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Prefrontal Cortex Response to Threat: Race by Age Variation in 9-10 Year Old Children

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Abstract

Background: Considerable research has suggested that race and age are two major determinants of brain development, including but not limited to development of the prefrontal cortex (PFC). Minorities' Diminished Returns (MDRs), however, suggests that race (as a proxy of racism) may interact with various determinants of human and brain development. Minimal knowledge, however, exists on whether age and race also interact on shaping PFC response to threat among American children.

Purpose: Using data from a task-based functional brain imaging study and considering race as a sociological rather than a biological construct, we investigated combined effects of race and age on prefrontal cortical (PFC) response to threat. We explored racial heterogeneities in the association between age and PFC response to threat by comparing Black and White children.

Methods: This study used the task-based functional Magnetic Resonance Imaging (fMRI) data from the Adolescents Brain Cognitive Development (ABCD) study, a national, landmark, multi-center brain imaging investigation of 9-10 years old children in the US. The primary outcomes were mean beta weights of n-back runs measuring PFC response to threating versus neutral face contrast in the following regions of interest (ROIs): left hemisphere-lateral orbito-frontal, left hemisphere -superior-frontal, right hemisphere -caudal middle frontal, and right hemisphere -superior frontal cortex. The independent variable was age. Covariates were sex, ethnicity, family socioeconomic status, and neighborhood socioeconomic status. Race was the focal moderator. To analyze the data, we used linear regression models without and with interactions and SES as covariates.

Results: We included 5,066 9-10 years old children. Age and race did not show direct effects on PFC response to threatening relative to neutral faces. While ethnicity, sex, and socioeconomic status were controlled, age and race showed a systematic interaction on PFC response to threatening relative to neutral faces.

Conclusions: For American children, race and age do not have direct effects but multiplicative effects on PFC response to threat. The results may be reflective of social inequalities in how Black and White children are socialized and developed. The results are important given the role of the PFC in regulating the limbic system response to threat. Coordinated work of the limbic system and PFC is a core element of children's behavioral and emotional development. Future research is needed on how social stratification and racism shape emotion processing and regulation of American children in response to threat.

Background

Age is one of the most salient determinants of child brain development[1-4]. While early childhood[5,6] and infancy[1,7,8] are also important, adolescence is a unique phase determined by a rapid change of brain maturation[9]. The National Institute of Health (NIH) notes about child brain development that: 1) the brain reaches its biggest size in early adolescence (11 and 14 years old for girls and boys respectively), 2) the prefrontal cortex undergoes maturation later than other parts of the brain, 3) a teenager's brain has considerable plasticity and resilience, meaning that it can successfully adapt and respond to its environment, 4) undergoes ongoing and rapid changes with 5) co-occurring physical, emotional, and social changes, and 6) exhibits the highest vulnerability to stress[9].

Response to threat[10-12], one of the major functions of the brain, has major implications for survival as well as social relations. Research has well shown that a large array of cortical and subcortical brain structures are involved in processing threat- and fear-related information[13-16], all being essential for maintaining social behavior, group affiliation, and attachment[17]. To increase survival, the brain needs to strongly respond to threat, as it encounters and processes negative stimuli (e.g. threat or fear related), as well as responding to stimuli that are unpredictable, ambiguous, and potentially dangerous[18]. An increased response to threat is also a part of psychopathologies such as anxiety[19], depression[20-23], poor decision making[24-26], aggression[27,28], and risk behaviors[29]. Research has shown that age[30-32], race[33-38], and socioeconomic status (SES)[39-41] are among the main predictors of the brain response to threat.

While age may alter how the brain evaluates and responds to threat, it is not the only factor. Race, family socioeconomic status, are all proxies of exposure to stress, adversities, trauma, and all other salient determinants of children brain response to threat[39-43]. As social adversities, stress, and trauma impact brain response to threat[43], there is a need to control if race and age still impact brain response to threat after socioeconomic status (as a proxy of stress and trauma) is controlled for.

Most of the existing research on the effect of age on brain response to threat is performed in White middle-class individuals. Research has, however, shown that what applied to the White middle-class may not necessarily apply to Blacks and other racial and ethnic groups. Any enhancement of these studies, however, require a large sample size. Such sample size requires large scale national studies that enhance statistical power for racial comparisons and also generate results that are generalizable to the US population. The Adolescents Brain Cognitive Development (ABCD), a national children's brain development study data with 10,000+ sample size[44-48] has generated an unprecedented opportunity to investigate how racial groups differ in the effects of risk and protective factors on brain development. As such, the ABCD study has also provided us a unique opportunity for comparison of Black and White children for age-related changes in those who live in low socioeconomic status families and neighborhoods. ABCD has a large sample size, national sampling, and has collected data on the brain imaging of 10,000+ American children[44-48].

Aims

To understand the separate, additive, and multiplicative effects of the race (as a social factor) and age on the brain development of children, we borrowed data from a national sample of American children, with two aims: First to test the additive and multiplicative effects of age and race on children's brain response to threat. By testing multiplicative effects, we mean to explore the differential associations between age and brain response to threat across racial groups. Using the ABCD data, we expected an interaction between race and age, which was an indicator of a difference between White and Black children for the effects of age on brain function. It is not race or age, but their combined and interactive effects that shape brain response to threat (negative face). This expectation is in line with the other research on behaviors and brain development showing that protective factors may have diminished effects for Black than White children[49-51].

Methods

Design and settings

This cross-sectional study was a secondary analysis of the existing data, borrowed from the ABCD study[44-48]. This analysis is limited to the wave 1 data of the ABCD study. As described elsewhere[44,52], ABCD is one of the largest brain imaging studies of child brain development that has ever been conducted. Among the main advantages of the ABCD study are being a national sample, a large sample size, a large sample of Blacks, public availability of the data, robust measurement of the brain development, and considerable psychiatric and psychosocial variables[44-48].

Participants and Sampling

Participants of the ABCD study were selected across multiple cities across states. This ABCD sample was primarily recruited through the school systems with sampling (school selection) informed by race, ethnicity, age, sex, socioeconomic status, and urbanicity. For additional methodological details of ABCD sampling and recruitment, please see the paper published elsewhere[53]. Analytical sample for this study was limited to White or Black children who had data on n-Back task (n=5,066).

Study Variables

Study constructs included age, race, ethnicity, sex, parental education (years), family income, financial difficulty, and neighborhood income and brain response to negative relative to neutral face (Table 1). PFC response to threatening (negative) relative to neutral face was captured by functional MRI measures during the N-Back task. A detailed description of the ABCD study procedures and harmonization of the fMRI studies are available elsewhere[45]. N-Back task measures a wide range of brain functions such as emotion process, emotion regulation, impulsivity, working memory, encoding, retrieval, forgetting, and recognition. This task is ideal for measurement of dorsolateral prefrontal, parietal and premotor cortex, hippocampus, parahippocampus, and amygdala response.

Outcome

Outcomes in this study were brain response to threatening (negative) relative to neutral faces. These outcomes were selected because brain response to threatening (negative) faces is shown to be a leading brain function that is essential for socialization. These included the mean beta weight for n-Back run 1 threatening (negative) face versus neutral face contrast in APARC ROI left hemisphere-lateral orbito-frontal, left hemisphere -superior-frontal, right hemisphere -caudal middle frontal, and right hemisphere -superior frontal. Table A lists the name of the outcome variables and their explanations.

Moderator

Race. Race, a self-identified variable, was measured as bellow: Black = 1, White = 0 [reference].

Independent Variables

Age. Parents reported the age of the children. Age was calculated as the difference from date of birth to the date of the enrollment to the study. Age was a continuous measure in years.

Confounders

Parental education (years): Parents were asked, "What is the highest grade or level of school you have completed or the highest degree you have received?". This variable tanged from 1 (no official education) to 21 (doctoral degree).

Family income: Parents were asked "What is your total combined family income for the past 12 months? This should include income (before taxes and deductions) from all sources, wages, rent from properties, social security, disability and veteran's benefits, unemployment benefits, workman". Family income was a continuous measure ranging from 1 (Less than $5,000) to 10 ($200,000+), with a higher score indicating higher income.

Table A. The list of the outcome variables and their explanations.

Outcome	ABCD Study Variable	Variable	Task	Faces	Hemisphere	APARC ROI	Description
1	tfmri_nback_r1_757	Mean beta weight	n-Back run 1	Negative face versus neutral face contrast	Left	Lateral orbi-to-frontal	A part of the prefrontal cortex region, located in the frontal lobes of the brain, and involved in the cognitive processes such as decision-making.
2	tfmri_nback_r1_773	Mean beta weight	n-Back run 1	Negative face versus neutral face contrast	Left	Superior frontal	Also called as the marginal gyrus, is one of the frontal gyri, and makes up one third of the frontal lobe. This gy-rus is bounded laterally by the superior frontal sulcus.
3	tfmri_nback_r1_783	Mean beta weight	n-Back run 1	Negative face versus neutral face contrast	Right	Caudal middle frontal	The caudal part of the middle frontal gyrus, which makes up about one-third of the frontal lobe of the human brain.
4	tfmri_nback_r1_807	Mean beta weight	n-Back run 1	Negative face versus neutral face contrast	Right	Superior frontal	A gyrus that continues onto the medial surface of the brain hemisphere. Cingulate sulcus is the main boundary between the superior fron-tal gyrus and the adjunct and underlying limbic lobe. It is also parallel to the cor-pus callosum before it turns upwards to the superior margin of the brain hemi-sphere under the name pars marginalis (marginal part).

Financial difficulties: Financial difficulties were measured by the following seven items: "In the past 12 months, has there been a time when you and your immediate family experienced any of the following:" 1)"Needed food but could not afford to buy it or could not afford to go out to get it?", 2) "Were without telephone service because you could not afford it?" 3)" Did not pay the full amount of the rent or mortgage because you could not afford it?", 4) "Were evicted from your home for not paying the rent or mortgage?", 5)"Had services turned off by the gas or electric company, or the oil company would not deliver oil because payments were not made?", 6) "Had someone who needed to see a doctor or go to the hospital but did not go because you could not afford it?", and 7) "Had someone who needed a dentist but could not go because you could not afford it?" Responses to each item were either 0 or 1. We calculated a sum score with a potential range between 0 and 7, a higher score indicating lower family socioeconomic status. Our variable was a continuous measure. Financial difficulties are an accepted socioeconomic status indicator[54-60].

Neighborhood Income (Socioeconomic Status): Derived from ABCD residential history file, we used the median family income of the neighborhood as neighborhood socioeconomic status. This is in line with the Area Deprivation Index (ADI), based on the work done by the Health Resources & Services Administration (HRSA), Amy Kind, Ana Diez Roux, and others. We used the neighborhood income of the county-level / census block group/neighborhood. Extensive research suggests that ADI, and median family income, and neighborhood income are predictors of health. This variable was not calculated in terms of 1 USD but 100,000 USD[61-64].

Ethnicity: Parents reported if they are of Hispanic ethnic background. This variable was coded as Hispanic = 1 and non-Hispanic = 0.

Sex: Sex was a dichotomous variable with males as 1 and females as 0.

Data Analysis

We used SPSS for data analysis. For descriptive purposes, we reported frequency (%) and mean (standard deviation [SD]) for categorical and continuous variables, respectively. To conduct our bivariate analyses, we used Chi-square and independent samples t-test to compare Blacks and White children. To perform our multivariable analyses, we performed two series of four linear regressions for each outcome. The independent variable was age. The outcome were one of the structures namely 1) left hemisphere-lateral orbito-frontal cortex, 2) left hemisphere -superior-frontal cortex, 3) right hemisphere -caudal middle frontal cortex, and 4) right hemisphere -superior frontal cortex (Table 1). Our models first only controlled for sex. Then we ran models that also controlled for ethnicity and SES indicators namely parental education (years), family

Table 1. Descriptive data overall and by race.

	All (*n* = 5,066)		Whites (*n* = 3,782)		Blacks (*n* = 1,284)	
	n	**%**	**n**	**%**	**n**	**%**
Race*[a]						
White	3782	74.7	3782	100.0	-	-
Black	1284	25.3	-	-	1284	100.0
Ethnicity*[a]						
Non-Hispanic	4276	84.4	3098	81.9	1178	91.7
Hispanic	790	15.6	684	18.1	106	8.3
Sex*[a]						
Male	2431	48.0	1800	47.6	631	49.1
Female	2635	52.0	1982	52.4	653	50.9
	Mean	**SD**	**Mean**	**SD**	**Mean**	**SD**
Age (Year)	9.44	0.50	9.43	0.50	9.45	0.51
Parental Education * [b]	16.80	2.50	17.25	2.34	15.46	2.49
Family income * [b]	7.18	2.46	7.86	1.98	5.20	2.67
Financial Difficulties * [b]	0.07	0.16	0.05	0.13	0.15	0.21
Neighborhood income * [b]	0.76	0.36	0.85	0.34	0.52	0.28
Activation of #1 in response to threatening than neutral faces	0.00	1.58	-0.02	1.58	0.06	1.59
Activation of #2 in response to threatening than neutral faces	-0.02	0.55	-0.02	0.46	-0.03	0.77
Activation of #3 in response to threatening than neutral faces	0.00	0.59	0.00	0.46	0.00	0.92
Activation of #4 in response to threatening than neutral faces	-0.01	0.55	-0.01	0.44	-0.01	0.82

Outcome #1: left hemisphere-lateral orbito-frontal, Outcome #2: left hemisphere -superior-frontal, Outcome #3: right hemisphere -caudal middle frontal, and Outcome #4: right hemisphere -superior frontal. All outcomes are mean beta weight for n-Back run 1 threatening face versus neutral face contrast. * $p < 0.05$ for comparison of Black and White people. [a]: Chi-Square test, [b]: independent samples t-test.

income, financial difficulty, and neighborhood income 100,000 USD. *Model 1* was a pooled sample model without any interaction term, *Model 2* was a pooled sample model with age by race interaction term, *Model 3* was performed in White and *Model 4* was performed in Black children. Identical models were run for each outcome, and without and with socioeconomic status covariates. Unstandardized regression coefficient (b), SE, and p-values were reported for each model. Given the explorative nature of this study, and given p values for interactions are larger, and interactions are hard to find, a p-value of equal or less than 0.1 was significant.

Ethical Aspect

The ABCD study protocol received approval from the University of California, San Diego (UCSD) Institutional Review Board (cIRB). Some other universities that were a part of the ABCD study also obtained local IRB approval. All the participating children gave assent. Parents also signed informed consent. More detailed information on the ABCD study is available elsewhere[52]. Given that the data used in this study were fully de-identified, our investigation was non-human subject research. Thus, it found to be exempt from a full IRB review.

Results

Descriptives

The current analysis was performed on 5,066 9-10 years old children who were either White (*n* = 3,782; %74.7) or Blacks (*n* = 1,284; %25.3). In Table 1 we have presented the descriptive demographic, socioeconomic status, and brain response to threat data. These data are presented for the pooled sample, as well as by race (Table 1).

As Table 1 shows, White and Black children did not differ in age and sex but differed in family socioeconomic status and neighborhood socioeconomic status. Compared to White children, Black children had lower SES. Black and White children did not differ in brain response to threat (Table 1).

Unadjusted bivariate correlations

Table 2 presents the results of the unadjusted bivariate correlations based on the Pearson test. Socioeconomic

Table 2. Bivariate correlations in the pooled sample and by race (n=5,066).

	1	2	3	4	5	6	7	8
All								
1 Parental education	1	-.44**	.56**	-.00	-.02	-.02	-.04*	-.02
2 Family income		1	-.28**	.00	.02	-.02	-.01	-.03
3 Financial difficulties			1	.02	-.01	-.02	-.02	-.01
4 Neighborhood income				1	.01	-.00	.00	-.01
5 Activation of #1 in response to threatening than neutral faces					1	.10**	.05**	.08**
6 Activation of #2 in response to threatening than neutral faces						1	.79**	.93**
7 Activation of #3 in response to threatening than neutral faces							1	.85**
8 Activation of #4 in response to threatening than neutral faces								1
Whites								
1 Parental education	1	-.44**	.48**	.01	.01	-.03	-.04*	-.03
2 Family income		1	-.22**	.01	.00	-.00	.01	-.02
3 Financial difficulties			1	.03	.01	-.02	-.01	.00
4 Neighborhood income				1	.03	.03	.03	.03
5 Activation of #1 in response to threatening than neutral faces					1	.16**	.10**	.15**
6 Activation of #2 in response to threatening than neutral faces						1	.72**	.91**
7 Activation of #3 in response to threatening than neutral faces							1	.78**
8 Activation of #4 in response to threatening than neutral faces								1
Blacks								
1 Parental education	1	-.29**	.46**	.01	-.05	-.03	-.05	-.02
2 Family income		1	-.18**	-.01	.04	-.04	-.03	-.04
3 Financial difficulties			1	.04	-.05	-.05	-.06	-.05
4 Neighborhood income				1	-.05	-.07*	-.05	-.07
5 Activation of #1 in response to threatening than neutral faces					1	-.00	-.01	-.04
6 Activation of #2 in response to threatening than neutral faces						1	.87**	.95**
7 Activation of #3 in response to threatening than neutral faces							1	.91**
8 Activation of #4 in response to threatening than neutral faces								1

Outcome #1: left hemisphere-lateral orbito-frontal, Outcome #2: left hemisphere -superior-frontal, Outcome #3: right hemisphere -caudal middle frontal, and Outcome #4: right hemisphere -superior frontal. All outcomes are mean beta weight for n-Back run 1 threatening face versus neutral face contrast.

status indicators were not correlated with brain response to threatening versus neutral faces. These correlations were inconsistent between racial groups and were based on brain outcome.

Pooled-Sample Associations without Socioeconomic Status as Covariate

Table 3 reports the results of the two regression models in the pooled sample. *Models 1-a*, which only included the main effects, showed that age or race were not associated with activation of various brain regions in response to threatening than neutral faces. *Model 2-a* showed interactions between race and socioeconomic status on activation of the brain regions in response to threatening than neutral faces.

Race-Specific Associations without Socioeconomic Status as Covariate

Table 6 reports the results of race-specific models. *Model 3-a* was performed in White children and *Model 4-b* was performed in Black children. We found that age was not associated with brain response to threatening versus neutral faces in White or Black children.

Table 3. Linear regressions in the pooled sample, without controlling for socioeconomic status (n = 5,066).

	Model 1-a All Main Effects		Model 2-a All M1 + Interactions	
	B	p	b	P
Outcome: #1				
Race (Black)	0.08	.205	2.27	.044
Age	0.03	.562	0.08	.146
Sex (male)	0.01	.873	0.01	.843
Age x Race			-0.23	.052
Outcome: #2				
Race (Black)	-0.01	.622	1.27	.001
Age	0.00	.938	0.03	.126
Sex (male)	-0.01	.699	-0.01	.746
Age x Race			-0.14	.001
Outcome: #3				
Race (Black)	0.00	.987	1.02	.016
Age	0.00	.914	0.03	.206
Sex (male)	0.00	.942	0.00	.979
Age x Race			-0.11	.016
Outcome: #4				
Race (Black)	-0.01	.811	1.19	.002
Age	-0.01	.691	0.02	.257
Sex (male)	0.01	.748	0.01	.703
Age x Race			-0.13	.002

B: Unstandardized regression coefficient, SE: Standard Error, CI: Confidence Interval, Outcome #1: left hemisphere-lateral orbito-frontal, Outcome #2: left hemisphere -superior-frontal, Outcome #3: right hemisphere -caudal middle frontal, and Outcome #4: right hemisphere -superior frontal. All outcomes are mean beta weight for n-Back run 1 threatening face versus neutral face contrast.

Table 4. Linear regressions by race, without controlling for socioeconomic status (n=5,066).

	Model 3-a Whites		Model 3-b Blacks	
	B	p	b	P
Outcome: #1				
Age	0.01	.752	-0.17	.126
Sex (male)	0.10	.013	0.02	.878
Outcome: #2				
Age	0.01	.496	-0.12	.089
Sex (male)	0.01	.722	-0.07	.338
Outcome: #3				
Age	0.00	.950	-0.14	.083
Sex (male)	0.02	.304	-0.01	.865
Outcome: #4				
Age	-0.01	.717	-0.15	.051
Sex (male)	0.00	.839	-0.04	.570

B: Unstandardized regression coefficient, SE: Standard Error, CI: Confidence Interval, Outcome #1: left hemisphere-lateral orbito-frontal, Outcome #2: left hemisphere -superior-frontal, Outcome #3: right hemisphere -caudal middle frontal, and Outcome #4: right hemisphere -superior frontal. All outcomes are mean beta weight for n-Back run 1 threatening face versus neutral face contrast.

Pooled-Sample Associations with Socioeconomic Status as Covariate

Table 5 reports the results of two regression models in the pooled sample. *Models 1-b*, which only included the main effects showed that race or age were not associated with activation of various brain regions in response to threatening than neutral faces. *Model 2-b* showed interactions between race and socioeconomic status on activation of the brain regions in response to threatening versus neutral faces.

Race-Specific Associations with Socioeconomic Status as Covariate

Table 6 reports the results of race-specific models. *Model 3-b* was performed in White children and *Model 4-b* was performed in Black children. We found that age was not associated with brain response to threatening versus neutral faces in White or Black children. However, the association was positive for Whites and threatening for Blacks.

Discussion

We found race by age effects in children brain response to threat. This is indicative of racial variation in age-related changes in brain response to threat. We, however, showed that these race by age effects remain significant when SES is controlled for. That is, race, per se, not as a proxy of SES, alters age-related brain development.

We found race per se not to be associated with brain response to threatening versus neutral faces in White but not Black children. Age was also not directly associated with activation of the brain in response to threatening

Table 5. Linear regressions in the pooled sample, while controlled for socioeconomic status (n=5,066).

	Model 1-b All Main Effects		Model 2-b All M1 + Interactions	
	B	P	B	p
Outcome: #1				
Race (Black)	0.15	.010	1.71	.071
Age	-0.03	.418	0.00	.996
Sex (male)	0.06	.110	0.06	.107
Ethnicity (Hispanic)	0.05	.407	0.05	.412
Parental education (years)	-0.01	.183	-0.01	.189
Family income	-0.02	.208	-0.02	.208
Financial difficulty	0.14	.359	0.14	.363
Neighborhood income (100000)	0.04	.558	0.04	.555
Age x Race			-0.16	.099
Outcome: #2				
Race (Black)	0.00	.896	0.92	.058
Age	-0.02	.248	0.00	.840
Sex (male)	-0.01	.537	-0.01	.545
Ethnicity (Hispanic)	-0.02	.566	-0.02	.559
Parental education (years)	0.00	.645	0.00	.660
Family income	0.00	.620	0.00	.620
Financial difficulty	-0.13	.088	-0.13	.087
Neighborhood income (100000)	-0.06	.109	-0.06	.110
Age x Race			-0.10	.056
Outcome: #3				
Race (Black)	-0.02	.559	0.98	.063
Age	-0.03	.208	-0.01	.765
Sex (male)	0.00	.991	0.00	.980
Ethnicity (Hispanic)	-0.03	.434	-0.03	.428
Parental education (years)	0.00	.646	0.00	.660
Family income	-0.01	.296	-0.01	.295
Financial difficulty	-0.12	.138	-0.13	.135
Neighborhood income (100000)	-0.06	.149	-0.06	.150
Age x Race			-0.11	.058
Outcome: # 4				
Race (Black)	-0.01	.696	0.97	.048
Age	-0.04	.057	-0.02	.405
Sex (male)	-0.01	.635	-0.01	.645
Ethnicity (Hispanic)	-0.03	.373	-0.03	.367
Parental education (years)	0.00	.677	0.00	.692
Family income	-0.01	.393	-0.01	.392
Financial difficulty	-0.13	.086	-0.14	.084
Neighborhood income (100000)	-0.04	.228	-0.04	.230
Age x Race			-0.10	.045

B: Unstandardized regression coefficient, SE: Standard Error, CI: Confidence Interval, Outcome #1: left hemisphere-lateral orbitofrontal, Outcome #2: left hemisphere -superior-frontal, Outcome #3: right hemisphere -caudal middle frontal, and Outcome #4: right hemisphere -superior frontal. All outcomes are mean beta weight for n-Back run 1 threatening face versus neutral face contrast.

Table 6. Linear regressions by race, while controlled for socioeconomic status (n=5,066).

	Model 3-b Whites		Model 4-b Blacks	
	B	P	b	p
Outcome: # 1				
Age	0.00	.955	-0.15	.162
Sex (male)	0.09	.032	-0.02	.849
Ethnicity (Hispanic)	0.11	.069	0.01	.946
Parental education (years)	0.00	.895	-0.05	.049
Family income	0.00	.966	-0.03	.321
Financial difficulty	0.30	.117	-0.01	.959
Neighborhood income (100000)	0.06	.460	-0.08	.699
Outcome: # 2				
Age	-0.01	.763	-0.10	.154
Sex (male)	-0.01	.598	-0.02	.782
Ethnicity (Hispanic)	-0.02	.562	-0.05	.678
Parental education (years)	-0.01	.102	0.02	.225
Family income	0.00	.761	-0.01	.463
Financial difficulty	0.02	.853	-0.34	.063
Neighborhood income (100000)	-0.03	.377	-0.19	.167
Outcome: # 3				
Age	-0.01	.666	-0.11	.143
Sex (male)	0.00	.825	0.02	.773
Ethnicity (Hispanic)	-0.03	.315	-0.03	.842
Parental education (years)	-0.01	.018	0.04	.051
Family income	0.00	.910	-0.03	.170
Financial difficulty	0.01	.900	-0.33	.092
Neighborhood income (100000)	-0.02	.604	-0.25	.095
Outcome: # 4				
Age	-0.02	.280	-0.12	.100
Sex (male)	-0.01	.580	-0.01	.929
Ethnicity (Hispanic)	-0.04	.186	-0.04	.773
Parental education (years)	-0.01	.055	0.03	.150
Family income	0.00	.478	-0.01	.622
Financial difficulty	-0.03	.747	-0.30	.120
Neighborhood income (100000)	0.00	.978	-0.25	.089

B: Unstandardized regression coefficient, SE: Standard Error, CI: Confidence Interval, Outcome #1: left hemisphere-lateral orbitofrontal, Outcome #2: left hemisphere -superior-frontal, Outcome #3: right hemisphere -caudal middle frontal, and Outcome #4: right hemisphere -superior frontal. All outcomes are mean beta weight for n-Back run 1 threatening face versus neutral face contrast.

versus neutral faces. Race and age, however, showed combined effects. Age would have a different implication for recognition and response to threat (negative emotion faces), with diminished salience of age for Black than White children. Although this was the main observed pattern for the outcomes, our four variables, response in the left hemisphere-lateral orbito-frontal, left hemisphere -superior-frontal, right hemisphere -caudal middle frontal, and right hemisphere -superior frontal ROIs also showed differences and nuances in their correlates.

Race was not found to change the brain response to threat. Race in our study was a proxy of adversities, stress, and poverty. Childhood poverty may be linked to reduced connectivity between the amygdala and hippocampus and some other regions, including the superior frontal cortex, lingual gyrus, posterior cingulate, and putamen[65-68]. The study showed that while childhood poverty predicts connectivity between 1) the left hippocampus and the right superior frontal cortex and 2) the right amygdala and the right lingual gyrus, this brain connectivity mediates the effect of childhood poverty on children depression[69]. Others have established hyperactivation of the reward network and hypoactivation of the executive network in low socioeconomic status individuals[70]. The effects of low socioeconomic status and stress on how the brain reacts to threat go beyond amygdala hyper-reactivity to threat and also impacts many other brain structures involved in memory and cognition[71].

Research has shown that each additional year spent in poverty may be associated with a lower level of connectivity in neural networks involved in emotion regulation. However, these effects may be more pronounced for children who receive low levels of supportive parenting[72]. Blacks, compared to Whites, receive lower levels of protective parenting and live longer under poverty.

Our finding is indicative of double jeopardy for the brain development of Black children. The first risk is that race may be associated with poor brain development, as race is a proxy of exposure to poverty and racism. In addition, age-related brain development may be delayed, again, probably as a result of racism and discrimination, for Black children. Studies have shown that racial discrimination results in an increase in amygdala connectivity with multiple brain regions. In the presence of racial discrimination, the amygdala shows more strong connection with the thalamus. Discrimination increased the connections between the amygdala and the putamen, caudate, anterior insula, anterior cingulate, and medial frontal gyrus[73].

The more salient effect of age for White than Black children's brain development may be due to the lack of supportive elements and environment in Black lives. Other stressors such as racial and ethnic discrimination are unique in the life of racial minorities. Many studies have shown that social and physical environment is more enriched and resource filled for White than Black families. Libraries, schools, and houses where White families live have many books and educational resources. For Black families, however, such resources are scarce. As a result of growing in a rich or poor environment, age may not have the same effect on the brain development of White and Black children.

The results are related to a pattern called Minorities' Diminished Returns (MDRs)[50,51]. MDRs refer to protective and risk factors that differently influence outcomes for Black and White families. For example, socioeconomic status interact with race on anxiety[74], depression[75], poor health[76], poor school performance[77,78], as well as high-risk behaviors[49] such as aggression[49] and tobacco use[79,80]. Black-White differences in correlates of health and development seem to be rules rather than exceptions[76,81-84]. For example, in the Fragile Families and Child Wellbeing Study (FFCWS), correlates of impulsivity, school performance, school bonding, attention-deficit/hyperactivity disorder (ADHD), obesity, aggression, depression, and self-rated health differed for White and Black children[84-87]. These differences between Black and White children[84-87] are due to differential effects of precursors on a wide range of developmental and health outcomes of Blacks and Whites[76,81,83,88-92]. As a result of these MDRs, Black children show diminished returns on health outcomes regardless of their profile of exposure to risk and protective factors, while for Whites, risk and protective effects alter the outcomes[49,86,93-95]. The same patterns of diminished returns are also shown for age[96]. Our study proposes that the same interaction may be seen for the effects of age on brain development.

Some cautionary notes

Here we list six points that need caution. First, the use of age as a primary independent variable using cross-sectional data from a longitudinal cohort study may be inappropriate. There is some age variability, with a range of 8-11 years old, but this cohort was recruited intentionally to be roughly the same age. Future data releases will allow for within-person evaluations of longitudinal change in neural activation that will be better suited for answering the questions posed by this paper. Second, this study is simplistic as it used age as a primary independent variable using cross-sectional data from a longitudinal cohort study. Although there is some age variability, with a range of 8-11 years old, the ABCD cohort was recruited intentionally to be with low age range at baseline. Future data releases will allow for within-person evaluations of longitudinal change in neural activation that will be better suited for answering questions posed in this paper. Third, we should emphasize that we see race as a social factor (a proxy of poverty and socioeconomic status) on how the brain is affected by low or high socioeconomic status (parental education). Across various brain mechanisms, we focused on the amygdala, which is highly involved in emotional regulation, emotional expression, aggression, and impulsivity. An alteration of the amygdala response is expected to be involved in a wide range of emotional, cognitive, and behavioral outcomes. To be more specific, we tested if race, as a proxy of racism, adversities, and stress alters age-related brain development of children, with a specific focus on brain response to threatening (negative) relative to neutral face, which is shown to be one of the brain functions profoundly affected by race, socioeconomic status, stress, and adversity[40,41,97-99]. Fourth, this study was exploratory. The ABCD data provides an opportunity to answer important questions with high statistical power. Studies utilizing the ABCD data have the potential to have a major contribution to the field. This paper is the first step in this regard. Fifth, no matter how responsible we attempt to be in our interpretations, studies arguing for racial differences in biological functioning are controversial. They have the potential to be abused. They are at an increased risk of it being used to harm or stigmatize already marginalized groups. Sixth, in almost all epidemiological studies, race has an imbalanced distribution, and this has implications for the power of the study. Thus, the results of race-stratified models should be interpreted with caution. However, most of our analyses were in the pooled sample, which is less affected by the distribution of race.

Conclusions

In summary, in a large national sample of American children, age and race do not have independent (separate) but inter-dependent (multiplicative) effects on PFC response to threatening (negative) relative to neutral faces. This suggests that age-related brain development of children might be under the influence of race (as a social rather than biological construct). More research is needed on how social factors such as race, racism, social environment, adversities, and stress influence children brain development as a function of age.

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