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Minor Physical Anomalies: Modifiers of Environmental Risks for Psychiatric Impairment?

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ABSTRACT

Objective: To test the hypothesis that minor physical anomalies (MPAs) modify an adolescent's vulnerability to environmental risk factors for psychopathology. **Method:** One hundred eighteen unreferred male adolescents who had been evaluated as 7-year-olds received a comprehensive neuropsychiatric evaluation. The evaluation included standardized assessments of environmental risk factors for psychiatric impairment, neurological signs, IQ, MPAs, and psychiatric impairment. The relationship between psychiatric status and environmental risk was examined as a function of the MPA profile. **Results:** There was a significant interaction between MPAs and environmental risk in predicting psychiatric status. Environmental risk was more predictive of psychiatric impairment at age 17 in subjects with high scores on the MPA scale than in subjects with low scores on the scale. This relationship was particularly apparent in subjects with conduct disorder. MPAs also exhibited relationships with two childhood factors, neurological soft signs and Verbal IQ, that had been shown to predict adolescent psychopathology in prior reports on this cohort. **Conclusions:** MPAs may contribute to psychiatric impairment by influencing an individual's vulnerability to environmental risk factors for psychopathology. These suggestive findings are consistent with an emerging body of literature examining the role of biopsychosocial interactions in psychiatric disorders. *J. Am. Acad. Child Adolesc. Psychiatry*, 1997, 36(3):395-403.

Key Words: minor physical anomalies, conduct disorder, neurological soft signs.

The term "minor physical anomaly" (MPA) refers to a set of congenital malformations of the head or extremity that are characteristically associated with Down syndrome. Typical MPAs include hypertelorism, large epicanthal folds, malformed ears, a high-arched palate, or a single transverse palmar crease. Because the integument and the CNS share common embryological origins, MPAs are considered markers for CNS

maldevelopment (Firestone and Peters, 1983). Although they are attributed to both genetic and environmental factors, the exact origins of MPAs remain poorly understood, and their validity as a marker of neurological dysfunction is not firmly established (Cantor-Graae et al., 1994; Deutsch et al., 1990).

In clinical settings, a number of studies using the standardized MPA scale developed by Waldrop and Halverson (1971) found an association between elevated MPA scores and psychopathology in children. As reviewed elsewhere, MPAs are associated with various psychiatric disorders in the clinic but are found most consistently with disruptive, pervasive developmental, and psychotic disorders (Cantor-Graae et al., 1994; Deutsch et al., 1990; Pomeroy et al., 1988).

In contrast to clinic samples, associations between MPAs and psychopathology are not consistently found in nonreferred samples. Waldrop and Halverson (1971) did find a longitudinal association in a community-based sample between neonatal MPAs and disruptive behavior in boys or shyness in girls at age 7, but three subsequent prospective studies using similar designs

Accepted March 7, 1996.

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Portions of this manuscript were presented at the Annual Meeting of the American Academy of Child and Adolescent Psychiatry, New York, 1994.

This project was supported by NIMH grants MH 30606-01-03, 2T01-MH-07715-19, and T32-MH-16434-04; a grant from the Lowenstein Foundation; NIMH Research Training Grant MH-16432; and NIMH Center Grant MH-43878 to the Center to Study Youth Anxiety, Suicide, and Depression.

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0890-8567/97/3603-0395\$03.00/0©1997 by the American Academy of Child and Adolescent Psychiatry.

found weak and mostly nonsignificant associations (Burg et al., 1980; Jacklin et al., 1980; Quinn and Rapoport, 1974). There are also inconsistent findings in cross-sectional, school-based studies. Some researchers reported that MPAs are associated with high ratings on scales measuring behavior problems or psychiatric impairment (Fogel et al., 1985; Gillberg et al., 1983; Halverson et al., 1976; O'Donnell et al., 1979). Other investigators, however, found either inconsistent or no relationships in these areas (Firestone et al., 1976; Rosenberg and Weller, 1973; Sandberg et al., 1980).

While various factors could account for the more consistent findings in this area among clinically referred than community-based samples, sampling variability may be particularly important (Cohen and Cohen, 1984). This may be especially true if associations between MPAs and psychopathology are moderated by factors associated with psychiatric referral. Further studies in nonreferred samples might resolve the inconsistencies.

Beyond the direct association of MPAs with psychopathology, there is interest in the impact of MPAs on the relationship between environmental factors and psychopathology. MPAs, like other subtle biological factors, may predispose to psychopathology only in particular environments (Raine et al., in press; Sameroff, 1993). A number of community-based studies, using diverse indices of biological risk, suggest that the relationship between biology and behavior is indeed dependent on the type of environment in which a child is reared (Breslau, 1995; Raine et al., in press; 1994; Sameroff, 1993). Two studies in nonreferred samples found that MPAs, in particular, might moderate the relationship between environmental risk and antisocial behavior. First, Mednick and Kandel (1988) reported that the combination of MPAs and an unstable home environment at age 12 predicted arrest for violent crime by age 21 better than either MPAs or an unstable environment alone. Second, in a cross-sectional study of 226 boys, aged 5 to 9 years, Sandberg et al. (1980) found an interaction between MPAs and environmental disadvantage as a predictor of behavior problems.

No study, to our knowledge, has considered whether MPAs moderate the association between the environment and *DSM*-based psychiatric disorders or psychiatric impairment in youth. The current study examines this issue. Previous reports on the sample used in this study emphasized the links between childhood

neurological signs and adolescent emotional disorders and between cognitive function and adolescent conduct problems (Schonfeld et al., 1988; Shaffer et al., 1985). These prior findings are integrated into the examination of interactions between MPAs and environmental risk.

METHOD

Subjects

Subjects were drawn from the 1962–1963 Columbia Presbyterian Medical Center (CPMC) birth cohort of the Collaborative Perinatal Project (CPP). The sample frame originally comprised every fifth woman registering during pregnancy at the CPMC clinic. Subjects were prospectively followed from birth to age 7 and were then recruited for an adolescent follow-up (see Shaffer et al., 1985).

The adolescent follow-up study was designed to assess long-term sequelae of neurological "soft signs" in childhood. Subjects ($n = 126$) were all African-American males, since as a group they exhibited the highest rate of neurological signs at age 7. Index cases ($n = 63$) had received a positive rating on any one of eight neurological soft signs but were free of frank neurological disease or marked mental retardation ($IQ > 60$). For comparisons ($n = 63$), the next African-American male on the CPP register with no evidence of neurological abnormality was selected. One hundred eighteen boys (94%) were examined when they were between ages 16 and 18. Two probands refused examination, and three were excluded after the age 17 neurological examination found signs of frank CNS injury. Three controls were not located; three refused examination. Finally, while the original study also included a sample of 47 African-American females, females were not examined in the current report because there were more extensive missing data on MPAs in females than in males.

Neurological Assessment

Neurological examinations including tests for soft signs were conducted at age 7 according to the CPP protocol by pediatricians supervised by senior pediatric neurologists. The examination at age 17 used similar procedures. The reliability of these examinations was shown to be satisfactory (see Shaffer et al., 1985).

Cognitive and Behavioral Assessments at Age 7

At age 7, subjects completed seven subtests of the WISC, and the Full Scale IQ (FSIQ) was prorated (see Shaffer et al., 1985). During testing, examining psychologists blind to the child's status on all other examinations made behavioral observations. Three a priori scales were constructed from these ratings for all children ($n = 440$) in the 1962–1963 CPP CPMC birth cohort to denote (1) hyperactivity, (2) aggression, and (3) dependency-withdrawal (see Shaffer et al., 1985).

Minor Physical Anomalies

Each subject was assessed at age 17 for MPAs using the scale of Waldrop and Halverson (1971), which has been shown to have satisfactory interrater reliability in at least eight studies (.70 to .94 intraclass correlation) (Pomeroy et al., 1988). The MPA assessment was performed by a physician who was blind to all other data. Since subjects were all African-Americans, the presence of "fine

electric hair" or number of "hair whorls" was not scored. Because of discrepancies in MPA scoring across ethnic groups (Firestone and Prabhu, 1983), we defined hypertelorism as either 1 (a score of 1) or 1½ (a score of 2) standard deviations beyond the mean distance between pupils in our sample. Subjects were not assessed for the presence of a "geographic tongue," based on recommendations from Waldrop and Halverson (1971). In all analyses, the "weighted MPA score" was used, as this is the measure that has been used in most MPA studies. Because only four subjects in our sample had weighted MPA scores greater than 4, boys with a score of 4 or more were combined into a single category.

IQ and Psychiatric Assessments at Age 17

The WAIS was administered to 112 boys who then received a comprehensive psychiatric evaluation. As described in Shaffer et al. (1985), this evaluation included semistructured clinician-administered interviews of both subject and parent. Clinicians rated overall functioning on the Global Assessment Scale (GAS) after each interview, and a set of questionnaires was completed by each of three high school teachers.

Subjects receiving GAS scores below 70 after either interview were evaluated further, using best-estimate procedures. A summary of all information was reviewed by a committee of two senior child psychiatrists and one senior child psychologist blind to a subject's neurological or MPA status. This committee assigned a final GAS rating and as many *DSM-III* Axis I diagnoses as appropriate. Hierarchical exclusionary rules were not applied.

Environmental Risk Factors

During interviews with parents at age 17, 12 dichotomously coded items assessed the presence of factors considered external to a child's neurological state but commonly associated with psychopathology. The scale items comprised mother not being married to biological father, having four or more siblings, incomplete maternal and paternal education, either parent having had psychiatric treatment or police record, welfare dependency, low income, dissatisfaction with housing, and disturbance in spousal relationship.

An a priori "environmental disadvantage" scale was constructed by summing these 12 items without knowledge of their distribution across groups. The scale had acceptable internal consistency ($\alpha = .64$) and previously was shown to predict concurrent psychopathology in this sample (Shaffer et al., 1985). The scale was correlated with a more limited assessment of environmental adversity that had been conducted 10 years earlier (see Schonfeld et al., 1988). For our analyses, we used a z -transformed scale (mean = 0, SD = 1) such that higher scores were assigned to increasing disadvantage.

Data Analysis

We used logistic regression to test for a moderating effect of MPAs on the relation of environmental disadvantage to psychopathology. Psychopathology at age 17, dummy-coded so that 1 represented impaired status, was regressed on MPA score, psychosocial disadvantage score, and their product interaction. A significant interaction in this statistical model would imply that the strength of the association between environmental disadvantage and psychopathology is dependent on the MPA score. As such, MPAs might be conceptualized as an "effect modifier," which influences the degree to which environmental disadvantage is associated with psychopathology.

We first conducted regressions treating *any* psychiatric diagnosis as opposed to *no* psychiatric diagnosis as the dependent measure.

We then conducted regressions using more specific categorizations. Because prior reports on this cohort (Shaffer et al., 1985) linked adolescent psychopathology to other age 7 and age 17 factors, these factors also were included as covariates in the regression models.

Beyond the analysis to test our primary hypothesis, we also examined the association between MPAs and potential confounders that had been shown to predict the development of adolescent psychopathology in the sample. Thus, we used the χ^2 statistic to examine the association between neurological soft sign status and number of MPAs, hypothesizing that there would be a positive association between MPAs and the presence of neurological signs (dichotomously coded). We used Pearson correlations to examine the relationship between MPA score and IQ. Verbal IQ (VIQ) deficits appear particularly relevant for youth psychopathology in general and disruptive disorders in particular (Moffitt, 1993; Schonfeld et al., 1988). Therefore, we examined associations separately between MPAs and VIQ, Performance IQ (PIQ), as well as FSIQ. All statistical tests are two-tailed with an a priori $\alpha = .05$.

RESULTS

Sample Characteristics

Of the 115 boys examined at age 17 who were without evidence of frank CNS illness or injury, 101 (88%) had complete data. There were no differences between cases with missing data and other cases on any of the variables used in the current study.

Characteristics of this sample have been described previously (Schonfeld et al., 1988; Shaffer et al., 1985). The average age 17 weighted MPA score was 2.2 ± 1.4 (range: 0 to 6). The mean age 7 and age 17 IQ scores were 92.1 ± 10.0 and 95.1 ± 11.1 , respectively. By design, a nearly equal number of subjects had at least one ($n = 57$) versus no soft signs ($n = 58$) at age 7. Fifty-one subjects received a GAS rating of less than 70. The distribution of *DSM-III* diagnoses in these 51 subjects is shown in Table 1.

Univariate Relationships

Prior results in this cohort found that psychopathology was related to neurological soft signs, IQ, and environmental disadvantage. Therefore, before examining relationships among psychopathology, environmental disadvantage, and MPAs, we examined univariate relationships between MPAs and neurological signs as well as among MPAs, environmental disadvantage, and IQ. Furthermore, while the primary goal of this report was to examine the interaction between MPAs and environmental risk factors as a predictor of psychiatric status, we first examined the univariate relationship between MPAs and psychopathology before examining interactions.

TABLE 1
Distribution of Psychiatric Disorders

Disorder and <i>DSM-III</i> code	No. ^a
Disruptive behavior disorders	
Conduct disorder: 312	22
Other disruptive disorders	
Oppositional defiant disorder: 313.81	5
Attention-deficit disorder with or without hyperactivity: 314.01 or 314.80	4
Psychotic disorders	
Schizoaffective disorder: 295.70	1
Affective disorder	
Major depression: 296.2x or 296.3x	7
Bipolar disorder: 296.56	1
Atypical depression: 296.82	3
Dysthymia: 300.40	5
Adjustment disorder with depressed mood: 309.00	3
Any anxiety diagnosis	
<i>DSM-III</i> codes: 300.00; 300.29; 301.22; 309.21; 313.00; 313.21; 313.22	15
Any substance use disorder: 305.xx	7

^a Number of youths who meet criteria for disorder. Total exceeds 51, the total number with Global Assessment Scale score <70, due to comorbidity.

Neurological Signs. Age 7 neurological signs were associated with age 17 MPAs (continuity-corrected Pearson $\chi^2[4] = 12.2$; $p = .01$; Mantel-Haenszel Test for Linear Association $\chi^2[4] = 9.9$; $p = .001$) (Table 2). While there was a trend in a similar direction for age 17 soft signs, this relationship was not significant (continuity-corrected Pearson $\chi^2 = 5.5$; $df = 4$; $p = .14$).

IQ. Table 3 shows correlations among age 17 MPAs, VIQ, PIQ, and FSIQ, at both age 7 and age 17. As shown in the table, MPA score was inversely correlated with age 7 VIQ but was unrelated to other IQ indices. MPA score also correlated with the VIQ - PIQ difference ($r = -.24$; $p = .009$), and the partial correlation between age 7 VIQ and age 17 MPAs was significant ($r = -.29$; $p = .003$), controlling for age 7 PIQ.

TABLE 2
Relationship Between Age 7 Soft Signs and Age 17 Minor Physical Anomaly (MPA) Score

Age 7 Soft Signs	Age 17 Weighted MPA Score				
	0	1	2	3	≥4
No signs	11	14	13	8	7
≥1 Sign	2	8	15	17	11

Note: Pearson $\chi^2(3) = 12.2$; $p = .01$. Mantel-Haenszel Test for Linear Association; $\chi^2(1) = 9.8$; $p = .001$.

Environmental Disadvantage. As shown in Table 3, there was no relationship between environmental disadvantage and MPAs.

Psychiatric Disorders. There was no difference ($t_{104} = 1.2$; $p = .23$) in MPA scores between the psychiatrically unimpaired ($n = 59$; MPA score = 2.0 ± 1.3) and impaired subjects ($n = 47$; MPA score = 2.4 ± 1.5).

Interactions Between MPAs and Environmental Disadvantage

Any Psychiatric Disorder. To test the principal hypothesis for this study, the presence of any psychiatric disorder was regressed on MPA score, disadvantage score, and the product interaction between these two variables. Based on prior results in this cohort (Shaffer et al., 1985), the following covariates were included: age 7 neurological signs, age 7 VIQ, age 7 PIQ, and the three age 7 behavioral scales. This analysis demonstrated a significant (Wald $\chi^2[1] = 6.4$; $p = .01$) interaction between MPAs and disadvantage as a predictor of psychopathology. Results yield very similar point estimates, with identical levels of statistical significance, if age 17 instead of age 7 VIQ and PIQ are used. For this analysis, the data were shown to adequately fit the model (goodness-of-fit $\chi^2 = 94.1$; $p = .39$).

To further elucidate the nature of this interaction, subjects were dichotomized at the median MPA score (weighted score of 2). One regression model was then fit with separate coefficients for the disadvantage scale in subjects with high (>2) and low (≤ 2) MPA scores. As shown in Table 4, there was a significant association between disadvantage and psychiatric impairment only among boys with high MPA scores. The regression coefficient in the model suggested that each standard deviation increase in the disadvantage score among subjects with a high MPA score was associated with a threefold increased risk for psychiatric impairment (95% confidence interval for odds ratio: 1.3 to 7.9). In contrast, the odds ratio for disadvantage in boys with a low MPA score was not significantly different from 1.0, and based on the statistical test on the interaction term, this odds ratio was significantly lower than the odds ratio for disadvantage among the subjects with a high MPA score. Age 7 neurological signs (Wald $\chi^2[1] = 3.2$; $p = .04$) and age 7 aggression score (Wald $\chi^2[1] = 5.0$; $p = .03$) were significant predictors of psychiatric disorder, as reported previously (Schonfeld et al., 1988; Shaffer et al., 1985).

TABLE 3
Pearson Correlations Among Minor Physical Anomaly (MPA) Score, IQ, and Environmental Disadvantage

	MPA Score	VIQ Age 7	PIQ Age 7	FSIQ Age 7	VIQ Age 17	PIQ Age 17	FSIQ Age 17
VIQ Age 7	-.24**						
PIQ Age 7	-.01	+.51***					
FSIQ Age 7	-.14	+.87***	+.86***				
VIQ Age 17	+.02	+.69***	+.46***	+.67***			
PIQ Age 17	-.02	+.42***	+.54***	+.55***	+.61***		
FSIQ Age 17	+.01	+.64***	+.55***	+.69***	+.92***	+.87***	
Disadvantage	+.02	-.11	+.08	-.03	-.22*	-.01	-.13

Note: VIQ = Verbal IQ; PIQ = Performance IQ; FSIQ = Full Scale IQ.

* $p < .05$; ** $p < .01$; *** $p < .001$.

Specific Psychiatric Disorders. Categories of nosologically related diagnoses were assembled as shown in Table 1. Because few boys had either isolated substance abuse disorders or psychotic disorders, these two classes of disorder were not examined. Three separate logistic regression models were fit, contrasting subjects having a specific class of disorder (disruptive; affective; anxiety) against subjects having no disorder.

Based on the reported interaction between MPAs and environmental factors as a predictor of criminal behavior (Mednick and Kandel, 1988), we first considered the disruptive disorders. In a univariate analysis,

there was a difference of marginal significance ($t_{86} = 1.72$; $p = .09$) in MPA scores between psychiatrically unimpaired ($n = 59$; 2.0 ± 1.3) and disruptive subjects ($n = 31$; 2.6 ± 1.5). However, as with analysis for psychopathology in general, our main interest was in the interaction between MPAs and environmental disadvantage. Based on prior results (Schonfeld et al., 1988), in the analysis treating disruptive disorders as the dependent measure, only VIQ and the age 7 aggression scale were included as covariates. Soft signs were not included as they were unrelated to disruptive disorders (Shaffer et al., 1985). As with the analysis for psychopathology in general, there was a significant interaction (Wald $\chi^2[1] = 5.2$; $p = .03$) between MPA score and environmental disadvantage. Furthermore, these data were shown to adequately fit the model (goodness-of-fit $\chi^2 = 76.3$; $p = .44$).

A regression model was again fit after dichotomizing subjects at the median MPA score (2). As shown in Table 5, the association between environmental disadvantage and disruptive disorders occurred only among boys with a high MPA score. The regression coefficient in the model suggests that each standard deviation increase in the disadvantage score among subjects with a high MPA score was associated with a threefold increased risk for disruptive disorders (95% confidence interval for odds ratio: 1.2 to 8.5). In contrast, the odds ratio for disadvantage in subjects with low MPA scores was not significantly different from 1.0 and was significantly less than the odds ratio between disadvantage and conduct disorder among subjects with a high MPA score (Wald $\chi^2[1] = 5.2$; $p = .03$). As reported earlier (Schonfeld et al., 1988), the age 7 aggression score remained a significant predictor of age 17 disruptive disorder in this analysis.

TABLE 4
Predictors of Any Psychiatric Disorder

Variable	B^a	SE	Wald χ^2
MPA score	-0.01	0.19	0.0
Disadvantage score (low MPAs) ^{b,c}	0.26	0.32	0.7
Disadvantage score (high MPAs) ^{b,c}	1.17	0.46	6.5**
Age 7 soft signs	0.50	0.28	3.2*
Age 7 VIQ	-0.01	0.02	0.1
Age 7 PIQ	-0.03	0.02	1.6
Age 7 aggression ^c	1.47	0.72	5.0*
Age 7 hyperactivity ^c	-0.06	0.28	.01
Age 7 anxiety ^c	-0.26	0.28	1.1

Note: All nine variables are entered in one logistic regression model. MPA = major physical anomaly; VIQ = Verbal IQ; PIQ = Performance IQ.

^a B represents the unstandardized regression coefficient such that a one-unit change in each variable is associated with an e^B change in the risk for psychiatric impairment.

^b In the initial model, the interaction between the disadvantage score and the MPA score treated continuously was significant (Wald $\chi^2[1] = 6.4$; $p = .01$). In the model presented in the table, separate disadvantage scale variables are entered for boys below (low MPAs) and above (high MPAs) the median on the MPA scale.

^c z -Transformed variable (mean = 0; SD = 1).

* $p < .05$; ** $p < .01$.

TABLE 5
Predictors of Disruptive Behavior Disorders

Variable	<i>B</i> ^a	SE	Wald χ^2
MPA score	-0.01	0.19	0.0
Disadvantage score (low MPAs) ^{b,c}	0.33	0.32	0.07
Disadvantage score (high MPAs) ^{b,c}	1.24	0.47	6.5**
Age 7 aggression ^c	1.31	0.70	5.0*
Age 7 VIQ	-0.01	0.02	0.1

Note: All five variables are entered in one logistic regression model. MPA = major physical anomaly

^a *B* represents the unstandardized regression coefficient such that a one-unit change in each variable is associated with an e^B change in the risk for conduct disorder.

^b In the initial model, the interaction between the disadvantage score and the MPA score treated continuously was significant (Wald $\chi^2[1] = 5.2$; $p = .03$). In the model presented in the table, separate disadvantage scale variables are entered for boys below (low MPAs) and above (high MPAs) the median on the MPA scale.

^c *z*-Transformed variable (mean = 0; SD = 1).

* $p < .05$; ** $p < .01$.

Finally, it should be noted that two thirds of boys with disruptive disorders had conduct disorder (Table 1). When the above analysis was repeated treating conduct disorder as the dependent measure, similar results were obtained, with a significant MPA by environmental disadvantage interaction (Wald $\chi^2[1] = 4.8$; $p = .04$) as a predictor of conduct disorder.

In the analyses predicting affective or anxiety disorders, the age 7 dependency-withdrawal score and age 7 soft sign score were included as covariates based on prior analyses from this cohort (Shaffer et al., 1985). For MPAs, no main effects or interactions with environmental disadvantage were found in predicting affective or anxiety disorders (results from these analysis available on request).

DISCUSSION

Three main findings emerged from this study. First, there was a significant interaction between MPAs and environmental risk factors for psychopathology as a predictor of psychiatric impairment. Second, the interaction was related specifically to disruptive disorders, particularly conduct disorder. Finally, MPAs at age 17 related to an age 7 VIQ/PIQ discrepancy and age 7 neurological soft signs, two potential markers of subtle neurological impairment that had been shown to predict age 17 psychopathology.

Clinical Implications

Our findings suggest that subtle biological abnormalities such as MPAs may act to increase a child's susceptibility to environmental risk factors for psychiatric impairment, especially impairment that is accompanied by conduct problems. This suggests that clinicians might be particularly concerned about the development of conduct problems in children who have subtle biological abnormalities and who are living under psychosocial adversity. With regard to prevention or treatment, our findings suggest that clinical interventions aimed at alleviating psychosocial adversity might be particularly useful in the care of children who have subtle biological abnormalities. Clinicians might accordingly examine the effects of psychosocial interventions in these children.

Biological Implications

MPAs, Soft Signs, and IQ. The associations in this study among MPAs, soft signs, and IQ, in a sample free of frank neuropathology, support the view that MPAs index subtle neurological abnormalities (Cantor-Graae et al., 1994). It is interesting to note that associations were specific to soft sign and VIQ measured in childhood but not adolescence.

The specificity of the association between age 17 MPAs and age 7 soft signs may relate to the fact that only age 7 soft signs predicted adolescent psychopathology in this sample (Shaffer et al., 1985). These findings are consistent with the theory that childhood soft signs index neurodevelopmental abnormalities. Comparable signs of neurodevelopmental abnormalities may either be absent or less easily detected in adolescence.

To consider explanations for the specificity of the association between MPAs and age 7 VIQ, we conducted further post hoc analyses. One explanation could be that environmental factors might lead to changes between age 7 and age 17 VIQ, attenuating the association between childhood IQ and measures, such as MPAs, that presumably relate to early childhood factors. Consistent with this possibility, disadvantage at age 17 was associated with a lower age 17, but not age 7, VIQ, as shown in Table 3. Furthermore, in a regression model, age 17 disadvantage predicted age 17 VIQ ($B = -1.7$; $SE = 0.8$; $t_{105} = 2.2$; $p = .02$) while controlling for age 7 VIQ ($B = +0.6$; $SE B = 0.05$; $t_{105} = 9.2$; $p < .001$). A second explanation for

the age specificity could be that MPAs specifically relate to VIQ subtests administered at age 7. However, MPAs did not relate to these subtests at age 17.

The association between an early childhood VIQ deficit and MPAs in the current study may relate to prior reports from this and other samples suggesting that an early childhood VIQ deficit is a precursor of conduct problems later in life (Moffitt, 1993; Schonfeld et al., 1988). In fact, results from our multivariate model suggest that the relationship between a deficit in VIQ and conduct problems may result because both VIQ and conduct problems relate to common antecedent factors. Namely, the interaction between MPAs and environmental disadvantage appeared to account for the association between an early childhood VIQ deficit and conduct problems. While VIQ related to conduct disorder without MPAs in the model (Schonfeld et al., 1988), including MPAs and the MPA by environmental disadvantage interaction eliminated the association between VIQ and conduct disorder.

Interactions Between MPAs and the Environment. The interaction between MPAs and environmental disadvantage might be placed in the context of recent research on the association between perinatal adversity and childhood psychopathology. Though the interaction between environmental adversity and adolescent MPAs in the current study was demonstrated in a cross-sectional analysis, MPAs measured in adolescence, or even adulthood, are believed to index early childhood factors. To our knowledge, the only long-term prospective study on the stability of MPAs found a correlation of $r = .71$ for the weighted Waldrop score, the score used in our analyses, from age 2 through 7 (Waldrop and Halverson, 1971). Cantor-Graae et al. (1994) also showed that perinatal complications predict adulthood MPA scores.

The interaction found in this study is therefore relevant to research demonstrating interactions between perinatal and environmental factors. Both low birth weight (Breslau, 1995) and birth complications (Raine et al., 1994) predict disruptive behavior or violence among children raised in disadvantaged environments but not among children raised under less adverse circumstances.

Care should be used when interpreting interactions between environmental and biological variables. While such interactions can imply that biological factors moderate the strength of environmental-behavioral associa-

tions, they do not necessarily imply that environmental factors are unrelated to behavior in the absence of biological risk. For example, in the current study, the association between environmental disadvantage and conduct disorder was not statistically significant in boys with low MPA scores. Nevertheless, the point estimate on the regression coefficient in Table 5 still suggested that high degrees of social disadvantage relate to conduct disorder in the absence of a high MPA score. That this regression coefficient was not *statistically* different from zero, corresponding to an odds ratio of 1.0, could result from a type II error, given the small number of conduct disorder cases with low MPA scores.

Further research aimed at elucidating a mechanism by which MPAs could potentiate the effects of environmental disadvantage seems warranted. One possibility is that MPAs serve as markers of CNS dysfunction, which predisposes children to psychopathology. Animal-based research supports this notion, finding that common embryonic cell lines give rise to anomalies of the skin and CNS, particularly the cerebellum (Le Douarin, 1993). This is consistent with an emerging line of research linking this brain region to higher-order thinking (Middelton and Strick, 1994). A second related possibility, as put forth by Deutsch et al. (1990), is that MPAs index heritable components of the disruptive disorders. This might suggest that the association in the current study with conduct disorder reflects a gene-environment interaction (Cadoret et al., 1995).

Limitations and Strengths

The first and perhaps most significant limitation in this study relates to the unclear generalizability of our findings. Children were selected into this study on the basis of neurological soft sign status. This design is likely to enrich the biological vulnerability of the sample, and, as a result, the associations might not generalize to less biologically vulnerable samples. Furthermore, the sample consisted of children in an urban community and included only African-Americans, which also may limit generalizability by increasing the proportion of environmentally disadvantaged subjects. Nevertheless, the study did control for some of the more important factors limiting the generalizability of findings in case-control studies examining biological correlates of psychopathology. These include referral

biases and the presence of comorbid neurological illness or neurocognitive dysfunction. Moreover, in prior research, among nonminority samples, interactions were found between MPAs and disadvantage in Scandinavian and British youth as determinants of either violent crime (Mednick and Kandel, 1988) or behavior problems (Sandberg et al., 1980). The best evidence for generalizability derives from replications across studies. When findings are replicated in very different populations using different measures of behavior, such as the results in our sample and in the Scandinavian or British samples, this offers particularly strong evidence of generalizability.

Second, since this sample was nonreferred, the rate of rare disorders was low. Hence, we could not assess relations between MPAs and psychosis or pervasive developmental disorders, two classes of disorder frequently emphasized in studies of MPAs (Cantor-Graae et al., 1994; Gillberg et al., 1983).

Third, the use of *DSM-III* nosology is a limitation. While this might affect conclusions concerning specificity, the instrument used to assess psychiatric impairment, the GAS, remains valid. Furthermore, *DSM-IV* conduct disorder criteria draw heavily on the criteria in *DSM-III*, since the *DSM-III* categorization possesses significant predictive validity (Robins and Price, 1991).

Fourth, we chose to leave multiple comparisons unprotected in this study, since we entered the study with a set of distinct hypotheses that were supported by our findings. While this may increase the chance of type I errors, given the paucity of research in this area among nonreferred children and the importance of research on biopsychosocial interactions, we felt that it was important to guard against type II errors while findings are accumulating.

Finally, despite some evidence of stability in MPA score (Waldrop and Halverson, 1971) and our indicators of environmental disadvantage (Schonfeld et al., 1988), our findings for psychiatric impairment were cross-sectional. Prospective studies are therefore needed that examine the interaction between childhood MPAs and childhood environmental risk factors as predictors of adolescent psychopathology or conduct problems.

Strengths of this study include the fact that sampling and screening procedures removed biases found in many prior studies of MPAs and the fact that all assessments, neurological as well as psychiatric, were completed by experienced clinicians who remained

blind to all other data. Psychiatric assessments integrated large amounts of data from five sources—the child, parental informant, and three schoolteachers. Best-estimate methodology among senior research-oriented clinicians was used to assign diagnoses and final GAS score. Finally, although the study extended over a period of 10 years, an acceptably high proportion of the sample was retained.

Conclusions

Results from this study suggest that MPAs may relate to psychopathology through an interaction with environmental risk factors. Furthermore, this study found a relationship between MPAs and two possible markers of subtle neurological dysfunction in childhood that previously have been linked to psychopathology. Hence, the interaction between environmental disadvantage and high MPA scores might be placed in the context of other research suggesting that subtle biological abnormalities relate to psychopathology through interactions with the environment (Raine et al., in press; Sameroff, 1993).

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