.05	0.031	-0.05	
Race								
Black	0.007	0.013	0.573		-0.065	0.047	-0.065	
Asian	-0.009	0.026	0.731		-0.013	0.168	-0.013	
Other/Mixed	-0.003	0.011	0.785		-0.016	0.046	-0.016	
Sex (Male)	-0.018	0.008	0.016	*	-0.018	0.008	-0.018	*
Age (Months)	0.001	0.001	0.217		0.001	0.001	0.001	
Married Family	-0.028	0.009	0.004	**	-0.029	0.009	-0.029	**
Hispanic	-0.009	0.01	0.377		-0.009	0.011	-0.009	
Black x HS Diploma/GED					0.1	0.055	0.099	#
Black x Some College					0.069	0.05	0.069	
Black x Bachelor					0.072	0.055	0.072	
Black x Post Graduate Degree					0.054	0.054	0.05	
Asian x HS Diploma/GED					-0.472	0.29	-0.472	
Asian x Some College					-0.072	0.192	-0.072	
Asian x Bachelor					0.063	0.175	0.063	
Asian x Post Graduate Degree					-0.002	0.172	-0.002	
Other/Mixed x HS Diploma/GED					-0.029	0.058	-0.029	
Other/Mixed x Some College					-0.008	0.05	-0.008	
Other/Mixed x Bachelor					0.042	0.051	0.042	
Other/Mixed x Post Graduate Degree					0.027	0.05	0.027	

Linear mixed effects regressions are used.
Outcome: Nucleus accumbens Function During MID Task (fMRI).
#p <0.1; *p <0.05; **p <0.001.



the striatum, jointly works with the prefrontal cortex to participate in decision-making and reward-seeking [118]. Activation of this reward network can be stimulated by the substances such as amphetamine, cocaine, nicotine, alcohol, and opioids leading to pleasurable experiences and addictions [119].

The nucleus accumbens, a component of the striatum, is part of the mesolimbic dopamine pathway. Nucleus accumbens is highly stimulated by drugs such as cocaine [120], opioids, psychostimulants [121], and methamphetamine [122]. These effects occur through various mechanisms, including reinstating drug-seeking behaviors [123] or directing behavioral sequence from drug use with reward [124]. In the nucleus accumbens, GABA, a hormone released by the

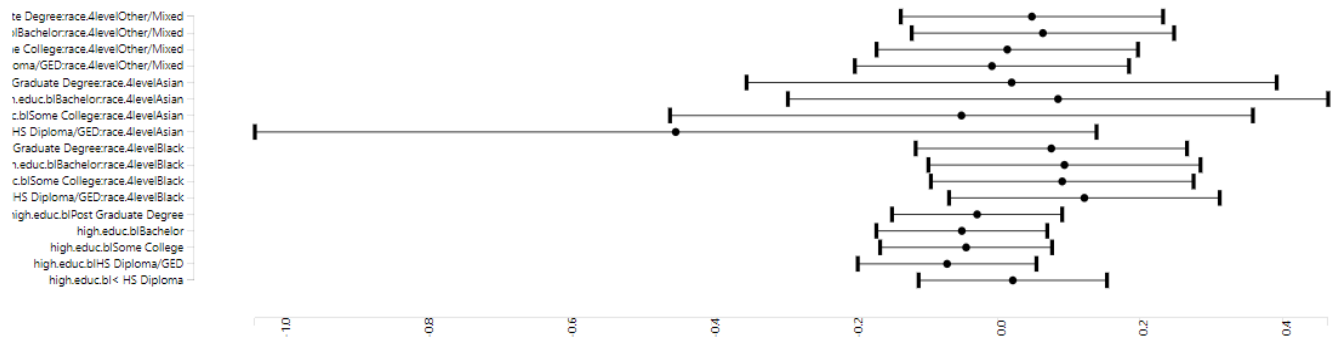


Figure 1: Association between Parental Education and Right Nucleus acumens Function Overall.

brain to regulate dopamine levels in the reward, mesolimbic pathway determines the association of drug and rewarding sensation [92]. The nucleus accumbens regulates various motivational behaviors as a part of the brain reward system [125]. The nucleus accumbens function, as a result, has an impact on the amount of GABA that is being released.

High family SES is a factor in higher quantity and quality of parenting, including more time spent with children, more resources in promoting child's growth, and safer neighborhood [126-128]. The effects of SES in the family may be explained by the scarcity of resources [23], risky parental behaviors such as smoking [132], alcohol consumption and substance use [38], and risky/unsafe neighborhood that leads to early exposure, peer pressure, and easy access to alcohol and substances [58,133]. These effects, however, vary by race as a proxy of racism.

The racial variations in brain function reported here are not due to genes but differential SES effects. In addition, high family SES also means exposure of children to lower parental risk behaviors [99,129,130]. These parenting behaviors play a key factor in explaining the SES effects on children development [131]. In contrast, minority children face cumulative stress from social exclusion and discrimination across all SES levels [32,131].

We should emphasize that race in our study was considered a social determinant, not a biological determinant of nucleus accumbens function. When SES is controlled, race is a proxy of racism, differential access to resources, and society's unequal treatment that leads to social inequalities. In other words, race and SES reflect how individuals and groups are treated by society. This view is different from biological frameworks that conceptualize race as an innate biological marker [134]. We have clearly emphasized this point in our other MDRs papers [135].

The first limitation of our study is that the participants had no exposure to drugs and substances. We used cross-sectional data of the first wave of the ABCD study in which the participants' ages were 9-10 years old. There was a limited number of participants that were exposed to any drugs or substances. Longitudinal studies are necessary throughout the ten-year follow-up period of the ABCD study. We only focused on the nucleus accumbens, which correlates with risky behaviors such as substance use.

More research is needed on the longitudinal changes in SES, nucleus accumbens function and structure, and substance use throughout the ABCD study. Race and SES, as two major social determinants, may have multiplicative and complex effects on nucleus accumbens activity, a proxy of brain reward processing. Future research may explore the role of other SES indicators and other brain regions. Finally, this study only compared racial groups. Other social identities such as ethnicity, LGBT status, or immigration also marginalize people.

Conclusion

In summary, high parental education, as a proxy of high family SES, correlates with less right nucleus accumbens function during anticipation of loss in a national sample of 9-10 year of US children. However, this effect varies across racial groups. Weaker SES effects for Black than White children suggests that SES is less protective among racial minority groups who are racialized, a pattern which can be explained by Minorities Diminished Returns (MDRs).

Declaration

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