

Predictors of Internalizing Symptoms Among Very Low Birth Weight Young Women

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ABSTRACT. As part of a longitudinal study of the outcomes of very low birth weight children (<1.5 kg), we sought to examine the perinatal, childhood, and young adult predictors of internalizing symptoms among very low birth weight young women and their normal birth weight controls. The cohort included 125 very low birth weight and 124 normal birth weight 20-year-old subjects. Perinatal, childhood, and young adult predictors were examined via stepwise multivariate analyses. Results revealed very low birth weight to be a significant predictor of parent-reported internalizing symptoms of their daughters but only among white subjects who had mothers with high levels of psychological distress. Additional significant predictors of 20-year internalizing symptoms included child I.Q. and internalizing symptoms at age 8 years and family expressiveness. When the results were analyzed according to the young adult self-report, additional predictors of internalizing symptoms included a history of asthma and exposure to violence. Perinatal risk factors were not found to be predictive of internalizing symptoms at age 20 years. Future studies should prospectively examine social and environmental factors associated with the neonatal intensive care experience that might explain the effect of very low birth weight on later psychopathology. *J Dev Behav Pediatr* 26:93–104, 2005. Index terms: *perinatal, predictors, very low birth weight, internalizing.*

As part of a longitudinal study of very low birth weight infants (VLBW, <1.5 kg), we recently examined behavioral outcomes and evidence of psychopathology in a cohort of VLBW young adults.¹ The most significant finding was an increase in internalizing symptoms among VLBW young women compared with normal birth weight (NBW) controls.² These include anxious, depressed, and withdrawn symptoms. The primary objective of the present study was thus to examine the perinatal, childhood, and young adult predictors of internalizing symptoms in

this 20-year-old cohort. We also sought to examine the outcomes associated with high levels of internalizing symptoms.

Adult affective disorders including depression and anxiety are predicted by multiple risk factors.³ These include genetic disposition,⁴ maternal depression,^{5,6} smoking during pregnancy,^{7,8} low birth weight,⁹ neonatal health problems,¹⁰ parental loss and family disadvantage,⁹ and poor parenting during infancy and early childhood.^{11–16} Poor intrauterine growth has been associated with increased malaise (stress) in adulthood, which is ameliorated by catch-up growth during childhood.^{17–19} Additional predictors of internalizing symptoms during childhood include low cognition,²⁰ poor motor functioning,²¹ soft neurologic signs,^{22–24} learning disability, need for special education,^{25,26} chronic health problems,^{27–29} childhood depression,^{9,30,31} and poor social support and stressful life events.^{11,32–35}

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Many of the above-described perinatal and childhood risk factors for adult affective disorders are also prevalent in VLBW populations. We thus hypothesized that VLBW would be a significant risk factor for internalizing symptoms in 20-year-old young women even after controlling for confounding risk factors.

POPULATION AND METHODS

Very Low Birth Weight Group

The 20-year study of behavioral outcomes included 116 men and 125 women.¹ The very low birth weight (VLBW, <1.5 kg) women were drawn from a cohort of 163 VLBW female infant survivors who were treated at Rainbow Babies and Children's Hospital in Cleveland, OH, between 1977 and 1979 and followed longitudinally since birth. One hundred twenty-five of the subjects were followed to 20 years of age and completed the Achenbach Young Adult Self-Report (YASR) of Behavior.² The study population comprised 77% (125/163) of the surviving birth cohort of VLBW female infants and 118/125 (94%) of those studied at age 8 years. In addition, seven children who were not studied at age 8 years were seen at age 20 years. One parent of 119 of these study participants (95%) was also interviewed and completed the Young Adult Behavioral Checklist (YABCL).² The biologic, adoptive, or stepmother was the parent interviewed in 93% of the cases.

The VLBW women had a mean birth weight of 1168 g and were born at a mean gestational age of 29.8 weeks. Twenty-four (19%) were born small for gestational age (birth weight ≤ 2 SD for gestational age³⁶). The cohort was born before the advent of cerebral ultrasonography; thus, the rates of periventricular hemorrhage and leukomalacia are unknown. There were no major congenital malformations or infections. At the time of the children's birth, 40 (22%) of their mothers were unmarried, 27 (22%) had less than a high school education, 56 (45%) had a high school education, and 42 (34%) had more than a high school education.

The VLBW participants had significantly higher mean I.Q. scores at age 8 years compared with those who did not participate at 20 years (97 ± 16 vs 82 ± 20 , $p = .003$), but their 8-year internalizing and externalizing behavior scores on the Child Behavior Checklist (CBCL) did not differ.³⁷ Mothers of the VLBW participants had higher levels of education at the time of the children's birth than those who did not participate at 20 years (22% vs 39% less than a high school education, $p = .04$), but they did not differ significantly in terms of race (52% vs 44% black, $p = .36$) or marital status (32% vs 46% unmarried, $p = .11$). More participants were born at the perinatal center than those who did not participate at age 20 years (38% vs 25%, $p = .04$). Participants had a significantly higher birth weight (1167 vs 995 g) and gestational age (29.8 vs 28.4 weeks, $p < .05$) but did not differ in neonatal complications.

Normal Birth Weight Group

The 20-year normal birth weight (NBW) population included 108 men and 124 women. The women represented

64% of the 193 female NBW controls who were born at term gestation and who had been recruited at age 8 years. One parent of 115 of the controls (93%) was also interviewed and completed the YABCL. The parent interviewed was the biologic, adoptive, or stepmother in 98% of cases.

The NBW participants had significantly higher mean I.Q. scores at 8 years of age compared with those who did not participate at 20 years (103 ± 16 vs 92 ± 15 , $p < .001$), but internalizing and externalizing behavior scores on the CBCL at age 8 years did not differ. Fewer of the mothers of the participants were unmarried when their children were 8 years of age (33% vs 60%, $p < .001$), fewer had less than a high school education (11% vs 28%, $p < .01$), and fewer were black (58% vs 77%, $p < .05$) for all comparisons.

The study was approved by the Institutional Review Board, and all subjects and their parents provided written informed consent to participate in the study.

Measures and Variables

The VLBW participants had been studied at birth, at 8 and 20 months corrected age, and at 8 and 20 years post-natal age.³⁸ The NBW controls were studied when recruited at age 8 years and then at age 20 years. At 20 years, young adult problem behavior was assessed from the perspective of the young adults and of their parents via self-administration of the YASR and the YABCL for parents or adult care givers, respectively.² Eight syndromes have been derived from the problem items on the YASR and YABCL, including two designated as internalizing (anxious/depressed, withdrawn) and three as externalizing (aggressive, delinquent, and intrusive behavior). Validity has been demonstrated by showing significantly higher scores for subjects referred for mental health services than for matched nonreferred subjects.³⁹⁻⁴¹ The 83rd percentile is considered the borderline clinical cutoff and the 90th percentile the clinical cutoff for the Internalizing, Externalizing, and Total Problem scales.²

Perinatal, birth, infancy, and early childhood information was available for the VLBW cohort only and included maternal race, education, and marital status at the time of the children's birth; birth weight; gestational age; Hibel antepartum, intrapartum, and neonatal risk scores⁴²; re-hospitalization before 20 months; and growth parameters at each study time period. The risk scores are cumulative composites of risk factors. For example, the neonatal risk score includes neonatal risk factors such as respiratory distress syndrome, infection, jaundice, and seizures.

Maternal sociodemographic descriptors at the time that the children were 8 years old were available for both the VLBW and NBW subjects. Additional variables available from the 8- and 20-year assessments are listed in Table 1.

Statistical Analyses

Univariate comparisons between the VLBW and NBW groups were made using Student's *t* test for continuous variables and with the chi-square test or Fisher's exact test for discrete variables. Correlation coefficients quantified

Table 1. Outcomes at 8 and 20 Years by Birth Weight Groups

	Very Low Birth Weight (n = 125)	Normal Birth Weight (n = 124)
Outcomes at 8 yr		
Major neurosensory abnormality ^a	13 (10%)	0***
WISC-R IQ ⁴³	97 ± 16	103 ± 16***
Academic achievement composite z score ^b	-0.5 ± 1.1	-0.0 ± 0.7***
Total motor z score ^c	-1.1 ± 1.4	0.0 ± 1.1***
Child Behavior Checklist ³⁷		
Internalizing	10.4 ± 7.7	9.2 ± 7.6
Externalizing	16.9 ± 12.0	14.4 ± 11.2
Outcomes at 20 yr		
Total chronic conditions ^d	27 (22%)	20 (16%)
Asthma ^e	11 (9%)	7 (6%)
WAIS-R IQ ⁵⁰	86 ± 13	90 ± 14*
High school graduation ^f	102 (82%)	111 (90%)
Postsecondary study	64 (51%)	68 (55%)
4-yr college	42 (34%)	47 (38%)
Unemployed	24 (19%)	13 (11%) ^g
Family environment scale ^{53h}		
Cohesion	7.6 ± 1.6	7.5 ± 1.7
Expressiveness	5.9 ± 1.8	6.1 ± 1.8
Conflict	2.3 ± 1.9	2.5 ± 2.0
Stressful life events ^{34h}	2.6 ± 1.7	2.6 ± 1.7
Exposure to violence ^{51h}	1.2 ± 0.3	1.2 ± 0.2
Psychosocial maturity ^{52h}		
Work orientation	3.1 ± 0.5	3.1 ± 0.5
Self-reliance	3.3 ± 0.5	3.5 ± 0.4*
Maternal Brief Symptom Inventory ⁵⁴		
Global severity index ≥ 63	17 (14%)	16 (14%)

^aIncludes cerebral palsy, hydrocephalus, blindness, and deafness.

^bAcademic achievement composite includes reading,⁴⁴ math,⁴⁵ and spelling.⁴⁶

^cTotal motor score includes visuomotor,⁴⁷ fine motor,⁴⁸ and gross motor⁴⁹ function.

^dChronic medical conditions were defined as those with a duration of 12 months or more. Data for neurosensory and chronic medical conditions are the numbers and percentages of participants with at least one condition in that category.

^eData are for participants who has had an asthma attack in the previous 12 months, were taking asthma medication, or both.

^fIncludes participants who had a General Equivalency Diploma.

^g*p* = .053.

^hHigher scores indicate an increase in the item measured.

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

the strength of bivariate association among the variables. Regression analyses determined which variables predicted internalizing outcomes even after adjusting for covariates. Logistic regression was used for dichotomous outcomes, and multiple linear regression was used for continuous outcomes. Raw internalizing scores were used in all analyses.

Because this was an exploratory study, a hierarchical procedure was used to establish independent factors predictive of 20-year internalizing symptoms during the three periods of study: (a) factors present during the perinatal and early childhood period, (b) factors present or recorded at the 8-year assessment, and (c) factors present or recorded at the 20-year assessment. Since perinatal and early childhood data were unavailable for the NBW controls, we

undertook two main analyses. In the first analysis (Model I), we examined the effects of birth weight status (VLBW vs NBW) on 20-year internalizing symptoms after controlling for other confounding risk factors. In this model, birth weight status was considered to represent perinatal risk factors. Birth weight status was included in all the regression models regardless of statistical significance because of its conceptual importance in the present study. Similarly, sociodemographic status was included as a covariate in all models regardless of statistical significance. In the second analysis (Model II), we sought to examine the effects of perinatal risk factors within the VLBW cohort. Again, sociodemographic status was always included in the regression model. In both sets of models, predictors of internalizing symptoms at age 20 years were considered separately according to parent report and according to young adult self-report (Models Ia and Ib and Models IIa and IIb, respectively).

Variables considered for inclusion in the models during the three sequential time periods of study were based conceptually on evidence from the literature and on their availability in the longitudinal database.³⁻³⁵ Because of the known effects of sociodemographic factors on behavioral outcomes, sociodemographic status was forced to be included in all analyses.⁵⁵ A composite score representing the mothers' sociodemographic status, which we have previously used, was calculated by assigning one point for each of the following factors: unmarried status, less than a high school education, and black race.⁵⁶ The composite score ranged from 0 to 3. In Model I, we used the maternal sociodemographic status at the time the child was 8 years old because maternal sociodemographic descriptors at the time of birth of the controls were unavailable. In Model II, which included only VLBW subjects, we used the maternal sociodemographic descriptors at the time of the children's birth since these were more relevant to the perinatal period.

Model I: VLBW and NBW Subjects. Step I of the regression model included birth weight status (VLBW vs NBW) as the only perinatal/early childhood predictor variable. Step II included birth weight status, which was forced in and a backward stepwise procedure was used to examine the other 8-year variables, which included maternal sociodemographic status, major neurosensory abnormality, the WISC-R I.Q., the composite motor z score, and the internalizing symptom raw score of the 8-year CBCL. The composite score of academic achievement was not considered in the model due to its high correlation with I.Q. (*r* = .74). The 8-year externalizing symptom score was similarly not entered in the model because of its high correlation (*r* = .72) with internalizing symptoms.

Step III included birth weight status along with the variables selected in Steps I and II (*p* < .1) and then included the other 20-year predictor variables retained with a significance of < .10 using a backward stepwise procedure. These included asthma, stressful life events, exposure to violence, family cohesion, expressiveness and conflict, and maternal psychological symptoms.

Model Ia considered internalizing symptoms according to parent-report and Model Ib according to the young adult

self-report. When constructing the models, once main effect terms were entered using the stated criteria, we investigated two-way interactions on covariates included in the models. If any two-way interactions were significant, we examined three-way interactions involving the variables involved in the two-way interactions. If an interaction was included, then all lower order main effects and interactions were also included.

Model II: VLBW Subjects Only. Only VLBW subjects were included in Model II. Step I examined maternal sociodemographic status as a forced variable, birth weight *z* score (a measure of intrauterine growth), prenatal risk, neonatal risk, and rehospitalization before 8 months corrected age. Gestational age was not considered in the model due to its narrow range within the category of VLBW infants. Step II included the predictor variables selected in Step I in addition to considering the 8-year predictor variables: major neurosensory abnormality, the WISC-R I.Q., the motor *z* score, internalizing scores on the CBCL, and change in weight *z* score between birth and 8 years, which is a measure of catch-up growth.⁵⁷

Step III examined 20-year variables, as described in Model I, after including variables selected in Steps I and II. Within each step, predictors were chosen using a backward selection procedure, retaining variables with a significance of $p < .10$.

We also compared the outcomes of VLBW women who had internalizing symptoms above the borderline clinical range² with those with scores within the normal range with respect to sociodemographic factors, behaviors, and functioning at 20 years. Odds ratios and mean differences, adjusted for sociodemographic status, were calculated using logistic and linear regression, respectively.

RESULTS

Comparison of Sociodemographic Status, Birth Data, and 8- and 20-Year Outcomes of the Very Low Birth Weight and Normal Birth Weight Groups

The very low birth weight (VLBW) and normal birth weight (NBW) women did not differ significantly with regard to maternal marital status, race, education, or in the composite index of sociodemographic status (Table 2). At age 8 years, VLBW girls, when compared with NBW controls, had significantly higher rates of major neurologic abnormality, lower I.Q. scores, and poorer scores on the composites of academic achievement and motor functioning but did not differ significantly in internalizing or externalizing symptoms (Table 1). At 20 years, the VLBW subjects, now women, continued to have a significantly lower I.Q. than NBW controls. Their rates of unemployment tended to be higher. They did not differ from the controls in the measures of family environment including family cohesiveness, expressiveness, or conflict or in stressful life events, exposure to violence, or in their mothers' psychological status. They reported similar work orientation but significantly less self-reliance. As previously reported, VLBW women compared with their controls also reported signifi-

cantly less alcohol (61% vs 83%) and illicit drug (30% vs 44%) use during the last year, fewer days drunk during the past 6 months (2.4 vs 7.0), and less sexual activity and child birth (13% vs 24%) than controls.^{1,38}

Predictors of Internalizing Symptoms at Age 20 Years

The Pearson correlation matrices for all the variables used in Models I and II are provided in Tables 3 and 4. Examination of the tables indicates that multicollinearity is not likely to substantially affect the findings in the regression models.

When considering pooled data from VLBW and NBW groups combined (Table 3), significant univariate correlates of parent-reported internalizing included social status, birth weight status (VLBW vs NBW), the motor composite score, internalizing symptoms at age 8 years and asthma, maternal psychological distress, and family cohesion, expressiveness, and conflict reported at age 20 years. Significant correlates of young adult self-reported internalizing included internalizing symptoms at age 8 years and asthma, stressful life events, and exposure to violence at age 20 years (Table 3). Within the VLBW group, significant correlates of parent-reported internalizing included social status, prenatal and neonatal risk, internalizing symptoms at age 8 years, and asthma and family expressiveness, cohesion, and conflict at 20 years. Significant correlates of self-reported internalizing included the birth weight *z* score and exposure to violence (Table 4).

Table 2. Maternal Demographic Status and Birth Data by Birth Weight Groups

	Very Low Birth Weight (n = 125)	Normal Birth Weight (n = 124)
Maternal factors^a		
Unmarried	50 (40%)	41 (33%)
Black race	65 (52%)	72 (58%)
Education^a		
< High School	21 (17%)	14 (11%)
High School	73 (58%)	63 (51%)
> High School	31 (25%)	47 (38%)
Composite sociodemographic score^b		
0	44 (35%)	46 (37%)
1	38 (30%)	38 (31%)
2	31 (25%)	31 (25%)
3	12 (10%)	9 (7%)
Birth data		
Birth weight, g (mean \pm SD)	1168 \pm 222	3134 \pm 495
Gestational age, wk (mean \pm SD)	29.8 \pm 2.3	$\geq 37^c$
Multiple birth ^d	24 (19%)	1 (1%)

^aThe maternal status at the time that the participant was 8 years old is given.

^bIn the calculation of this composite score, one point was assigned for each of the following factors: unmarried status, black race, and less than a high school education.

^cSpecific information on gestational age was not available for the control group.

^dData are for participants born either a twin or, in one case, a triplet.

Table 3. Pearson Correlations of Predictors of Internalizing Symptoms Used in Models Ia and b

	1	2	3	4	5	6	7	8	9	10	11	12	13	14
1. Social risk														
2. Bwt status	.03													
3. Neuro imp.	-.05	.23**												
4. I.Q.	-.47**	-.20**	-.03											
5. Motor	-.27**	-.39**	-.40**	.60**										
6. Int. at 8 yr	.01	.08	-.03	-.04	-.07									
7. Asthma	.03	.06	.07	.03	-.05	.08								
8. Life stressors	.25**	.01	-.09	-.17**	-.13	.09	.03							
9. Violence exp.	.31**	-.07	.05	-.26**	-.18**	.01	.07	.25**						
10. Mat. GSI	.03	.01	-.02	-.10	-.04	.50**	.13	.10	.05					
11. Fam. cohesion	-.06	.04	-.02	.11	.03	-.26**	-.12	-.04	-.03	-.40**				
12. Fam. express.	-.18**	-.05	-.04	.12	.05	-.13	-.08	-.05	-.04	-.23**	.29**			
13. Fam. conflict	.09	-.06	.02	-.13*	-.09	.31**	.01	.13	.13	.45**	-.45**	-.06		
14. Int (YABCL)	-.14*	.20**	.04	-.12	-.16*	.44**	.15*	-.03	.04	.47**	-.28**	-.20**	.28**	
15. Int (YASR)	-.01	.11	.06	.05	-.05	.20**	.18**	.16*	.24**	.09	-.07	.04	.08	.38**

Social risk, maternal sociodemographic risk based on unmarried status, black race, and education (< high school); Bwt status, birth weight status (0 = normal birth weight, 1 = very low birth weight); Neuro imp., neurosensory impairment including cerebral palsy, blindness, and deafness; I.Q., 8-year WISC-R I.Q.⁴³; Motor, motor composite of fine motor,⁴⁷ gross motor,⁴⁹ and visuomotor⁴⁸ function; Int. at 8 yr, internalizing score on the Child Behavior Checklist³⁷; Asthma, asthma attack in the previous 12 months, on asthma medication, or both; Life Stressors, young adult report of stressful life events³⁴; Violence exp., exposure to violence in the previous 12 months⁵¹; Mat. GSI, maternal score on the General Severity Index of the Brief Symptom Inventory⁵⁴; Fam. cohesion, Fam. express, Fam. conflict, family cohesion, expression, and conflict scores on the Family Environment Scale⁵³; Int (YABCL), internalizing score reported by parent on the Young Adult Behavior Checklist²; Int (YASR), internalizing score on the Young Adult Self-Report.²

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

Multivariate Analyses

Model I: Effects of Birth Weight Status. *Model Ia:* VLBW status had a significant effect on 20-year parent-reported internalizing scores (Table 5). A significant three-way interaction ($p = .04$) was found between social status, maternal psychological distress, and birth weight status. Examination of the regression coefficients in this model and of the means of VLBW and NBW groups by tertiles of the General Severity Index of the Brief Symptom Inventory and social status both indicate that the effect of VLBW on internalizing scores was highest among subjects with low social risk who had mothers with high levels of psychological stress, with relatively little effect of birth weight status among those with moderate or high levels of social risk. To clarify which of the components of sociodemographic risk might explain these findings, we performed exploratory analyses that examined the individual effects of maternal education, marital status, and race in the model. The results revealed that the inverse effect of social risk (i.e., low social risk) was due to race (i.e., white race was predictive of internalizing scores: $\beta = -3.9$, 95% confidence interval [CI] -5.57 to -2.2 , $p < .001$), whereas the effect of maternal education and marital status was not significant. The effect of VLBW on internalizing scores was similarly highest among subjects who were both white and who had mothers with high levels of psychological distress. Additional significant predictors of internalizing scores at 20 years included internalizing scores and I.Q. at 8 years and family expressiveness. In exploratory models, when 8-year externalizing and internalizing scores were both entered in the model, the results were similar to those when only internalizing scores were included. When 8-year

externalizing but not internalizing scores were entered in the model, they predicted internalizing symptoms at 20 years ($\beta = 0.20$, 95% CI 0.13 – 0.27 , $p = .001$).

Model Ib. Significant predictors of 20-year self-reported internalizing symptoms included lower sociodemographic risk, asthma, and exposure to violence. The effect of VLBW status approached significance, $p = .12$, as did the effect of stressful life events ($p = .054$). There were no significant interactions between birth weight status and other covariates in this model. Examination of the individual components of the sociodemographic risk index revealed that none of the three components (race, maternal education, or marital status) individually had a significant effect.

Model II: Effects of Perinatal Risk Factors Among VLBW Subjects. *Model IIa.* Significant predictors of parent-reported internalizing scores among VLBW subjects included lower social risk, increased maternal psychological symptoms, and less family expressiveness (Table 6). Similar to Model Ia, the effect of lower social risk was due to race (i.e., white race was predictive of internalizing behavior: $\beta = -5.4$, 95% CI -7.9 to -3.0 , $p < .001$), whereas the effects of maternal education and marital status were not significant. Neonatal risk had a significant effect when only birth or birth and 8-year variables were included in the model ($p < .01$), but this effect diminished when the 20-year variables were added. In additional exploratory models, 8-year externalizing symptoms had no effect on 20-year internalizing symptoms when entered together with 8-year internalizing scores or after excluding 8-year internalizing scores from the model.

Model IIb. Significant predictors of 20-year self-reported internalizing symptoms included intrauterine growth as measured by the birth weight z score and exposure to violence. Birth weight z score had a positive relationship to

Table 4. Pearson Correlations of Predictors of Internalizing Symptoms Used in Models 1a and b

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18
1. Social risk																		
2. Prenatal risk	-.04																	
3. Birth weight z	-.18*																	
4. Neonatal risk	-.11	-.01																
5. Rehosp.	.14	.15	-.07															
6. Weight change	.28**	.13	-.61**	.31**														
7. Neuro imp.	-.09	-.02	.03	.25**	.05													
8. I.Q.	-.41**	-.06	.23*	-.24**	-.24**	-.23*												
9. Motor	-.12	-.05	.12	-.42**	.14	-.11	.03											
10. Int. at 8 yr	-.19*	.26**	.12	.03	-.21*	-.02	-.44**	.53**										
11. Asthma	-.02	-.02	.13	.31**	.10	-.04	.08	.08	-.03									
12. Life stressors	.39**	-.04	-.14	-.11	.10	.29**	-.13	-.10	-.05	.04								
13. Violence exp.	.33**	-.07	-.14	.11	.30**	.11	.09	-.31**	-.21*	-.06	.06							
14. Mat. GSI	-.08	.16	-.02	.05	-.06	.06	-.02	-.04	-.07	.58**	.14	.05						
15. Fam. cohesion	.02	-.15	-.03	-.13	.05	.03	-.05	.13	.09	-.30**	-.02	-.03	-.03					
16. Fam. express.	-.21*	-.01	-.03	-.13	-.14	-.04	-.04	.17	.09	-.15	-.09	-.09	-.04	-.39**				
17. Fam. conflict	-.15	.30**	-.04	.03	.04	.04	.05	-.15	-.12	.46**	.001	.08	.03	.51**	.35**			
18. Int (YABCL)	-.32**	.19*	.14	.21*	.05	-.09	-.002	-.05	-.09	.42**	.18*	-.11	.03	.53**	-.39**	-.11		
19. Int (YASR)	.01	-.03	.22*	.05	.10	-.04	.05	.12	.06	.16	.17	.12	.26**	.10	-.04	-.25**	.27**	
20. Int (YASR)																-.05	.11	.34**

Social risk, maternal sociodemographic risk based on unmarried status, black race, and education (< high school); Prenatal risk, cumulative prenatal risk score⁴²; Birth weight z, birth weight z (SD) score⁴⁶; Neonatal risk, cumulative neonatal risk score⁴²; Rehosp, rehospitalization before 8-months corrected age; Weight change, change in weight z score between birth and 8 years; Neuro imp., neurosensory impairment including cerebral palsy, blindness, and deafness; I.Q., 8-year WISC-R I.Q.⁴³; Motor, motor composite of fine motor,⁴⁷ gross motor,⁴⁸ and visuomotor⁴⁸ function; Int. at 8 yr internalizing score on the Child Behavior Checklist³⁷; Asthma, asthma attack in the previous 12 months, on asthma medication, or both; Life stressors, young adult report of stressful life events³⁸; Violence exp., exposure to violence in the previous 12 months⁵¹; Mat. GSI, maternal score on the General Severity Index of the Brief Symptom Inventory⁵⁴; Fam. cohesion, Fam. express., Fam. conflict, family cohesion, expression, and conflict scores on the Family Environment Scale⁵³; Int (YABCL), internalizing score on the Young Adult Behavior Checklist²; Int (YASR), internalizing score reported by parent on the Young Adult Self-Report.²

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

Table 5. Predictors of Internalizing Behaviors for the Total Population (Models 1a and b)

	At Birth β (95% CI)	At 8 Years β (95% CI)	At 20 Years β (95% CI)
Parent Report (Model 1a)			
Significant variables adjusted for ^a	(n = 234)	(n = 217)	(n = 218)
Birth weight status	2.7 (1.0 to 4.4)**	1.8 (0.1 to 3.4)*	1.4 (-1.3 to 4.2)
Sociodemographic risk ^b		-1.8 (-2.7 to -0.8)***	-0.2 (-1.6 to 1.3)
8-year WISC-R I.Q.		-0.08 (-0.1 to -0.02)*	-0.06 (-0.1 to -0.01)*
8-year internalizing on CBCL ^c		0.4 (0.3 to 0.5)***	0.2 (0.1 to 0.4)***
Asthma at age 20 yr ^d			2.4 (-0.4 to 5.2)
Maternal psychologic symptoms on GSI ^e			3.2 (-0.4 to 6.9)
Family expressiveness on FES ^f			-0.5 (-0.8 to -0.1)*
Birth weight status \times sociodemographic status			-0.9 (-2.9 to 1.1)
Birth weight status \times GSI			7.9 (3.0 to 12.7)**
Sociodemographic status \times GSI			-1.0 (3.7 to 1.8)
Birth weight status \times sociodemographic status \times GSI			-3.8 (-7.5 to -0.2)*
R^2	.04	.28	.47
p value	.002	<.001	<.001
Young Adult Self-Report (Model 1b)			
Significant variables adjusted for ^a	(n = 249)	(n = 230)	(n = 219)
Birth weight status	1.9 (-0.3 to 4.0)	1.6 (-0.6 to 3.8)	1.7 (-0.4 to 3.8)
Sociodemographic risk ^b		-0.6 (-1.7 to 0.5)	-1.8 (-3.0 to -0.6)**
8-yr internalizing on CBCL ^c		0.2 (0.1 to 0.4)**	0.2 (0.1 to 0.3)**
Asthma at age 20 yr ^d			4.3 (0.1 to 8.4)*
Stressful life events ³⁴			0.6 (-0.01 to 1.3)
Exposure to violence ⁵¹			7.1 (2.8 to 11.5)**
R^2	.01	.05	.16
p value	.092	.007	<.001

CI, confidence interval.

^aIncludes all variables significant at $p < .1$ except for birth weight status and sociodemographic status, which were forced in regardless of significance level.^bRepresents a composite score for which one point was assigned for each of the following factors: maternal unmarried status, education less than high school at the child's 8th year and black race.^cChild Behavior Checklist (CBCL).³⁷^dData are for participants who had had an asthma attack in the previous 12 months, were taking asthma medication, or both.^eGeneral Severity Index (GSI) of the Brief Symptom Inventory (BSI).⁵⁴^fFamily Environment Scale (FES).⁵³* $p < .05$; ** $p < .01$; *** $p < .001$.

internalizing symptoms (i.e., the better the intrauterine growth, the greater the number of internalizing symptoms). Birth weight in the VLBW cohort (<1 kg vs 1–1.49 kg) did not have an effect when considered in the model.

Outcomes of VLBW Women with High Levels of Internalizing Symptoms. VLBW women who had internalizing scores above the borderline clinical range on parent-reported internalizing symptoms compared with those with normal scores were more likely to be white and have lower rates of high school graduation and lower rates of enrollment in postsecondary (high school) educational programs (Table 7). They were more likely to use illicit drugs and have poorer work orientation and self-reliance. Those with self-reported internalizing scores above the borderline clinical range, similarly, had poorer work orientation, less self-reliance, and a tendency toward substance and tobacco use.

DISCUSSION

We sought to examine the perinatal, childhood, and young adult predictors of internalizing symptoms among 20-year-old very low birth weight (VLBW) and normal birth weight (NBW) women born during the early years of

neonatal intensive care. Results revealed VLBW status to be a significant predictor of parent-reported internalizing symptoms, but only among subjects who were white and had mothers with high levels of psychological distress. Additional significant predictors of internalizing symptoms included child I.Q. and internalizing symptoms assessed at age 8 years and family expressiveness. When the results were analyzed according to self-reported internalizing symptoms, the association with VLBW approached significance, and a history of asthma and exposure to violence were also predictive. Our findings that VLBW subjects who had high levels of internalizing symptoms had poorer educational achievement and tended to smoke, drink, and abuse drugs more than those in the normal range is in agreement with the literature on adolescent girls.⁵⁸

This is the first study to examine the predictors of psychopathology among VLBW young adults. We focused on women in this report since internalizing symptoms, which include anxious/depressed and withdrawn symptoms, are prevalent in adolescent and young women. These results cannot be generalized to VLBW men who, in general, demonstrate poorer educational outcomes than VLBW women.³⁸ Strengths of the study include its longitudinal

nature, the variables considered, and the relatively large population size. Weaknesses include the absence of information on maternal drug use and smoking during pregnancy⁸ and on maternal depression, maternal/infant interactions, and child abuse during the early formative years.^{59,60} The perinatal history of the NBW controls was also lacking. The results may possibly differ in populations of different sociodemographic background or with a more in-depth psychiatric evaluation of internalizing symptomatology.

Although cumbersome, our method of analyzing the results according to both parent report and young adult self-report provides information on symptomatology from different perspectives. Self-report of subjective symptoms such as anxiety and depression would be expected to be reported best by young adults rather than by their parents, as has been found in adolescents.⁶¹ However, parents are considered to know their offspring well into their mid-20s and to be able to contribute valuable information at this age.^{2,62,63} Parent ratings of their children's mental health have been found to be more predictive of concurrent signs of mental health than those of the young adults themselves.² In fact, our predictive model explained 47% of the variance of internalizing symptoms when analyzed according to parent report but only 16% according to self-report. This might reflect shared variance since maternal psychopathology was moderately correlated with internalizing symptoms. However, Saigal et al⁶⁴ similarly found that predictors of psychopathology were identified by parent report of behavior of extremely low birth weight adolescents but not by teen self-report.

The significant predictors of internalizing symptoms in our cohort, which are in agreement with the literature,

include low cognition,^{20,25,65} internalizing symptoms and/or depression during childhood,^{9,11,66} asthma,^{27,29} family expressiveness,⁹ and exposure to violence.^{11,67} Our finding that externalizing symptoms at age 8 years were associated with internalizing symptoms in young adulthood is in agreement with reports that childhood depression may co-occur or be preceded by externalizing symptoms.⁶⁸ However, our findings of an inverse relationship between sociodemographic status and internalizing symptoms contradicts the well-known relationship between social risk and adult depression.^{55,69,70} This direct relationship is, however, less evident in childhood and adolescence, where social risk factors tend to be related mainly to externalizing than to internalizing symptoms.⁷¹ When social risk factors are related to internalizing symptoms in adolescence, they tend to be associated with alcohol, tobacco, and drug use.⁷²

Indices of poverty, such as income and material resources rather than maternal education and marital status have mainly been used to examine the effect of social risk on depression.^{14,73,74} Our composite measure of social disadvantage included maternal education, marital status, and race. When we examined each component separately, we found white race to be the main determinant of internalizing symptoms, specifically among subjects who had mothers with high levels of psychological distress. Inhibition of emotions via either repression or conscious suppression and/or unwillingness to express private feelings among the black population may have played a role in our study. Social context and social cognition play a role in how emotions are expressed, and cultural influences on symptom problem recognition need to be considered in our sample, half of which were from the inner city of Cleveland.⁷⁵

Table 6. Predictors of Internalizing Behaviors for Very Low Birth Weight Females (Models IIa and b)

	At Birth β (95% CI)	At 8 Years β (95% CI)	At 20 Years β (95% CI)
Parent Report			
Significant variables adjusted for ^a	(n = 117)	(n = 103)	(n = 104)
Sociodemographic risk ^b	-2.3 (-3.6 to -1.1)***	-2.2 (-3.5 to -0.9)**	-2.1 (-3.4 to -0.9)**
Prenatal risk ⁴²	0.1 (-0.0 to 0.2)	0.03 (-0.1 to 0.2)	0.03 (-0.1 to 0.1)
Neonatal risk ⁴²	0.1 (0.0 to 0.1)*	0.1 (0.02 to 0.1)**	0.04 (-0.0 to 0.1)
8-yr internalizing on CBCL ^c		0.4 (0.2 to 0.6)***	0.1 (-0.1 to 0.3)
Asthma at age 20 yr ^d			4.4 (-0.4 to 9.1)
Maternal psychological symptoms on GSI ^e			6.9 (3.7 to 10.0)***
Family expressiveness on FES ^f			-0.8 (-1.5 to 0.1)*
R ²	.18	.31	.47
p value	<.001	<.001	<.001
Young Adult Self-Report			
Significant variables adjusted for ^a :	(n = 123)	(n = 108)	(n = 118)
Sociodemographic risk ^f	0.4 (-1.2 to 1.9)	-0.2 (-1.8 to 1.4)	-0.6 (-2.2 to 1.0)
Birth weight z-score ⁹⁸	2.0 (0.4 to 3.7)*	1.8 (0.1 to 3.5)*	2.3 (0.7 to 3.8)**
Exposure to violence ⁵¹			8.5 (2.3 to 14.7)**
R ²	.05	.05	.11
p value	.049	.088	.004

^aIncludes all variables significant at $p < .1$ except for sociodemographic status, which was forced in regardless of significance level.

^bRepresents a composite score for which one point was assigned for each of the following factors: unmarried status, less than a high school education, and black race.

^cChild Behavior Checklist (CBCL).³⁷

^dAsthma is defined as asthma attack in the previous 12 months, taking asthma medication, or both.

^eGeneral Severity Index (GSI) of the Brief Symptom Inventory (BSI).⁵⁴

^fFamily Environment Scale (FES).⁵³

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

Table 7. Sociodemographic Factors and 20-Year Functioning of Very Low Birth Weight Women According to Young Adult and Parent Report of Internalizing Above the Borderline Clinical Cutoff (83rd Percentile)

	Self-Report			Parent-Report		
	Internalizing ≥ Cutoff (n = 37)	Internalizing < Cutoff (n = 88)	Odds Ratio ^a (95% CI)	Internalizing ≥ Cutoff (n = 34)	Internalizing < Cutoff (n = 85)	Odds Ratio ^a (95% CI)
Sociodemographic variables ^b						
White	18 (49%)	42 (48%)	1.0 (0.5 to 2.2)	23 (68%)	36 (42%)	2.8 (1.2 to 6.6)***
Maternal education <high school	7 (19%)	14 (16%)	1.2 (0.5 to 3.4)	4 (12%)	15 (18%)	0.6 (0.2 to 2.0)
Mother unmarried	13 (35%)	37 (42%)	0.7 (0.3 to 1.7)	10 (29%)	35 (41%)	0.6 (0.3 to 1.4)
High school or GED completed	28 (76%)	74 (84%)	0.5 (0.2 to 1.5)	26 (77%)	73 (86%)	0.3 (0.1 to 0.9)***
Postsecondary study	17 (46%)	47 (53%)	0.7 (0.3 to 1.6)	14 (41%)	49 (58%)	0.4 (0.1 to 0.9)***
4-year college	11 (30%)	31 (35%)	0.7 (0.3 to 1.7)	9 (27%)	33 (39%)	0.4 (0.2 to 1.0)**
Unemployed	8 (22%)	16 (18%)	1.3 (0.5 to 3.5)	7 (21%)	16 (19%)	1.6 (0.5 to 4.7)
Substance use ^c						
Alcohol	26 (70%)	51 (59%)	1.7 (0.7 to 3.8)	21 (62%)	51 (61%)	1.0 (0.4 to 2.4)
Tobacco	19 (51%)	31 (35%)	2.0 (0.9 to 4.3)	12 (35%)	35 (41%)	0.8 (0.4 to 1.9)
Marijuana	15 (41%)	22 (25%)	2.1 (0.9 to 4.8)	10 (30%)	25 (30%)	1.1 (0.5 to 2.8)
Other illicit drugs	3 (8%)	2 (2%)	3.7 (0.6 to 23.6)	4 (12%)	1 (1%)	8.8 (0.9 to 84.6)*
Pregnancy and Delivery						
Pregnancy (ever)	10 (28%)	26 (30%)	1.0 (0.4 to 2.5)	10 (30%)	24 (29%)	1.7 (0.6 to 4.7)
Live birth (ever)	4 (11%)	13 (15%)	0.7 (0.2 to 2.7)	3 (9%)	12 (14%)	0.8 (0.2 to 3.9)
	Mean Difference		(95% CI)	Mean Difference		(95% CI)
Psychosocial maturity ⁵²						
Work orientation	2.7 ± 0.6	3.2 ± 0.4	−0.5 (−0.7 to −.04) [†]	2.8 ± 0.6	3.2 ± 0.5	−0.4 (−0.6 to −0.2) [†]
Self-reliance	3.1 ± 0.6	3.4 ± 0.4	−0.4 (−0.6 to −0.2) [†]	3.1 ± 0.5	3.4 ± 0.5	−0.3 (−0.5 to −0.1) [†]
Friends ²	6.3 ± 2.4	6.8 ± 2.1	−0.6 (−1.4 to 0.3)	6.4 ± 2.3	6.9 ± 2.0	−0.7 (−1.5 to 0.2)

CI, confidence interval.

^aWith the exception of sociodemographic variables, the odds ratios and mean differences were adjusted for sociodemographic status.^bMaternal status at the time that the participants were 8 years old.^cDuring the previous year.**p* < .06; ***p* < .057; ****p* < .05; [†]*p* < .001.

Richardson et al⁷⁶ reported racial and ethnic disparities in the diagnosis and treatment of depression among Medicaid-covered youths and, similar to our results, found that the prevalence of diagnoses of depression, based on medical claims, to be 7% for white 15- to 18-year-old females compared with 2% for similarly aged black females. The reason for this discrepancy was considered to be due to multiple factors including physician diagnosis, trust in the physician, and cultural differences. Katz et al⁷⁷ reported that respondents from the upper social classes may be more informed about psychopathology and be more inclined to report their symptoms. Those of lower social class may fail to give an accurate report of the emotions that they feel or are less psychologically minded and unable to engage in introspection.

The positive association between the mother's own psychological stress and internalizing symptoms in their daughters, which we have documented, may be related to genetic vulnerability^{4,78} and/or reporting bias with projection of maternal anxious and depressive thoughts onto their children.^{6,61,79} We did not measure maternal psychological status before their child's 20th year, but it is likely that parents with high levels of psychological stress had similar symptoms during their younger years. This may have affected parenting with persistent effects on their children.^{16,74}

Among VLBW children, predictors of anxiety and/or depression have included the quality of the family environment,^{80,81} family dysfunction,⁶⁴ maternal mood, birth weight,^{64,80,81} intelligence,⁸¹ grade level,⁸² and reading comprehension.⁸¹ Predictors of overall internalizing symptoms have included maternal age and single marital status,⁸³ a disadvantaged home,⁸⁴ school location in urban areas,⁸⁵ maternal smoking,⁸³ birth weight,⁸⁶ and maternal responsiveness.⁸⁴ Duration of neonatal hospital stay, a measure of neonatal health, has been associated with anxiety.^{86,87} We found a significant association between internalizing symptoms and neonatal risk when the birth and 8-year variables were considered in the model but not when the 20-year variables were added (see Model IIa, Table 6). With the exception of an association between periventricular leukomalacia and anxiety at age 6 years reported by Whitaker et al,⁸⁸ specific neonatal risk factors have not been found to be predictive of anxiety, depression, or overall internalizing symptoms in VLBW children.^{81,83,89,90} Hippocampal injury has been associated with depression in adulthood, and the hippocampus is one of the regions of the brain injured in preterm infants.⁹¹⁻⁹³ Our unexpected finding of a positive relationship between 20-year internalizing symptoms and intrauterine growth may be confounded by our method of population selection, which included infants with a birth weight of <1.5 kg irrespective of gestational age.

Thus, infants in the higher gestational age range tend to have intrauterine growth failure.⁹⁴ Such infants usually have accelerated rates of growth after birth, as evidenced by the significant inverse relationship between the birth weight z score and weight z score change between birth and 8 years ($r = -0.61$, $p < .01$; Table 4). Such catch-up growth may have had an ameliorating effect on internalizing symptoms, similar to that reported by Cheung et al¹⁷ for stress-related symptoms. Rodgers³² reported a trend toward a protective effect with fewer psychological symptoms among low birth weight (<2.3 kg) mainly term-born 36-year-old adults compared with larger birth weight subjects, which would also support our findings.

In summary, we found birth weight status to be a predictor of internalizing symptoms after controlling for other risk factors, although this applied to a subset of the population. It has been postulated that stresses during critical phases of human development, together with a

genetic disposition, may lower an individual's threshold for developing depression and anxiety later in life.⁹⁵ VLBW infants experience acute and chronic complications of prematurity, sensory isolation, repetitive painful exposures, and maternal separation, all of which could potentially predispose them to future psychopathology.⁹⁶ Future studies should prospectively examine the relationship between the neonatal intensive care experience, maternal psychologic symptoms, social risk factors, and possible interventions to prevent the development of later anxious and depressed symptoms.⁹⁷

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