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Research Paper: Sex Differences in the Association of Household Income with Amygdala Volume

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ABSTRACT

Background: Household income and other socioeconomic position (SEP) indicators are among the most salient social determinants of children's emotions and behaviors. Some research has shown that income and other SEP indicators may have certain sex-specific effects on the structures and functions of particular brain regions.

Objectives: To investigate sex differences in the association of household income with amygdala volumes in US children.

Materials & Methods: This is a cross-sectional study using data from the Adolescent Brain Cognitive Development (ABCD) study. The study data was collected between 2016 and 2018 across 21 sites distributed across US states. Wave 1 ABCD included 10262 American children aged between 9 and 10 years old. The independent variable was household income. The primary outcome was the left amygdala volume, which was measured by T1-weighted structural brain Magnetic Resonance Imaging (MRI). We used a data exploration and analysis portal for our data analysis.

Results: Overall, the household income was positively associated with left amygdala size in children. Sex showed a statistically significant interaction with household income on children's left amygdala volume, net of all confounders, indicating a stronger effect of high household income on male children compared to female children.

Conclusion: Household income is a more salient determinant of left amygdala volume for male children compared to female American children. Low-income male children remain at the highest risk of a small amygdala.

Keywords: Amygdala, Magnetic Resonance Imaging, Brain imaging, Socioeconomic status, Children, Sex

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Highlights

- The higher household income is associated with a larger volume of left amygdala.

- Sex may alter the influence of income on the left amygdala size of children. Income may be more influential on the left amygdala volume of boys than girls.

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1. Introduction

Household income and other socioeconomic position (SEP) indicators are among the most salient social determinants of children's emotions and behaviors [1-3]. Among all SEP indicators, household income is one of the most influential indicators [4-7]. Children from high-income families receive high levels of protective parenting, which boosts their outcomes across domains [8-12]. Some effects of household income on children's positive behavioral and emotional outcomes [4-7] are due to lower levels of stress and adversities typical of high-income families [13-15]. Income also partially explains some of the racial and ethnic parameters in children's behavioral outcomes [16-19]. As a result, higher-income may be a solution to eliminate social inequalities in children outcomes across social groups [20, 21].

Income, however, may have health effects across subgroups. In the presence of differential effects, income can become a source, rather than a solution to health inequalities [22-25]. In this case, any intervention to manipulate income has the risk of widening an existing gap [26], partly because the same research has suggested that any socially marginalized group shows weaker effects of income on health and behaviors [26-30].

Some research has shown that income and other SEP indicators may have certain sex-specific effects on the structures and functions of brain regions [31]. Javanbakht et al. [32] and Kim et al. [33] found that household income had larger effects on the brain function of female children than male children. Whittle and colleagues [34] and Mcdermott and colleagues [35] showed that boys were more sensitive than girls to environmental inputs such as income and parenting. Javanbakht et al. reported a larger effect of parenting on the amygdala volume of females than males [32]. Thus, while sex differences in the effects of income on brain development are likely, the direction of these sex differences are still inconsistent. As the literature is not conclusive, more research is needed on this topic.

In this investigation, we compared male and female American children (9-10 years old) for the effects of household income on their left amygdala volumes. While high household income was expected to be associated with large left amygdala volume, this effect is expected to be more salient for males than females. In line with the results reported by Whittle and colleagues [34] and Mcdermott and colleagues [35], male sex is expected to be associated with a higher vulnerability to environmental inputs, including but not limited to income and other SEP indicators.

2. Materials and Methods

This cross-sectional study was a secondary analysis of existing data. We borrowed data from the Adolescent Brain Cognitive Development (ABCD) study [36-40]. ABCD is a national children's brain development study with broad diversity based on race, ethnicity, sex, and SEP [36, 41].

Participants were recruited from multiple cities across various states in the US. This sample was enrolled through the US school system. The recruitment catchment area of ABCD, which was composed of 21 participating sites, encompasses over 20% of the entire United States population of 9- to 10-year-old children. ABCD applied a carefully designed sampling and recruitment process across various sites, described elsewhere [36, 37, 39, 41-56], to ensure that the sample is random and representative. Such local randomization efforts yielded a final overall ABCD sample that is a close approximation to the national sociodemographic factors. These sociodemographic factors include race, ethnicity, age, sex, SEP, and urban city.

The SEP target in ABCD has two sources: 1) the American Community Survey (ACS), and 2) annual 3rd- and 4th-grade school enrollment. A full description of the ABCD sample and sampling is published here [57]. The first is a large-scale survey of approximately 3.5 million households conducted annually by the US Census Bureau. The second data is maintained by the National Center for Education Statistics (NCES), which is affiliated with the US Department of Education.

Analytical sample

This study included 10262 children of 9-10 years old whose data on income and amygdala volume were available. Children from any race or ethnicity were included.

Outcome

Amygdala volume

The volume of the left amygdala was the outcome. For calculation of morphometry of brain structures such as amygdala, only MRI and computer were used. No human was involved in the morphometric calculation of the amygdala size [37]. This variable was treated as a continuous measure (in mm^2), and a higher score indicates a larger amygdala.

Although both functional (f)MRI and structural (s) MRI data were available, this analysis only used the sMRI data on the morphometry of the amygdala. As different MRI devices were utilized in this national study, we controlled for the MRI device. Casey et al. have described the MRI processes in detail. Building upon the efforts of these big data studies has led to the establishment of an optimized MRI acquisition protocol to measure brain structure and function that is harmonized to be compatible across three 3-tesla (T) scanner platforms: Siemens Prisma, General Electric 750, and Phillips at 21 sites [37]. To minimize the noise in the data, and maximize effective harmonization, a rigid protocol was used for MRI. Real-time motion detection and correction for the structural scans are implemented by the ABCD DAIC hardware and software. Besides, a real-time head motion monitoring system called FIRMM (fMRI Integrated Real-time Motion Monitor) (www.firmm.us) [58] collaboratively developed at Washington University, St. Louis and Oregon Health Sciences University was implemented for motion detection in resting-state fMRI scans at the Siemens sites [59]. Finally, to minimize head motion, the head was stabilized with foam padding around headphones/earbuds. As such, the technologist localizes the head position and ensured that the child can fully view the screen. As the scanner table moved to the center of the scanner bore, a child-appropriate movie was played and the staff made sure the child could see and hear it.

The volumes of 116 brain regions of interest (ROIs) were defined according to the SRI24 atlas [60]. Measuring the volumes of ROIs consisted of non-rigidly registering the SRI24 atlas to each brain-size corrected MRI via ANTS (Version: 2.1.0) [61, 62] and overlaying parcellations with the tissue segmentations from Atropos [63]. Volumetric segmentation of the brain was performed using FreeSurfer software, version 5.3.0 (Harvard University). Size, surface, and volume of various cortical and subcortical structures of the brain were calculated by parcellation and the use of standard brain atlas and ROI classifications that are widely used and accepted. All these data are freely available within the data release [59].

Independent variable

Household income

Household income was a three-level categorical measure. The item used to measure household income was "What is your total combined household 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." Responses included less than $50000 (reference category), $50000-100000, and $100000 or more.

Moderator

Sex: Regarding sex, 1 for males and 0 for females, was a dichotomous variable. This variable was the effect of the modifier.

Confounders

Race, ethnicity, age, parental marital status, and parental educational attainment were the confounders.

Race: Race, a self-identified variable, was a categorical variable, composing of Black, Asian, Mixed/Other, or White (reference group).

Ethnicity: Ethnicity was also a self-identified variable and a categorical variable, composing of Hispanics vs. non-Hispanics (reference category).

Age: Parents reported the age of the children. This variable was calculated in months.

Parental education: Parental education was asked using this item: "What is the highest grade or level of school you have completed or the highest degree you have received?" Responses were as follows: less than a high school diploma (reference category), high school diploma, some college, college degree, and graduate-level education.

Parental marital status: The household's marital status was a dichotomous variable: married=1 and non-married=0.

Data analysis

We used the data exploration and analysis portal (DEAP) for our data analysis. DEAP is an online platform that uses R statistical package to analyze the ABCD data. To conduct multivariable analysis, two mixed-effects regression models were performed. We adjusted for the nested nature of the data as participants were nested to MRI devices, families, and study sites. The left amygdala volume was the outcome. Household income, a three-level categorical variable, was the predictor. Sex was the moderator. Age, race, ethnicity, household income, parental education, and family marital status were confounders. Family and MRI machine were also controlled. Appendix 1 shows our model formulas. Both regression models were estimated in the overall/pooled sample. Model 1, the main effect model, was estimated in the absence of the household income by sex interaction term. Model 2 (the interaction model) added an interaction term between sex and household income. Regression coefficient (B), standard error, 95% t value, and P values were reported for each model.

Ethical aspect

For this study, we used a fully de-identified data set. As such, the study was non-human subject research. This study was exempted from a full review Institutional Review Board (IRB). However, the protocol of the main study, the ABCD, was approved by the IRB at the University of California, San Diego (UCSD), and several other institutions. The participants signed consent or assent depending on their age [41].

3. Results

Descriptives

Table 1 presents the summary statistics of the pooled/overall sample. The current analysis was performed on 10262 children (9-10 years old) of whom 52.3% were boys and 47.7% girls. Males had larger amygdala volume.

Overall multivariate analysis

Table 2 summarizes the results of two linear regression models in the overall (pooled) sample. Model 1 (main effect model) showed a positive relationship between household income and amygdala volume. Model 2 (interaction model) showed an interaction term between sex and household income on amygdala volume, suggesting that the effect of household income on amygdala volume was stronger for male than female children.

4. Discussion

Our findings showed that sex alters the effect of household income on amygdala volume in a national sample of American children, with a stronger effect being observed for males than female American adolescents.

Environmental input, including variation in SEP, may have some sex-specific effects on brain structure and function [31]. Javanbakht showed SEP effects on the amygdala of females but not males [32]. A study by Kim et al. found that household income was associated with an increase in the structural brain network efficiency of females aged 6-11 years, but not in male children in the same age group [33]. The study by Whittle and colleagues showed that boys were more sensitive than girls to a variation in environmental inputs such as positive caregiving and parenting. They showed that positive parenting and caregiving better predict the volumetric growth of the amygdala and the cortical thinning of the right anterior cingulate for boys than girls [34]. Mcdermott and colleagues also showed a stronger positive relationship between SEP and cortical surface area for males than females [35].

Thus, although sex differences are reported in the effects of SEP indicators such as household income on brain volume across essential developmental phases such as early to late adolescence, the direction of these sex differences is inconsistent. It is during adolescence that sex differences in brain and behavior may emerge or intensify [64].

A recent study tested whether biological sex shows any statistical interaction with income to explain brain morphology and volume across brain structures in a cross-sectional and longitudinal way. While on the whole, income affects cortical gray matter areas, including the cortex and sensorimotor processing areas, these effect sizes were more significant in males than in females. As such, biological sex should be regarded as an essential variable, more salient than a control variable. Thus the

Table 1. Descriptive data overall and by sex

Variables		All	Female	Male	P
N	Level	10262	4899	5363	
Left amygdala volume, Mean±SD		1570.10±231.89	1492.78±206.47	1640.72±231.33	<0.001
Household income (%)	[<$50 K]	2948 (28.7)	1429 (29.2)	1519 (28.3)	0.616
	[>=$100 K]	4373 (42.6)	2069 (42.2)	2304 (43.0)	
	[>=$50 K & <$100 K]	2941 (28.7)	1401 (28.6)	1540 (28.7)	
Race (%)	White	6832 (66.6)	3217 (65.7)	3615 (67.4)	0.256
	Black	1482 (14.4)	733 (15.0)	749 (14.0)	
	Asian	221 (2.2)	112 (2.3)	109 (2.0)	
	Other/Mixed	1727 (16.8)	837 (17.1)	890 (16.6)	
Parental Education (%)	<HS Diploma	374 (3.6)	188 (3.8)	186 (3.5)	0.619
	HS Diploma/GED	850 (8.3)	396 (8.1)	454 (8.5)	
	Some College	2637 (25.7)	1238 (25.3)	1399 (26.1)	
	Bachelor	2712 (26.4)	1293 (26.4)	1419 (26.5)	
	Post Graduate Degree	3689 (35.9)	1784 (36.4)	1905 (35.5)	
Married family (%)	No	3119 (30.4)	1527 (31.2)	1592 (29.7)	0.107
	Yes	7143 (69.6)	3372 (68.8)	3771 (70.3)	
Age (y), Mean±SD		118.97±7.47	118.80±7.44	119.13±7.49	0.023
Hispanic (%)	No	8321 (81.1)	3980 (81.2)	4341 (80.9)	0.719
	Yes	1941 (18.9)	919 (18.8)	1022 (19.1)	

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studies should go beyond controlling for sex and income if the interest is to study functional and structural neurodevelopment during adolescence [65].

For example, the effects of environmental risk factors such as income and other SEP markers depend on the nature of ongoing neurodevelopmental processes [66]. We already know that neurodevelopment is sexually dimorphic. For example, while some brain regions develop faster in males, others may tend to develop faster in girls [64, 67, 68]. Thus, sex differences in neurodevelopment [31, 64, 67, 68] and vulnerability to environmental exposures [34, 69, 70] may explain our findings.

Gender differences and various social experiences of males and females may also explain these findings. While sex differences are attributed to brain structure or function, sex differences may be caused by social networks, culture, norms, parents, and friends. It is possible that parenting of boys and girls are widely different across SEP levels. SEP likely has a more substantial impact on boys' brain development or behavioral coping than girls. Boys of high- vs. low-income families likely show a larger difference in exposure and response to stress and stimuli. High- and low-income girls may be less different in the level of parenting, stress, peers, and social risk. It is plausible that for males, the level of the risk of the peers and social network widely varies across

Table 2. Summary of the effect of household income on amygdala volume by sex

Variables		B	SE	t	P	Sig.
Model 1	Household income [≥$ 50 K & <$100 K]	23.67727	6.87591	3.44	0.0005765	* * *
	Household income [≥$100 K]	35.14168	7.66025	4.59	0.000045	* * *
Model 2	Household income [≥ $50 K & <$100 K]	19.87162	9.03332	2.20	0.0278423	*
	Household income [≥ $100 K]	20.71412	9.35860	2.21	0.0268936	*
	Sex (Male)	133.02916	7.81496	17.02	0.000001	* * *
	Household income [≥$50 K & <$100 K] Sex (Male)M	7.31207	11.13755	0.66	0.5115016	
	Household income [≥$100 K] x Sex (Male)	27.41879	10.19432	2.69	0.0071651	* *

*P<0.05, **P<0.01, ***P<0.001.

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the SEP spectrum. However, this variation is smaller for females.

How parents socialize or monitor their boys and girls widely varies [71-73]. The influence of peers also varies for boys and girls [74]. Coping mechanisms may also differ between males and females [75]. These differences may explain why boys and girls show differential effects of income on their amygdala volume.

It is likely that SEP better alters the parenting or the level of risk of the peers for boys than girls. That means, variation in the level of parenting and peers may be smaller for girls, and this variation may show a smaller impact of parental SEP. As a result, for girls, SEP may not similarly change the behavioral outcomes in no small degree. An explanation is lower variance and average of behavioral problems of females than male children. Girls' levels of behavioral problems may stay low and unaltered despite high or low SEP. For boys, however, behavioral problems are typically higher, but they would be SEP's function. Such behavioral problems would be low at high SEP and are high at low SEP. At the same time, we cannot expect the highest risk in low SEP girls; we would expect the worst level of behavioral problems in low SEP boys.

Another potential explanation is that boys' and girls' social experiences differ as peers, parents, teachers, and society may differently respond to a change in SEP for boys and girls. As suggested by several theories [76, 77], equal SEP indicators such as income can generate unequal outcomes across diverse demographic groups.

Sex differences are not specific to an age group (children), a SEP indicator (income), or a behavioral outcome (amygdala volume). This means that sex differential effects of a wide range of SEP indicators on many outcomes have been documented for children, adults, and older adults. Among adults, many studies have shown stronger health effects of income and other related SEP indicators for males than females [78-83].

We argue that studies on behaviors or development should not merely control for sex. This is particularly true for studies investigating how SEP indicators shape neural, behavioral, and social development of diverse groups of children. Most research has traditionally "controlled" for the statistical effect of sex. Researchers should be aware that sex may also alter SEP indicators' effect on behaviors and brain function and development.

Additional research is needed on parental, social, psychological, and even biological mechanisms that may explain why child gender or sex interfere with SEP indicators such as income on amygdala volume. According to the social reproduction theory, parental SEP may differently impact children's developmental and behavioral outcomes across social groups [84]. Also, not only sex but the intersection of sex, race, place, and class may also shape the outcomes of children in the US [85]. These results, however, require further research.

One limitation of this study is its cross-sectional design. This study only investigated sex differences in the effects of one SEP indicator, namely household income. It is unknown if there are differential marginal returns of other SEP indicators by sex. Future research may test the effects of wealth, parental education, parental marital status, employment, and even higher-level SEP indicators such as neighborhood SEP by sex. Future research may study biology and social processes to explain why household income influences male and female children differently. Some social processes may be peer influences, norms, expectations, parenting, and sex hormones.

5. Conclusions

Males show a stronger influence of high household income on amygdala volume than females. This means that girls from high- vs. low-income families would have more similar amygdala volume than boys from high- vs. low-income families. In other words, sex and SEP interact on brain development (e.g., amygdala volume).

Ethical Considerations

Compliance with ethical guidelines

This analysis was exempt from a full IRB review (IRB Net Number=1665000-1). Charles R. Drew University of Medicine and Science (CDU) does not provide a number for the exempt letters.

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Authors contributions

Conceptualization, formal analysis, writing the original draft preparation, writing, review and editing, funding acquisition, and approval of the final version of the manuscript: Shervin Assari.

Conflict of interest

The author declared no conflict of interest.

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Appendix 1. Formula used for study models

Model No.	Expressions
1	sMRI_vol_subcort.aseg_amygdala.lh ~ household.income.bl+race.4level+sex+high.educ.bl+married.bl+age+hisp Random: ~ (1|rel_family_id)
2	sMRI_vol_subcort.aseg_amygdala.lh ~ household.income.bl+race.4level+sex+high.educ.bl+married.bl+age+hisp+household.income.bl * sex Random: ~ (1|rel_family_id)

CJNS