

Protective Prevention Effects on the Association of Poverty With Brain Development

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IMPORTANCE This study was designed to determine whether a preventive intervention focused on enhancing supportive parenting could ameliorate the association between exposure to poverty and brain development in low socioeconomic status African American individuals from the rural South.

OBJECTIVE To determine whether participation in an efficacious prevention program designed to enhance supportive parenting for rural African American children will ameliorate the association between living in poverty and reduced hippocampal and amygdalar volumes in adulthood.

DESIGN, SETTING, AND PARTICIPANTS In the rural southeastern United States, African American parents and their 11-year-old children were assigned randomly to the Strong African American Families randomized prevention trial or to a control condition. Parents provided data used to calculate income-to-needs ratios when children were aged 11 to 13 years and 16 to 18 years. When the participants were aged 25 years, hippocampal and amygdalar volumes were measured using magnetic resonance imaging.

EXPOSURES Household poverty was measured by income-to-needs ratios.

MAIN OUTCOMES AND MEASURES Young adults' whole hippocampal, dentate gyrus, and CA3 hippocampal subfields as well as amygdalar volumes were assessed using magnetic resonance imaging.

RESULTS Of the 667 participants in the Strong African American Families randomized prevention trial, 119 right-handed African American individuals aged 25 years living in rural areas were recruited. Years lived in poverty across ages 11 to 18 years forecasted diminished left dentate gyrus (simple slope, -14.20 ; standard error, 5.22 ; $P = .008$) and CA3 (simple slope, -6.42 ; standard error, 2.42 ; $P = .009$) hippocampal subfields and left amygdalar (simple slope, -34.62 ; standard error, 12.74 ; $P = .008$) volumes among young adults in the control condition (mean [SD] time, 2.04 [1.88] years) but not among those who participated in the Strong African American Families program (mean [SD] time, 2.61 [1.77] years).

CONCLUSIONS AND RELEVANCE In this study, we described how participation in a randomized clinical trial designed to enhance supportive parenting ameliorated the association of years lived in poverty with left dentate gyrus and CA3 hippocampal subfields and left amygdalar volumes. These findings are consistent with a possible role for supportive parenting and suggest a strategy for narrowing social disparities.

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More than 1 in 5 children in the United States live in poverty.¹ Poverty and other markers of disadvantage are powerful variables that forecast developmental trajectories, including cognitive development,² psychosocial development,³ and physical health⁴ throughout life. As interest in the effects of poverty and disadvantage has surged in the pediatric research community, a parallel literature has been developing in which scientists have begun to investigate the possibility that growing up in poverty, where stressors are common and resources are scarce, will have implications for the maturation of the hippocampus and amygdala. These temporal lobe structures contribute to various facets of academic functioning and social development, and they support learning, memory, mood, and stress reactivity.⁵ Despite the importance of the hippocampus and amygdala to mental and physical health across the lifespan,⁶ little is actually known about the ways in which childhood exposure to poverty is associated with their development.

Reports from initial investigations show diminished hippocampal volumes among children living in poverty.⁷⁻¹² These reports mirror findings from animal models, which show hippocampal cell proliferation and neurogenesis to be greater among mice and rats reared in stimulating environments compared with those reared in relative deprivation.¹³ Results are less clear for the amygdala. Childhood poverty has been found to be associated with both larger¹¹ and smaller^{9,10} amygdalar volumes, and findings from animal models typically show associations between exposure to chronic stress and larger amygdalar volumes.¹⁴

Taken together, these findings underscore the need for further investigations of the association between childhood exposure to poverty and the development of the hippocampus and amygdala across time. The current study was designed to address this issue using a longitudinal, prospective design to determine whether duration of life in poverty across ages 11 to 18 years was associated with whole and subfield hippocampal volumes and amygdalar volumes at age 25 years. Translational studies show that the key consequences of stress exposure for the hippocampus are suppression of neurogenesis in the dentate gyrus (GCL) and dendritic remodeling in the CA3 subfield.^{15,16} In children, exposure to stress is also associated with smaller volumes in these subfields.^{17,18} Thus, this study examined the hypothesis that exposure to poverty would be associated with smaller volumes in the whole hippocampus, the GCL and CA3 hippocampal subfields, and the amygdala.

However, not all children and adolescents who grow up in poverty experience adverse consequences. Recent research suggests that a subset of youths who receive supportive parenting develop resilience to the consequences of poverty and low socioeconomic status environments. Studies show that parenting that includes high levels of warmth, sensitivity, and emotional support can offset many of the psychosocial disadvantages that beset children in poverty.^{19,20} Mounting evidence also reveals that supportive parenting can favorably mold stress-response tendencies among vulnerable children.²¹ In fact, supportive parenting may help mitigate some of the hormonal, metabolic, and cardiovascular changes that follow childhood adversity. In particular, supportive parenting buf-

Key Points

Question Can participation in a parenting-focused intervention program for children aged 11 years ameliorate the association between childhood poverty and brain development in adulthood?

Findings In this secondary analysis of data from the Strong African American Families randomized clinical trial, childhood poverty was associated with diminished volume of brain limbic regions in adulthood. The parenting-focused intervention was associated with attenuations in risk for poverty and reduced brain development.

Meaning The findings are consistent with a possible role for supportive parenting in brain development and suggest a strategy for narrowing social disparities.

fers the effects of poverty on adolescents' allostatic load, a measure of cardiometabolic risk.²² Such parenting also buffers the effects of low childhood socioeconomic status on proinflammatory signaling profiles²³ and metabolic profiles in adulthood.²⁴ Similarly, the benefits of supportive parenting may extend to hippocampal and amygdalar development, as vividly illustrated in a recent series of studies.²⁵⁻²⁷ Among children reared in poverty, those who received supportive parenting had larger hippocampal volumes than those who received parenting that was not as supportive.

These are important findings. To the extent that they reflect a causal process in which supportive parenting offsets some of the risks to brain maturation associated with poverty, these findings have implications for numerous pediatric research domains, including those focused on social disparities and resilience to adversity.²⁸ However, causal inferences cannot easily be made on the basis of existing studies because their observational designs are prone to residual confounding and reverse causal influences. Here, we avoid those problems by conducting secondary analyses of data from the Strong African American Families (SAAF) program, a randomized clinical trial.¹⁹ The SAAF program was designed to mitigate the negative effect of life stress on rural African American youths by increasing supportive parenting processes.²⁹ The program has demonstrated stress-buffering capacities for a range of psychosocial outcomes, such as self-control, drug use, and conduct problems.³⁰ It also has favorable effects on several health-relevant biological processes, including inflammation, catecholamine levels, telomere lengths, and epigenetic aging,³¹ all of which could, in turn, influence patterns of brain development.⁵ Accordingly, in this study, we tested the hypothesis that the cumulative number of years during which African American youths lived in poverty across preadolescence and adolescence would be associated with diminished volumes in the whole hippocampus, the GCL and CA3 hippocampal subfields, and the amygdala among young adults who had been randomly assigned to the control condition but not young adults who had been assigned to the SAAF condition.

In summary, in this study, analyses were performed on data gathered from rural African American youths and their primary caregivers who had taken part in the SAAF randomized prevention trial when the youths were aged 11 years. When

Table 1. Characteristics of Participants With and Without Brain Imaging Data at Age 11 Years

Characteristic	Mean (SD)				ANOVA	P Value
	With Brain Imaging Data		Without Brain Imaging Data			
	SAAF (n = 59)	Control (n = 57)	SAAF (n = 310)	Control (n = 241)		
Male, proportion	0.46 (0.50)	0.51 (0.50)	0.46 (0.50)	0.48 (0.50)	0.092 ^a	.76
Parent age, y	37.15 (8.70)	37.25 (5.91)	37.81 (7.59)	37.89 (7.78)	0.000 ^a	.99
Family poverty, proportion	0.47 (0.50)	0.37 (0.49)	0.39 (0.49)	0.34 (0.48)	0.329 ^a	.57
Parent education, y	4.53 (1.17)	4.61 (1.13)	4.57 (1.33) ^b	4.73 (1.50)	0.080 ^c	.78
Parent unemployment, proportion	0.24 (0.43)	0.11 (0.31)	0.24 (0.43) ^d	0.22 (0.41)	1.614 ^e	.20
Single-parent family, proportion	0.71 (0.46) ^f	0.58 (0.50)	0.55 (0.50) ^g	0.54 (0.50)	1.150 ^h	.28
Intervention sessions, No.	5.02 (2.47)	NA	4.64 (2.63)	NA	-1.022 ⁱ	.31
Family poverty (age 11-18 y), y	2.61 (1.77)	2.04 (1.88)	2.20 (1.85)	2.03 (1.87) ^j	1.177 ^e	.28

Abbreviations: ANOVA, analysis of variables; NA, not applicable; SAAF, Strong African American Families.

^a $F_{1, 663}$.

^b Of 307 participants.

^c $F_{1, 660}$.

^d Of 308 participants.

^e $F_{1, 661}$.

^f Of 58 participants.

^g Of 305 participants.

^h $F_{1, 657}$.

ⁱ By *t* testing (*t* [367]).

^j Of 239 participants.

youths were aged 11 to 13 years and 16 to 18 years, caregivers provided data that were used to calculate income-to-needs ratios. T1-weighted magnetic resonance imaging (MRI) data were obtained when the participants were aged 25 years to determine the volumes of their whole hippocampi, GCL and CA3 hippocampal subfields, and amygdalae.

equivalence of the demographic and study variables for participants who did or did not take part in the imaging study at age 25 years by prevention group assignment at age 11 years (Table 1). No significant main or interaction effects emerged. The University of Georgia Institutional Review Board reviewed and approved all study procedures, and all participants provided written informed consent.

Methods

Participants

A total of 119 right-handed rural African American individuals aged 25 years were recruited from the 667 participants in the SAAF randomized prevention trial. The SAAF sample was recruited randomly from rural communities in Georgia when the participants were aged 11 years (mean [SD] age at pretest, 11.2 [0.34] years²⁹). At pretest, the SAAF sample could be characterized as working poor; primary caregivers worked an average of 39.4 hours per week, yet 46.3% of the sample lived below federal poverty standards. The data collected from participants aged 25 years included 408 participants from the original SAAF sample, a retention rate of 61.2% across 14 years. Random selection of the subsample of 119 participants to take part in a neuroimaging session was made necessary by financial constraints associated with imaging.

The subsample was selected randomly from a list of the 408 participants in the age 25 years assessment until the targeted sample size was reached. All participants included in the subsample were screened for standard imaging contraindications and right-handedness prior to enrollment. Three participants were excluded because of excess motion in MRI images. The remaining 116 participants were included in the analyses. At age 11 years, 59 participants (50.9%) were assigned randomly to the SAAF condition and 57 (49.1%) were assigned randomly to the control condition. A 2-factor multivariate analysis of variance was executed to evaluate the

SAAF Intervention Implementation

The SAAF prevention program consisted of 7 consecutive, 2-hour weekly meetings held at community facilities, with separate skill-building curricula for youths and for their primary caregivers, and a family curriculum. Caregivers in the prevention condition were taught the consistent provision of instrumental and emotional support, high levels of monitoring and control, adaptive racial socialization strategies, and methods for communicating about sex and alcohol use. Youths learned the importance of forming goals for the future and making plans to attain them, resistance efficacy skills, and adaptive behaviors to use when encountering racism.

Measures

Family Poverty

When participants were aged 11 to 13 years and 16 to 18 years, caregivers provided data on their families' income-to-needs ratios, based on family size, that were used to compute household poverty. Poverty statuses at 6 assessment waves were summed to determine the number of years living below federal poverty guidelines (mean [SD], 2.30 [1.83]).

Intervention Status and Sex

Intervention status and sex were coded as follows: SAAF participants were coded 1 and control participants were coded 0, and male participants were coded 1 and female participants were coded 0.

Table 2. Family Poverty and Intervention as Predictors of Left Amygdalar, CA2/CA3, and CA4/GCL Volume at Age 25 Years

Predictors	Volume					
	Left Amygdalar		Left CA2/CA3		Left CA4/GCL	
	B (SE)	β	B (SE)	β	B (SE)	β
Sex (male)	114.129 (47.553)	.256 ^a	2.524 (9.021)	.034	6.711 (19.485)	.042
Intracranial volume (age 25 y)	90.672 (23.256)	.406 ^b	13.190 (4.412)	.359 ^c	30.976 (9.529)	.384 ^c
Intervention, SAAF (age 11 y)	32.764 (33.041)	.073	2.802 (6.268)	.038	11.091 (13.539)	.069
Family poverty (age 11-18 y)	-34.615 (12.743)	-.283 ^c	-6.420 (2.418)	-.319 ^c	-14.201 (5.222)	-.321 ^c
SAAF \times poverty	38.131 (18.704)	.213 ^a	7.019 (3.548)	.238 ^a	15.778 (7.664)	.244 ^a

Abbreviations: B, unstandardized coefficient; GCL, granule cell layer; SAAF, Strong African American Families.

^b $P < .001$.

^c $P < .01$.

^a $P < .05$.

Psychosocial Variables

At age 25 years, participants reported their frequencies of cigarette smoking and alcohol use in the past month. The response sets ranged from 0 (“not at all”) to 6 (“about 2 packs a day”) for cigarette smoking and from 0 (“none”) to 5 (“20 or more days”) for alcohol use. Because the distributions for smoking and alcohol use were skewed, a log transformation was applied to normalize the ratings. Depressive symptoms were assessed with the 20-item Center for Epidemiologic Studies Depression Scale.³² Consistent with psychometric studies of the Center for Epidemiologic Studies Depression Scale, 16 was used as the cutoff score to identify clinically significant depression.

MRI Acquisition

Imaging data were collected using the Signa HDx 3-T scanner (GE Health) at the University of Georgia Bio-Imaging Research Center. Structural imaging consisted of a high-resolution T1-weighted, fast-spoiled gradient echo scan (repetition time, 7.8 milliseconds; echo time, 3.1 milliseconds; flip angle, 20°; field of view, 25.6 cm; matrix, 256 \times 256; 160 contiguous 1-mm axial slices; voxel size, 1 mm³).

Image Analysis

Cortical reconstruction and volumetric segmentation were performed with the FreeSurfer version 5.3 image analysis suite, which is documented and freely available online for download (<http://surfer.nmr.mgh.harvard.edu/>). FreeSurfer morphometric procedures have demonstrated good test-retest reliability across scanner manufacturers and field strengths.^{33,34} The standard FreeSurfer pipeline (discussed in detail in prior publications, eg, Reuter et al³⁴) was used to process the MRI data and, specifically, to derive intracranial volume and amygdalar volumes for use in this study. Hippocampal subfield segmentation was derived using the new automated algorithm available in FreeSurfer version 6.0.³⁵ This method uses a refined probabilistic atlas built on a combination of manual annotations of the hippocampal subregions from 15 ultrahigh resolution, ex vivo images and of the neighboring subcortical structures from an independent data set of 39 in vivo, T1-weighted, 1-mm resolution MRI scans. Using Bayesian inference, the constructed atlas is used to automatically segment the hippocampal subregions. Recently published research³⁶ found the new segmentation procedure to have a high degree of test-retest and transplatform reliability across scanning

modalities (1.5-T vs 3-T scanners). Although this software enables isolation of CA4 and the granule cell layer of the GCL, these 2 subdivisions were combined in this study because they are both components of the dentate gyrus and because the ability to distinguish the molecular layer in T1-weighted images is limited.³⁵ The other regions quantified in this study, CA2 and CA3, were combined because of a lack of distinguishing T1-weighted MRI contrast. Results were blindly reviewed for surface quality, a process with well-established reliability.³⁷

Results

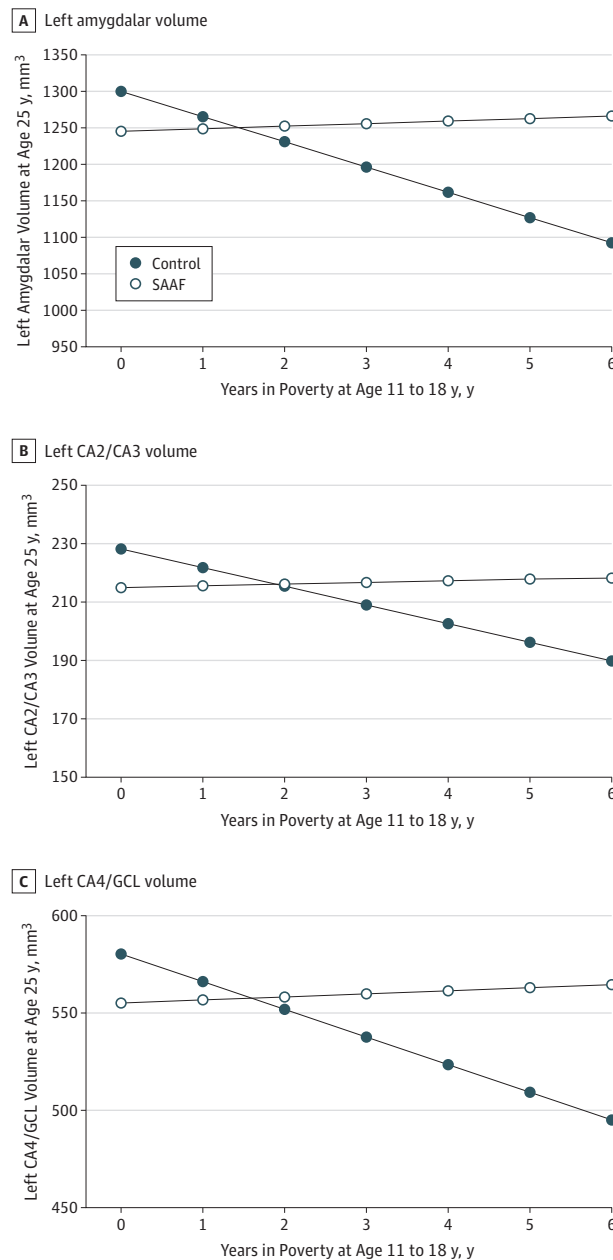
Family Poverty, the Hippocampi, and the Amygdalae

Our initial analysis was designed to determine whether family poverty was associated with hippocampal and amygdalar volumes among young adults in the control condition. Presumably, young adults in the control condition displayed normative associations between family poverty and the volumes of the hippocampi and amygdalae. Adjusted for sex and intracranial volume, the results of partial correlations between family poverty across time and the brain volumes of interest were consistent with the first study hypothesis. Control participants who spent more time in poverty evinced smaller left amygdalae ($r = -.296$; $P < .05$), left CA2/CA3 ($r = -.302$; $P < .05$), and left CA4/GCL ($r = -.300$; $P < .05$) than young adults who spent less time in poverty. Family poverty was not associated with right amygdalar, right CA2/CA3, or right CA4/GCL volume.

Participation in SAAF, Family Poverty, and Volumes of the Hippocampi and Amygdalae

Next, we tested the hypothesis that participation in SAAF would ameliorate the association of family poverty with the left amygdalar, left CA2/CA3, and left CA4/GCL volumes. To do this, we executed hierarchical multiple regression analyses that included main effects for family poverty, prevention status (SAAF = 1; control = 0), and the interaction of family poverty with prevention status. In all models, sex and intracranial volume were controlled. Interactions were interpreted through the plotting of estimated levels of hippocampal and amygdalar volumes by years in poverty and prevention status. The results of these analyses are presented in Table 2.

Figure. Effect of Family Poverty on Youths by Intervention Status



GCL indicates dentate gyrus; SAAF, Strong African American Families.

A main effect for family poverty and an interaction effect between family poverty and SAAF participation were found (Figure). More time spent living in family poverty from ages 11 to 18 years was associated with a smaller left amygdala volume (simple slope, -34.615 ; standard error [SE], 12.744 ; $P = .008$), a smaller left CA2/CA3 volume (simple slope, -6.420 ; SE, 2.418 ; $P = .009$), and a smaller left CA4/GCL volume (simple slope, -14.201 ; SE, 5.222 ; $P = .008$) among participants from the control condition. Family poverty was not associated with the volume of these regions among participants from the SAAF condition (left amygdala: simple slope, 3.516 ; SE, 13.329 ;

$P = .79$; left CA2/CA3: simple slope, 0.599 ; SE, 2.529 ; $P = .81$; and left CA4/GCL: simple slope, 1.577 ; SE, 5.462 ; $P = .77$).

To further describe the years in poverty \times SAAF interaction, we conducted planned group comparisons to test the hypothesis that adolescents who spent more years living in poverty and were assigned to the control condition would have smaller mean left amygdala volumes and left CA2/CA3 and CA4/GCL volumes than would similar youths assigned to the SAAF condition and youths who spent less time in poverty who were assigned to either the SAAF or the control condition (Table 3). The patterning of the means for each analysis conformed to the study hypothesis. Youths assigned to the control condition who spent more years during adolescence living in poverty had smaller left amygdalar and left hippocampal subfield volumes than did youths in the other 3 groups, who did not differ from one another.

Hippocampal Subfield Volumes, Amygdalar Volumes, and Psychosocial Functioning

To explore the significance of the study findings, we examined contemporaneous associations of the left hippocampal subfield volumes and left amygdalar volume with depression status, smoking, and alcohol use. To do this, we executed partial correlations and adjusted them for sex, intracranial volume, and prevention condition (SAAF or control). A score of 16 or greater on the Center for Epidemiologic Studies Depression Scale was associated with diminished left CA2/CA3 ($r, -0.245$; $P = .009$) and left CA4/GCL ($r, -0.215$; $P = .02$) volumes. Smoking was associated with diminished amygdalar volumes ($r, -0.225$; $P = .02$). No associations with alcohol use were found.

Discussion

Two important findings emerged from this study. First, we confirmed the association between childhood poverty and diminished volume of limbic regions in adulthood. These diminished volumes were significant to important outcomes, as the associations between the hippocampal subfield volumes and depression indicated. Second, we found evidence suggesting that a parenting-focused intervention during early adolescence attenuated associations between poverty and brain development. These results, made possible by the embedding of MRI assessments of hippocampal and amygdalar volumes in a parenting-focused randomized prevention trial, increases confidence in the causal nature of the linkages between supportive parenting and brain maturation. Observational research²⁵⁻²⁷ indicated that associations between living in poverty and reductions in hippocampal volume could be offset by supportive parenting processes. This study confirmed and extended those findings by demonstrating that exposure to prevention programming at age 11 years could have lasting protective effects on brain development into adulthood. Of relevance to pediatric clinical practice, efficacious family-centered programs designed to enhance supportive parenting are available for rural African American preadolescents,²⁹ adolescents,³⁰ and young adults.³⁸ Participation in these pro-

Table 3. Means of Left Amygdalar, CA2/CA3, and CA4/GCL Volume for Family Poverty by Intervention Condition Groups^a

Variables	Family Poverty × Intervention Condition Groups, Mean (SE)				ANOVA	P Value
	Low Poverty		High Poverty			
	Control (n = 35)	SAAF (n = 29)	Control (n = 22)	SAAF (n = 30)		
Left amygdalar volume	1273.62 (30.76)	1260.92 (33.70)	1160.11 (39.20)	1246.73 (33.82) ^b	5.256 ^c	.02
Left CA2/CA3 volume	223.86 (5.85)	217.13 (6.42)	201.31 (7.47)	213.80 (6.34)	4.147 ^d	.04
Left CA4/GCL volume	570.22 (12.69)	561.10 (13.91)	521.07 (16.18)	552.35 (13.74)	4.952 ^d	.03

Abbreviations: GCL, granule cell layer; SAAF, Strong African American Families.

^b Of 29 participants.

^a Low poverty was defined as 2 or less years living in poverty; high poverty, 3 or more. *F* tests refer to planned group comparisons of the high-poverty control group vs the other 3 groups. All tests controlled for sex and intracranial volume.

^c $F_{1,109}$.

^d $F_{1,110}$.

grams has demonstrated stress-buffering effects on adolescent catecholamine levels, cytokine levels, telomere lengths, epigenetic aging,³¹ and, as this report demonstrates, hippocampal subfield and amygdalar volumes.

The sample in this study was underpowered for detecting precise parenting practices that could be responsible for the buffering effects; additional research with larger samples is needed to identify specific mediators. Candidate parenting processes might include developmentally supportive emotional and instrumental behaviors and household routines, along with avoidance of harsh and coercive parenting processes. Future research should also examine the hypothesis that the SAAF program helped to ameliorate the effect of stressors common to families coping with economic hardship, such as parental depression and family conflict, both of which have implications for brain maturation.⁵ In past research, the SAAF program has been shown to decrease both of these risk factors.^{30,31}

Limitations

Several limitations of this study must be noted. First, the SAAF trial was not designed to examine change in hippocampal and amygdalar volumes. We did not assess pretrial hippocampal or amygdalar volumes; therefore, we could not determine whether the volumes in these regions changed differentially over time for members of the intervention and control groups. At study entry, the SAAF and control groups were similar in terms of family poverty, parental education, family structure, parental age, and youth sex, suggesting

that randomization worked to minimize pretrial group differences. These findings are consistent with the assumption that the groups began the trial with similar hippocampal and amygdalar volumes. Nevertheless, until pretest data become available, conclusions about the capacity of the SAAF program to influence changes in hippocampal and amygdalar volumes must be viewed as tentative. Second, only diminished left-side hippocampal subfield and amygdalar volumes were associated with poverty for control participants. The reasons for this lateralized finding currently are not clear, but these results are consistent with evidence of diminished hippocampal volumes on the left side but not the right side in adults with histories of childhood adversity.³⁹⁻⁴¹ Future research should be designed to determine whether links between exposure to poverty and lateralized hippocampal and amygdalar volumes have delayed effects that do not emerge until adulthood.⁴²

Conclusions

This study provides further evidence of the association between childhood poverty with brain development and initial evidence that a family-oriented intervention may be associated with a reduction in the effects of poverty. To the extent that they are substantiated in future research, these strategies may provide a means of narrowing social disparities.

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