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Research Article

Perceived Discrimination and Superior Frontal Cortex Surface Area in Children: Sex Differences

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Abstract

Background: Limited knowledge exists on the role of Perceived Discrimination (PD) as a social determinant and risk factor that influences children's brain development and whether this association is different for male and female children.

Aim: To examine the association between PD, the superior frontal cortex, and sex differences in a national sample of 9/10-year-old children in the US.

Methods: This cross-sectional study included 8,719 children from the Adolescent Brain Cognitive Development (ABCD) study. The exposure variable was PD, and the outcome variables were the right and left superior frontal cortex surface areas, measured using structural MRIs. Covariates included: age, family structure, parental education, household income, stressful life events, financial stress, neighborhood poverty, and neighborhood toxins/pollutants (lead, PM2.5, and NO_2). We used a mixed-effect regression model for data analysis to adjust to the nested nature of the ABCD data.

Results: There was an inverse association between PD and superior frontal cortex surface area in children. We found a statistically significant interaction between PD and the superior frontal cortex, indicating a more prominent inverse association between PD and superior frontal cortex surface area in males than females. Similar findings were observed for the right and left hemispheres.

Conclusion: High levels of PD may be a more salient determinant of superior frontal cortex surface area for male than female children. Sex may alter the relevance of high PD for the brain development of US children. More research is needed on the mechanism by which sex differences emerge in the association between PD and brain development.

Keywords: Discrimination; Stress; Race; Population groups; Sex; Children

Introduction

Perceived Discrimination (PD) is a specific type of stressor that increases the risk of a wide range of undesired mental and behavioral health outcomes [1,2] such as depression, anxiety, tobacco use, alcohol use, drug use, and suicide [3]. High PD may interfere with emotion regulation, reward processing, and cognitive control of the brain [3-5]. However, males and females may respond differently to PD [6,7]. While most research has shown that compared to females, males are more likely to develop undesired mental and behavioral outcomes in response to PD [8-15], some studies have shown null or opposite results [16-19]. These sex and gender differences in vulnerability to discrimination may be partially due to the different coping strategies employed by males and females to adjust to PD [20].

As a type of stressor, PD has a known association with altered brain structure and function [21], but, PD's effect on the superior frontal cortex area is less understood. The superior frontal cortex is a part of the prefrontal cortex (PFC) with major cognitive, emotional, and behavioral implications [22,23]. The superior PFC is involved in executive function, emotion regulation, decision making, and behavioral control [24-26]. We know less about the relevance of PD, as an independent risk factor of the superior frontal cortex area. Very few studies have reported the effect of PD on the superior frontal cortex while controlling for other types of stressors. We need large-scale data sets that have collected data on numerous social stressors and brain structure for such studies.

Although PD has been linked to children's developmental, emotional, and functional outcomes [3], these effects may depend on sex [16-19]. That is while PD is a risk factor for several undesired mental and behavioral outcomes, males and females may respond differently when they experience PD [27-29]. Therefore, PD may have different implications for substance use, depression, and physical health outcomes in males and females [29,30].

Any study of the contribution of PD to children's brain development requires careful control of potential confounders such as stress, family Socioeconomic Status (SES), neighborhood SES, and toxins/pollutants that affect brain development in children [31]. These effects include family SES, family resources, neighborhood SES, and other social and environmental factors [32-37]. Chronic exposure to adversity such as living in low-SES families or neighborhoods interfere with a child's normal brain development [38-41]. Therefore, such factors should be controlled when studying a social and environmental factor like PD as a risk factor for child brain

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development [42-46].

PD does not occur in vacuum. Exposure to PD is commonly experienced in conjunction with other stressors and risk factors [47]. Stress, family SES, neighborhood conditions, and toxins/pollutants may confound the effects of PD on a child's developmental outcomes [48-50]. Other types of stressors and SES indicators confound the effects of PD on brain development because most of these factors correlate with stressors such as PD and at the same time have undesired effects on child brain development [38,39,41,51-53]. For families, stress, low SES, high neighborhood stress, and exposure to toxins/pollutants may co-occur, and have a joint effects on the child's development [54,55]. Consequently, we need to conduct studies that extricate the effects of PD from co-occurring stressors, toxins/pollutants, and contextual conditions [56-58]. Therefore, we have decided to conduct this study while controlling for other potential contributing factors that may confound the effects of PD on children's brain development [55,59].

Aims

To extend the existing knowledge on the possible role of PD as a unique social determinant of 9/10-year-old children's brain development in the US, we tested the association between PD and the superior frontal cortex of children, while social, physical, and economic confounders were controlled. We also explored sex differences in the association between PD and the superior frontal cortex surface area of children. Our hypothesis is that males are more vulnerable to the effects of PD than females, as supported by previous work [8-15].

Methods

Design

This study is a secondary analysis of the baseline (wave 1) data (2016-2018) of the Adolescent Brain Cognitive Development (ABCD) study [60-64], a national study of children's brain development in the United States [60,65].

Sampling

In the ABCD study, participants were limited to 9/10-year-old children recruited from multiple cities across several states in the US. In total, 21 ABCD centers were involved in the recruitment of participants. The primary recruitment strategy was through the school systems [66]. The overall study included 10,875 children.

Eligibility

Race. Race/ ethnicity was a categorical variable and self-identified by the parents. All participants were non-Hispanic Black. This study did not include non-Hispanic White, Hispanic, Asian, Native American, or Mixed/Other racial groups. Participants were only included when their data corresponded with our variables: cognitive function, discrimination, SES, stress, and residential history (n = 1,123).

Study variables

Confounders:

Demographic factors: Age and sex were demographic confounders. Parental education, household income, and parental marital status were the SES control variables. Parents reported the children's ages, the child's age acting as a continuous variable, and measured in months. The sex of the child was a dichotomous variable with 1 representing males and 0 representing females.

Socioeconomic status: Household income was a nominal variable with three levels: Less than 50,000, 50,000-100,000 and 100,000+, as reported by the parent. Parental marital status was represented using 1 for married status and 0 for unmarried status. Parental education was a categorical variable with the following groupings: less than a high school degree, completed high school, college started but not completed, college completed, and postgraduate study. We also used a measure of neighborhood poverty that reflected the percent of households living under poverty in the neighborhood (derived from the zip code).

Stressful life events: Stressful life events were a categorical measurement and were evaluated using the K_SADS interview of the child. Items included (1) "A car accident in which your child or another person in the car was hurt bad enough to require medical attention," (2) "Another significant accident for which your child needed specialized and intensive medical treatment," (3) "Witnessed or caught in a fire that caused significant property damage or personal injury," (4) "Witnessed or caught in a natural disaster that caused significant property damage or personal injury," (5) "Witnessed or present during an act of terrorism (e.g., Boston marathon bombing)," (6) "Witnessed death or mass destruction in a war zone," (7) "Witnessed someone shot or stabbed in the community,"(8) "Shot, stabbed, or beaten brutally by a non-family member," (9) "Shot, stabbed, or beaten brutally by a grown up in the home,"(10) "Beaten to the point of having bruises by a grown up in the home," (11) "A non-family member threatened to kill your child," (12) "A family member threatened to kill your child," (13) "Witness the grownups in the home push, shove or hit one another," (14) "A grown up in the home touched your child in his or her privates, had your child touch their privates, or did other sexual things to your child," (15) "An adult outside your family touched your child in his or her privates, had your child touch their privates or did other sexual things to your child,"(16) "A peer forced your child to do something sexually," and (17) "Learned about the sudden unexpected death of a loved one." Response items for each item were 0 (no) or 1 (yes). Our variable was also binary, with 1 for the presence of any level of financial stress and 0 for the absence of financial stress.

Financial stress: Financial Stress was a categorical variable measured using the following items:

Subjective Family SES: Subjective family SES in this study was established as financial difficulties measured by the following seven items, with the listed options referring to the following prompt: 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. This variable was binary, with 1 indicating the presence of any financial stress and 0 for the absence of any financial stress.

Environmental toxins/pollutants: Based on residential history, we derived neighborhood poverty, neighborhood lead, PM2.5, and NO_2 levels. These variables were continuous measurements with a higher value indicating more environmental pollutants/toxins.

Primary outcome

Superior Frontal Cortex Surface Area. The ABCD study used MRIs to measure the surface area of the cortex, including the superior frontal gyrus. This variable is treated as a continuous measurement, and a high score indicated a large surface area. For a full description of MRI protocol, harmonization, quality control, movement reduction, and brain mapping, please see this paper.

Independent variable

Perceived Discrimination. The following items were used to measure PD: (1) "How often do the following people treat you unfairly or negatively because of your ethnic background? Teachers,"

(2) "How often do the following people treat you unfairly or negatively because of your ethnic background? Other adults outside school," (3) "How often do the following people treat you unfairly or negatively because of your ethnic background? Other students," (4) "I feel that others behave in an unfair or negative way toward my ethnic group," (5) "I feel that I am not wanted in American society," (6) "I don't feel accepted by other Americans," and (7) "I feel that other Americans have something against me." Responses included 1 for almost never; 2 for rarely; 3 for sometimes; 4 for often; 5 for very often; 777 for don't know; and 999 for refused to answer. We calculated a continuous measure with a higher score indicating more PD [67].

Data analysis

We used the Data Analysis and Exploration Portal (DEAP), an interface for analyzing ABCD data based on R package. First, we ruled out multi-collinearity between our studies variables and determined that our outcome had a normal distribution. Next, we applied mixed-effects linear regression models for our multivariable models; Model 1 and Model 2 were performed in the pooled sample, and Model 3 and Model 4 were performed in females and males, respectively. Model 1 did not include an interaction term but included all the confounders. Model 2, however, did include an interaction term between sex and PD, in addition to all the confounders. Overall, we performed four mixed-effects regression models and reported the values b, SE, t, and p.

Ethical considerations

This analysis was exempt from a full IRB review by Charles R Drew University of Medicine. The study of origin (ABCD), was approved by the Institutional Review Board (IRB) at the University of California, San Diego (UCSD). Assent and consent were received from children and their parents, respectively [65].

Results

Descriptives

Table 1 shows that 8,719 9/10-year-old children with complete data were included in the current analysis. The participants self-identified as either female (n = 4,148; 47.6%) or male (n = 4,571; 52.4%). Males were slightly older and had larger right and left superior frontal cortex surface area. Males also reported slightly higher PD than females. Males and females did not differ in their exposure to environmental toxins, financial stress, or by race, ethnicity, family structure, and parental SES.

Model fit

Table 2 presents the fit of mixed-effects regression models. This table shows that models explained a more significant proportion of the variance of right and left superior frontal cortex surface area when confounders were included.

Regression models

Table 3 shows that overall, higher PD was associated with a smaller superior frontal cortex surface area in children, net of all confounders such as age, race, ethnicity, SES, environmental toxins, and other stressors. We found a significant interaction between PD and sex on the right superior frontal cortex surface area in children. The inverse association between PD and right superior frontal cortex surface area was steeper for male children than female children.

Regression models

Table 4 shows that overall, higher PD was associated with a smaller left superior frontal cortex surface area. This negative association between PD and left superior frontal cortex surface area was steeper in males than females.

Figure 1 shows that overall, higher PD was inversely associated with superior frontal cortex surface area. However, this association was steeper for males than females. The same pattern holds for the right and left superior frontal cortex.

Discussion

Overall, PD was inversely associated with superior frontal cortex surface area in children; however, the inverse association between higher PD and smaller superior frontal cortex surface area was more pronounced in males than in females.

In this study, high PD levels were associated with smaller right and left superior frontal cortex surface areas in children. This finding can be explained by the notion that various stressors reduce brain development and function, such as executive function, learning, memory, inhibitory control, emotion regulation, and even reward processing [51,68,69]. PD is even more relevant to the superior frontal cortex surface area of males than females. This finding is in line with the observation that the effects of PD and associated stressors on depression and substance use may be more prominent in males than females [8-15].

While the effects of SES, neighborhoods, stress, and pollutants were controlled, PD remains a robust correlate of superior frontal cortex surface area, particularly in male children. A comprehensive list of risk factors, including PD, should be considered a social determinant of child brain development. Furthermore, the effect of PD is particularly significant in males, which supports previous studies that have reported higher vulnerability to PD in males than females [8-15].

Table 1: Descriptive data.

Level	Overall	Female	Male	p
	8719	4148	4571	
	Mean (SD)	Mean (SD)	Mean (SD)	
Age (Months)	119.12 (7.51)	118.91 (7.49)	119.30 (7.52)	0.015
Right Superior frontal Cortex Surface Area	7,775.06 (965.44)	7,407.75 (859.05)	8,108.38 (935.33)	< 0.001
Left Superior frontal Cortex Surface Area	8,002.79 (961.65)	7,619.58 (851.61)	8,350.54 (922.91)	< 0.001
Perceived Discrimination (1-7)	1.19 (0.42)	1.15 (0.37)	1.22 (0.45)	< 0.001
Neighborhood Poverty	19.88 (15.26)	19.97 (15.14)	19.80 (15.38)	0.606
Neighborhood Lead Risk	4.90 (3.07)	4.90 (3.06)	4.90 (3.07)	0.919
Neighborhood NO_2	2.35 (1.59)	2.36 (1.60)	2.34 (1.57)	0.663
Neighborhood PM 2.5	7.44 (2.57)	7.48 (2.58)	7.39 (2.57)	0.101
Body Mass Index (BMI)	18.60 (3.87)	18.66 (3.96)	18.55 (3.79)	0.199
	n (%)	n (%)	n (%)	
Race				
White	5,999 (68.8)	2,818 (67.9)	3,181 (69.6)	0.303
Black	1,123 (12.9)	557 (13.4)	566 (12.4)	
Asian	189 (2.2)	96 (2.3)	93 (2.0)	
Other/Mixed	1,408 (16.1)	677 (16.3)	731 (16.0)	
Married				
No	2,493 (28.6)	1,214 (29.3)	1,279 (28.0)	0.192
Yes	6,226 (71.4)	2,934 (70.7)	3,292 (72.0)	
Parental Education				
< HS Diploma	280 (3.2)	136 (3.3)	144 (3.2)	0.776
HS Diploma/GED	655 (7.5)	307 (7.4)	348 (7.6)	
Some College	2,172 (24.9)	1,014 (24.4)	1,158 (25.3)	
Bachelor	2,368 (27.2)	1,122 (27.0)	1,246 (27.3)	
Post Graduate Degree	3,244 (37.2)	1,569 (37.8)	1,675 (36.6)	
Household Income				
< 50K	2,334 (26.8)	1,114 (26.9)	1,220 (26.7)	0.677
≥ 50K& < 100K	2,534 (29.1)	1,221 (29.4)	1,313 (28.7)	
≥ 100K	3,851 (44.2)	1,813 (43.7)	2,038 (44.6)	
Hispanic				
No	7,110 (81.5)	3,396 (81.9)	3,714 (81.3)	0.473
Yes	1,609 (18.5)	752 (18.1)	857 (18.7)	
Stressful Life Events (Any)				
No	5,732 (65.7)	2,694 (64.9)	3,038 (66.5)	0.142
Yes	2,987 (34.3)	1,454 (35.1)	1,533 (33.5)	
Financial Stress (Any)				
No	7,021 (80.5)	3,374 (81.3)	3,647 (79.8)	0.071
Yes	1,698 (19.5)	774 (18.7)	924 (20.2)	

Other than PD, a wide range of societal factors correlated with superior frontal cortex surface area in this study. Race, sex, SES, and other stressors were linked to superior frontal cortex surface area. Therefore, social and environmental risk factors cumulatively hinder children's brain development, and these harmful effects are especially strong for children raised in low SES families who experience high stress and reside in neighborhoods with pollutants. Even in the context of these risk factors, any unit increase in exposure to PD may result in additional deterioration of brain development in children.

In reality, many US children experience various adversities across multiple domains [70-72]. For example, many non-Hispanic

Table 2: Model fits.

	Right		Left	
	Model 1 All No Interaction	**Model 2 All M1 + Interaction**	**Model 1 All No Interaction**	**Model 2 All M1 + Interaction**
N	8,719	8,719	8,719	8,719
R-squared	0.18968	0.20086	0.19011	0.2012
ΔR-squared	0.00146	0.00177	0.14702	0.16036
ΔR-squared (%)	0.15%	0.18%	14.70%	16.04%

Table 3: Summary of mixed-effects regressions on the association between PD and children's right superior frontal cortex surface area.

	Model 1				Model 2			
	Estimate	**SE**	**P**	**Sig**	**Estimate**	**SE**	**P**	**Sig**
Perceived Discrimination (1-7)	-79.05304	22.13936	0.0003579	***	-20.03908	35.24444	0.5696599	
Race								
White	-							
Black	-386.21987	35.24767	<0.001	***	-387.39766	35.24965	<0.001	***
Asian	-405.34987	65.30782	<0.001	***	-407.33014	65.30711	<0.001	***
Other/Mixed	-143.49157	27.63994	<0.001	***	-143.11902	27.63876	<0.001	***
Sex (Male)	706.44995	18.27638	<0.001	***	817.78907	54.88221	<0.001	***
Age (Month)	2.1434	1.18908	0.0714912	.	2.11833	1.18874	0.0747847	.
Married Family	26.73602	25.57244	0.2958204		26.4756	25.57169	0.3005352	
Parental Education								
Less than High School								
HS Diploma/GED	-7.52387	63.34861	0.9054608		-7.71594	63.34402	0.9030522	
Some College	47.11017	58.49551	0.4206317		46.99441	58.49146	0.4217422	
Bachelor	109.24075	61.94113	0.0778307	.	108.0121	61.93959	0.0812241	.
Post Graduate Degree	166.56452	62.66971	0.0078793	**	166.46992	62.66573	0.0079107	**
Household Income								
<50K								
≥100K	96.63388	35.73591	0.0068621	**	96.7895	35.73421	0.0067701	**
≥50K& < 100K	23.42004	31.02664	0.4503676		23.22221	31.02504	0.4541796	
Hispanic	-176.42459	30.43736	<0.001	***	-176.75674	30.43569	<0.001	***
Neighborhood Poverty	-2.68703	1.02149	0.0085409	**	-2.69903	1.02144	0.0082475	**
Neighborhood Lead Risk	10.24332	4.83165	0.0340306	*	10.288	4.83151	0.033253	*
Neighborhood NO_2	12.73061	13.71072	0.353166		13.14877	13.71101	0.3375885	
Neighborhood PM25	-9.73848	8.56306	0.2554586		-9.68434	8.56269	0.2580896	
Stressful Events (Any)	-3.20034	19.91874	0.8723574		-3.13975	19.9157	0.8747345	
Financial Stress (Any)	-52.95403	27.06217	0.0504083	.	-52.80719	27.06004	0.0510318	.
Body Mass Index (BMI)	8.53665	2.49895	0.0006382	***	8.47067	2.49866	0.0007018	***
Perceived Discrimination (1-7) × sex (Male)					-94.52963	43.94135	0.0314825	*

#p<0.1; *p<0.05; **p<0.01; ***p<0.001.

Black children are more likely to be a member of a low SES family, experience financial stress, reside in poor urban areas with high pollutants, and experience high levels of PD [73]. The cumulative nature of risk requires us to reduce exposures to PD and other risk factors in order to eliminate disparities in the brain development of all US children.

PD takes a toll on children's brain development. High levels of PD may also explain why we observe different levels of brain function and structure across socially privileged and marginalized groups. The harmful effect of PD and interpersonal racial discrimination is well known [16,74]. This effect asserts that group differences in brain development and cognitive performance are partly due to modifiable social factors (PD, stress, and pollutants) rather than genes or biological differences. These differential exposures to risk factors place low-SES and racial minorities at a relative disadvantage across multiple domains. However, to reiterate, this variation across social groups should not be attributed to fixed biological variation (i.e.,

Table 4: Summary of mixed-effects regressions on the association between PD and left superior frontal cortex surface area.

	Model 1				Model 2			
	Estimate	**SE**	**P**	**Sig**	**Estimate**	**SE**	**P**	**Sig**
Perceived Discrimination (1-7)	-85.85595	21.84397	8.55E-05	***	-33.81147	34.77083	0.3308742	
Race								
White								
Black	-398.77184	34.83812	<0.001	***	-399.79429	34.83939	<0.001	***
Asian	-329.82925	64.52616	<0.001	***	-331.56455	64.52569	<0.001	***
Other/Mixed	-109.77969	27.31664	<0.001	***	-109.45182	27.31499	<0.001	***
Sex (Male)	734.43701	18.04318	<0.001	***	832.62764	54.15138	<0.001	***
Age (Month)	1.57986	1.17271	0.1779542		1.55823	1.17251	0.1838924	
Married Family	36.74132	25.27642	0.1460986		36.51364	25.27498	0.1485906	
Parental Education								
Less than High School								
HS Diploma/GED	-45.0198	62.60178	0.4720704		-45.17029	62.5965	0.4705534	
Some College	4.39701	57.80771	0.939371		4.29991	57.80293	0.9407024	
Bachelor	58.01885	61.21459	0.3432605		56.94475	61.21213	0.3522491	
Post Graduate Degree	111.02641	61.93531	0.0730686	.	110.95803	61.93035	0.0732225	.
Household Income								
< 50K								
≥100K	88.55307	35.32091	0.0121907	*	88.69124	35.3184	0.0120504	*
≥50K& < 100K	37.57488	30.66448	0.2204745		37.40882	30.66226	0.2224873	
Hispanic	-185.63176	30.09128	<0.001	***	-185.91809	30.08908	<0.001	***
Neighborhood Poverty	-2.86265	1.00975	0.0045931	**	-2.87338	1.00968	0.0044402	**
Neighborhood Lead Risk	12.5925	4.77705	0.0084028	**	12.63138	4.77676	0.0081997	**
Neighborhood NO_2	17.63121	13.65035	0.1965192		18.00446	13.64967	0.1871905	
Neighborhood PM25	-18.18536	8.50934	0.0326171	*	-18.14113	8.50838	0.0330225	*
Stressful Events (Any)	-18.87319	19.67164	0.3373785		-18.82553	19.66916	0.3385387	
Financial Stress (Any)	-49.91857	26.7408	0.0619692	.	-49.79166	26.73849	0.0626126	.
Body Mass Index (BMI)	11.83751	2.46731	<0.001	***	11.78088	2.46712	<0.001	***
Perceived Discrimination (1-7) × sex (Male)					-83.37202	43.35195	0.05	*

#p<0.1, *p<0.05, **p<0.01, ***p<0.001.

determinist view) [75].

Study Limitation

Our study had a few methodological limitations. First, given the cross-sectional design of this study, we cannot determine causal associations between PD and brain development. While we controlled for a wide range of SES indicators, other factors such as parental occupation, family wealth, physical health, psychiatric conditions, and learning disabilities were omitted confounders. Furthermore, the sample was not random, and consequently, the results are not representative or generalizable. Lastly, this study included all racial and ethnic groups, and the studied links may differ for non-Hispanic Black and White children. Therefore, future research should compare diverse racial and ethnic groups of children for the association between PD and brain development.

Future Directions

This study provides preliminary results on the association between PD and brain development. Future research may test the additive, sub-additive, and multiplicative effects of race, ethnicity, sexual and gender minority status, and PD on brain development. Research may also test how PD changes exposure and vulnerability to other types of stress in childhood. Similar tests should also be run to explore these results in relation to other brain structures and networks. Future researchers may also use instrumental variables in order to address the problem of indigeneity and residual confounding variables.

Conclusion

Higher levels of PD are linked to lower levels of right and left superior frontal cortex surface area in 9/10-year-old children, an association that can be detected above and beyond SES, neighborhoods, stress, and environmental toxins/pollutants. The impact of PD varies between male and female children, exemplified by differences in the surface area of their respective superior frontal cortexes. High PD is more strongly associated with less superior frontal cortex surface area in male children than female children.

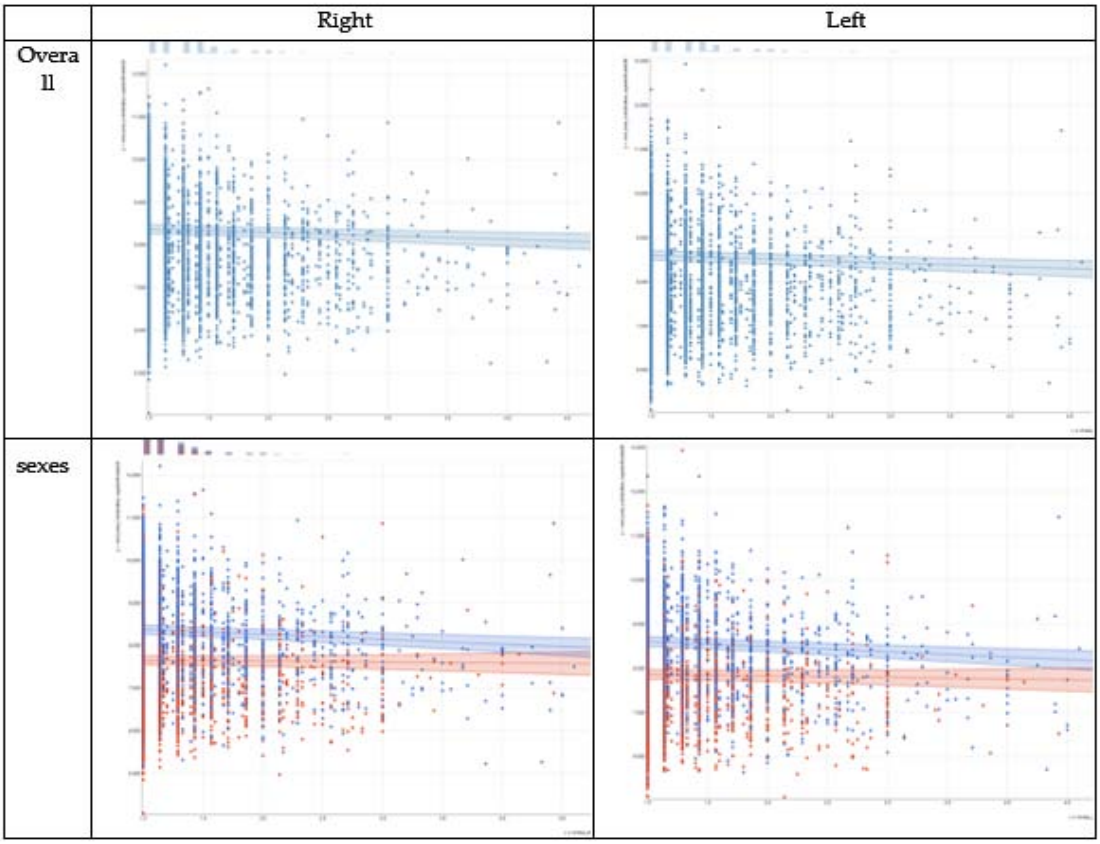

Figure 1: Association between PD and left superior frontal cortex surface area in 9/10-yr-old children.

Reducing PD (through enforcing anti-discriminatory policies) is necessary to reduce disparities in children's brain development. Particular attention should be given to males and members of social groups who commonly face discrimination (e.g., Blacks).

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