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Effect of ethnicity and race on cognitive and language testing at 18 – 22 months in extremely preterm infants

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Abstract

Objective—To evaluate the relationship of race/ethnicity to cognitive and language scores on the Bayley Scales of Infant and Toddler Development 3rd edition (BSID-III) in extremely preterm toddlers (<28+0 weeks' estimated gestational age).

Study design—Extremely preterm toddlers at NICHD Neonatal Research Network Centers evaluated at 18–22 months adjusted age from 3 race/ethnic groups (White, Black, and Hispanic-White) were included in this cohort study. Multivariable regression modeling was used to identify race/ethnic differences adjusting for medical and psychosocial factors.

Results—Children included 369 Whites, 352 Blacks and 144 Hispanic-Whites. Cognitive scores differed between groups in unadjusted analysis ($p < 0.001$), but not after adjusting for medical and psychosocial factors ($p = 0.13$). Language scores differed in adjusted and unadjusted analyses. Whites scored higher than Blacks or Hispanic-Whites, and Blacks scored higher than Hispanic-Whites.

Conclusions—A combination of medical variables and primary caretaker education accounted for differences in BSID-III cognitive scores between groups. Black and Hispanic-White toddlers had lower language scores than Whites, even after adjustment. Early intervention should be targeted to these identified risk factors. Assessment of early language development among minority groups may be warranted.

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development; prematurity; Bayley Scales; BSID

Children born premature and extremely low birth weight (<1000 grams) are at high risk of developing intellectual and language difficulties.¹⁻³ These children are more likely to receive special educational assistance and/or repeat a grade than their normal birth weight peers.^{4,5} Early childhood intervention can improve cognitive, academic, and social outcomes.^{6,7} Early assessment of cognitive functioning in preterm children permits delivery of appropriate interventions to improve their cognitive and behavioral outcomes. In order to determine which interventions are needed, early assessment tools must identify the specific nature of developmental deficiencies.

Prior to 2005, the Bayley Scales of Infant and Toddler Development 2nd edition (BSID-II) was the standard tool for assessing outcomes for high risk infants at age two.⁸ The BSID-II had several design weaknesses, including the fact that language skills were not evaluated separately from cognition, but were distilled into a single score, the Mental Developmental Index (MDI). We demonstrated higher overall BSID-II MDI scores in White children than in Hispanic-White or Black children that were not explained by socioeconomic status or maternal education.⁹ The cause of this difference is undetermined. A third edition of the Bayley Scales of Infant and Toddler Development (BSID-III) has been developed,¹⁰ and is now being used exclusively throughout the Eunice Kennedy Shriver National Institute of Child Health and Human Development Neonatal Research Network (NRN) centers. The newer BSID-III has a separate language composite score that is further subdivided into expressive and receptive components. This more detailed characterization of language development may facilitate a better understanding of the development of cognitive function. However, the effect of race and ethnicity on BSID-III scores has not been described, and must be assessed in order to determine whether this may be a psychosocial factor associated with BSID-III scores, as was the case with the BSID-II. In addition, the inclusion of a separate language domain may affect the previously noted association between race/ethnicity and BSID scores, but this has yet to be determined.

The objectives of this study were to compare cognition and language scores in extremely preterm children at 18 to 22 months corrected age as measured by the BSID-III among different racial and ethnic groups while adjusting for various medical and psychosocial factors, including maternal education level. We hypothesized that 1) differences would be found between groups on the BSID-III composite scores of cognition and language at 18 to 22 months corrected age in children who were born <28+0 weeks estimated gestational age (EGA), 2) differences between groups would be found in the expressive language subtest,¹¹ and 3) identifiable medical and psychosocial factors would be associated with any observed racial and ethnic differences in cognitive and language skills measured on the BSID-III.

METHODS

This study was a retrospective cohort study of children born at <28+0 weeks EGA at the sixteen centers of the NRN who were evaluated at 18 to 22 months adjusted age during the period of January, 2008 to June, 2009. Based on historic enrollment patterns in the NRN, we restricted this study to infants coded "White", "Black" and "Hispanic-White" to have an adequate sample size in each cell of >30 subjects. Sample size calculations indicated that a sample size of 369 Whites, 162 Blacks and 79 Hispanic-Whites would be adequate to detect a difference between groups of one-half standard deviation on each of the BSID-III cognitive and language composite scores with 90% power. Therefore, given past NRN

enrollment patterns, the population anticipated to be evaluated January, 2008 to June, 2009 was considered more than adequate to evaluate the hypotheses proposed for this study. All subject data were collected prospectively.

The study sample included all children born <28+0 weeks EGA in the three race and ethnic groups who were evaluated using the BSID-III examination and a neuromotor examination at 18 to 22 months corrected age. Children with missing values for BSID-III scores or race and ethnicity were excluded from this study, as were children in race and ethnic groups containing 30 children as described above. Subject data were collected from the NRN Generic Follow-up Database.¹²

Bayley Scales of Infant Development, 3rd edition

BSID-III scores range from 55–145 for the cognitive scale and 45–155 for the language composite scale, with scores of 100 ± 15 representing the mean $\pm$ 1 SD. The average reliability coefficients for the BSID-III scales in premature infants are all greater than 0.94.¹⁰ For this study, the BSID-III was administered by experienced testers at each site who had been certified by one of four NRN gold standard examiners. The BSID-III was administered in Spanish to those children whose primary language was identified as Spanish. In these instances, either a bilingual examiner administered the test or an interpreter was used to translate the test items.

BSID-III Cognitive scale: Cognitive function is assessed by examining the following cognitive constructs: 1) Sensorimotor development, 2) Exploration and manipulation, 3) Object relatedness, 4) Concept formation, 5) Memory, 6) Habituation, 7) Visual acuity, 8) Visual preference, and 9) Object permanence.

BSID-III Composite Language scale: Language development scores are composed of the combination of the expressive and receptive scores. The Expressive Language subtest measures the ability to communicate, either through words or gestures. The Receptive Language subtest tests the ability to comprehend and respond appropriately to words and requests.

Neuromotor Examination

The neuromotor examination is performed by a certified NRN examiner. The Gross Motor Function Classification System (GMFCS)¹³ for cerebral palsy is a classification system that spans from 0–5 (0 = normal) and is based on self-initiated movement with emphasis on sitting (truncal control) and walking. Moderate to severe cerebral palsy is defined as a nonprogressive central nervous system disorder characterized by abnormal muscle tone in at least one extremity and abnormal control of movement and posture which interfered with or prevented age appropriate activities and a GMFCS score of ≥ 2 .

Statistical Analysis

Primary outcome variables included the mean BSID-III Cognitive score, Composite Language score, Expressive Language score, and Receptive Language score. Race and ethnicity group was the primary independent variable. Key medical and psychosocial variables previously shown to adversely impact neurodevelopmental outcomes in at-risk children^{14–16} were specifically chosen as covariates and were collected from the NRN database. Medical and psychosocial variables that were adjusted for included: sex, center, adjusted age at testing, primary caretaker education, birth weight, gestational age, multiple gestation, presence of culture positive nosocomial sepsis, bronchopulmonary dysplasia (BPD), Grade III or IV intraventricular hemorrhage (IVH) or cystic periventricular leukomalacia (PVL), postnatal steroid use, GMFCS Level ≥ 2 , and blindness or deafness at

18–22 month follow-up. Center was included as a covariate as a proxy for socioeconomic status, as each center may serve patients of in different socioeconomic strata.

Demographic characteristics of the three groups were compared using chi-square tests for categorical characteristics. BSID-III mean scores were first compared between groups using Analysis of Variance (ANOVA) with BSID-III score as the outcome variable and race and ethnicity category as the sole explanatory variable. Next, multivariable regression modeling using Analysis of Covariance (ANCOVA) was performed to examine the association of BSID-III score with race and ethnicity while controlling for medical and psychosocial variables. The adjusted means from these models were compared among groups and provide an estimate of the mean BSID-III scores by group for the average value of the specified medical and psychosocial confounders included in the model. Adjusted p-values comparing BSID-III score between race and ethnic groups were obtained from this second model. A p-value<0.05 determined statistical significance. Pairwise comparisons between race groups were adjusted for multiple comparisons using the Bonferroni correction.

RESULTS

The study population consisted of 865 extremely preterm children. Population characteristics are shown in Tables I, II, and III.

Cognitive Scale

The mean BSID-III cognitive score was significantly lower than the expected mean of 100 in all three groups. However, the score was significantly higher in the White group than in either the Black or Hispanic-White groups when no adjustment was made for medical or psychosocial covariates (Table IV). When cognitive scores were adjusted for either medical or psychosocial covariates alone, this difference remained. However, adding medical and psycho-social factors together resulted in loss of significance between groups. Backward selection was then performed, retaining only factors at p 0.05 level. In this model, birth weight, grade III or IV IVH, nosocomial sepsis, multiple gestation, GMFCS 2, blindness, sex and primary caretaker education appeared to jointly account for the loss of significance in scores between groups.

Language Scales

The mean BSID-III composite language score was significantly lower than the expected mean of 100 in all three groups. Analyses showed that both the mean composite language score and the receptive and expressive language scale scores were significantly different among the three race and ethnic groups both with and without adjustment for medical and psychosocial covariates. Post-hoc analyses showed that White children had higher scores than the other two groups on all three scales. Composite and expressive language scores were not different between Blacks and Hispanic-White. Although Blacks scored higher than Hispanic-Whites on the receptive language subscale this difference was not significant once adjustment was made.

Early Intervention

In our study population, 63.4% of White infants, 55.1% of Black infants and 54.9% of Hispanic-White infants were reported as needing early intervention. For White infants, 57.8% were receiving early intervention at 18–22 months and an additional 17.9% had received early intervention at some point but discontinued prior to their 18–22 month visit. For Black infants, 43.8% were still receiving early intervention, and 16.8% had received early intervention but discontinued. For Hispanic-White infants, 47.5% were still receiving early intervention, and 20.8% had received early intervention but discontinued. The p-value

for comparing receipt of early intervention (yes or no) between race/ethnicity groups was <0.001 . Furthermore, infants that received early intervention at any point (discontinued or still receiving) tended to have lower cognition scores, and infants that were still receiving early intervention at 18 to 22 months tended to have lower scores for all language outcomes. As a post-hoc analyses, we included receipt of early intervention in the models described above as an additional covariate. The inclusion of this variable did not change the relationship between race and ethnicity and the cognitive or language scores.

DISCUSSION

We have shown that race and ethnicity are associated with cognitive and language scores on the BSID-III. Even though differences in the cognitive scores were explained by a combination of medical and psychosocial factors, these factors did not account for the differences identified in language scores. The identification of specific medical and psychosocial factors associated with increased risk for cognitive impairment may allow more targeted early intervention. Our finding that language differences were sustained in minority groups regardless of other risk factors provides a compelling argument for focusing early intervention programs on the attainment of language in these groups. In addition, as BSID-III scores were below expected in *all three* race and ethnic groups included, this study highlights the continued need for monitoring and provision of early intervention in all at-risk groups.

Difficulties with cognition, attention and self-regulation seen in children born at lower birth weights can persist throughout childhood and are associated with an increased incidence of learning difficulties.¹⁻⁵ Because early childhood intervention results in improvements in developmental and social outcomes,^{6,7} early assessment of cognitive functioning in these children is extremely important. We have shown that cognition and language scores were lower for infants receiving early intervention. Receipt of early intervention identified infants in our database that were likely to have lowered cognitive/language scores. It is thus likely that infants that receive early intervention are selected to receive this intervention because caretakers believe they are predisposed to have developmental deficits.

In the current study, we found that BSID-III cognitive scores were no longer different between race and ethnic groups after adjustment for a combination of psychosocial and medical factors. In our previous study using the BSID-II, however, race and ethnic differences remained even after adjustment.⁹ This difference may be due to the inclusion of a separate language domain in the BSID-III. Ethnic and cultural influences may be of less concern for cognitive development than previously believed, and our results highlight the importance of conducting future studies of assessment of language development in this population.

In a recent meta-analysis, Aylward¹ found that expressive language skills, such as verbal production and mean length of utterances, were lower in preterm children, and that these skills were susceptible to environmental influences. The BSID-III language scales now provide us with a tool to look specifically at language skills in preterm children, and separate out receptive and expressive language skills. Because receptive language skills were lower in Hispanic-White children than Black children, we speculate that non-English primary language may contribute to this finding. However, language scores were lower in both Black and Hispanic-White children compared with Whites, indicating that language delays may be more prevalent in both groups, but this requires further study.

This study had several important limitations that should be addressed in future studies. First, defining race and ethnicity is often difficult due to the variability in reporting of the

measure. For instance, race and ethnicity may be collected via subject self-report, direct observation of the subject, proxy report, or extraction from medical records. This variability may decrease the reliability and validity of the measure. Self-report is the most reliable method of collecting race and ethnicity information, and is thus preferred for data collection and study;¹⁷ this is the method which we utilized. In addition, the Office of Management and Budget has defined minimum acceptable standards for collecting and presenting race and ethnicity data, and we have met those standards.¹⁷ Though we have used the most reliable method of measurement of race/ethnicity, the risk of error in this measurement still exists, and the influence of such an error on the study results is unknown. We have attempted to limit the effect of this possible confounding by including socioeconomic status as a separate variable in the analysis.

Perhaps the greatest limitation of this study is the fact that there is not a standardized Spanish version of the BSID-III, and there is thus no evidence that the BSID-III administered to Spanish-speaking children in the manner that we have described is valid or reliable. There may have been differences in interpretation between test administrators, and the effect of this is unknown. In addition, it is not known whether those children for whom their primary language was identified as Spanish were bilingual Spanish/English speakers or monolingual Spanish speakers. This heterogeneity could bias our results and makes interpretation of the language score data difficult. Further study on how language use during BSID-III administration influences test results is greatly needed. The association between race and ethnicity and language score should not be completely discounted, however, as Black children also scored significantly lower than Whites on the language portion of the BSID-III, and this difference is unexplained by non-English language, as there was only one child in the study identified as Black for whom the primary language was identified as Spanish.

The use of backward selection in our secondary post-hoc analyses may also be a limitation of this study, and in future studies a cross-validation approach might be more useful in identifying predictive factors. The inclusion of receipt of early intervention may also be a limitation of the study, as there was no control for the *type* of early intervention given; our data collection included only whether or not the child received any early intervention. Early intervention services may be extremely heterogeneous, and future studies should consider comparison of intervention types in at-risk children of different races and ethnicities. Finally, though we have shown important associations between psychosocial factors such as race and ethnicity and medical morbidities with BSID-III scores, our study design does not allow causal inference based upon our results. Though we have attempted to address this by adjusting for medical and psychosocial factors, we do not know whether we have adjusted for all potentially important covariates or confounders. Future studies should be designed to specifically assess whether there is differential prediction of developmental outcomes between groups.

In conclusion, the racial and ethnic group differences on the BSID-III cognitive scale observed in this study were explained by a combination of medical and psychosocial factors. Black and Hispanic-White children were at greater risk for delayed language than White children, highlighting the need for further study and possibly specific programs focused on language skills in these groups. This study provides an important step in better understanding the impact of race and ethnicity on the newly revised BSID-III and has important implications for the refinement of early intervention strategies among children with a history of preterm birth by delineating modifiable factors underlying race and ethnic disparities in neurodevelopmental test results in these children.

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List of Abbreviations

ANCOVA	Analysis of Covariance
ANOVA	Analysis of Variance
BPD	Bronchopulmonary Dysplasia
BSID	Bayley Scales of Infant and Toddler Development
BSID-II	Bayley Scales of Infant and Toddler Development, 2 nd edition
BSID-III	Bayley Scales of Infant and Toddler Development, 3 rd edition
EGA	Estimated Gestational Age
GMFCS	Gross Motor Function Classification System
IVH	Intraventricular Hemorrhage
MDI	Mental Developmental Index
NICHD	Eunice Kennedy Shriver National Institute of Child Health and Human Development
NRN	Eunice Kennedy Shriver National Institute of Child Health and Human Development Neonatal Research Network
PVL	periventricular leukomalacia

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Appendix

Data collected at participating sites of the NICHD Neonatal Research Network (NRN) were transmitted to RTI International, the data coordinating center (DCC) for the network, which stored, managed and analyzed the data for this study.

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Table 1

Study Population Demographic and Baseline Characteristics During Hospitalization

	White (N=369)	Black (N=352)	Hispanic-White (N=144)	Total (N=865)	P-value
Gestational age at birth (weeks)					
n	369	352	144	865	0.1061
Mean (StdDev)	25.5 (1.12)	25.3 (1.24)	25.4 (1.09)	25.4 (1.16)	
Range	23–27	22–27	22–27	22–27	
Multiple gestation: n (%)					
No	251/369 (68.0)	274/352 (77.8)	105/144 (72.9)	630/865 (72.8)	0.0125
Yes	118/369 (32.0)	78/352 (22.2)	39/144 (27.1)	235/865 (27.2)	
Birth weight (g)					
n	369	352	144	865	0.0145
Mean (StdDev)	811 (173)	777 (162)	810 (159)	797 (167)	
Range	440–1276	410–1250	510–1230	410–1276	
Sex: n (%)					
Female	181/369 (49.1)	178/352 (50.6)	68/144 (47.2)	427/865 (49.4)	0.7857
Male	188/369 (50.9)	174/352 (49.4)	76/144 (52.8)	438/865 (50.6)	
BPD: n (%)					
No	160/365 (43.8)	188/348 (54.0)	78/142 (54.9)	426/855 (49.8)	0.0103
Yes	205/365 (56.2)	160/348 (46.0)	64/142 (45.1)	429/855 (50.2)	
Postnatal steroids: n (%)					
No	312/362 (86.2)	311/348 (89.4)	125/144 (86.8)	748/854 (87.6)	0.4177
Yes	50/362 (13.8)	37/348 (10.6)	19/144 (13.2)	106/854 (12.4)	
Grade III or IV IVH: n (%)					
No	316/368 (85.9)	306/349 (87.7)	119/143 (83.2)	741/860 (86.2)	0.4193
Yes	52/368 (14.1)	43/349 (12.3)	24/143 (16.8)	119/860 (13.8)	
Cystic PVL: n (%)					
No	352/369 (95.4)	334/351 (95.2)	136/144 (94.4)	822/864 (95.1)	0.9041
Yes	17/369 (4.6)	17/351 (4.8)	8/144 (5.6)	42/864 (4.9)	
Nosocomial sepsis: n (%)					
No	250/369 (67.8)	187/352 (53.1)	88/144 (61.1)	525/865 (60.7)	0.0003

	White (N=369)	Black (N=352)	Hispanic-White (N=144)	Total (N=865)	P-value
Yes	119/369 (32.2)	165/352 (46.9)	56/144 (38.9)	340/865 (39.3)	

Table 2

Study Population Demographic and Baseline Characteristics at 18–22 Month Follow-up

	White (N=369)	Black (N=352)	Hispanic-White (N=144)	Total (N=865)	P-value
Adjusted age for BSID-III cognitive subscale (months)					
n	368	351	144	863	0.0986
Mean (StdDev)	19.7 (1.38)	19.5 (1.39)	19.5 (1.35)	19.6 (1.38)	
Range	18–22	18–22	18–22	18–22	
Adjusted age for BSID-III receptive language subscale (months)					
n	366	346	141	853	0.1297
Mean (StdDev)	19.7 (1.38)	19.5 (1.39)	19.5 (1.36)	19.6 (1.38)	
Range	18–22	18–22	18–22	18–22	
Adjusted age for BSID-III expressive language subscale (months)					
n	362	348	139	849	0.0885
Mean (StdDev)	19.7 (1.38)	19.5 (1.39)	19.5 (1.37)	19.6 (1.38)	
Range	18–22	18–22	18–22	18–22	
Weight at testing (kg)					
n	369	352	143	864	0.4282
Mean (StdDev)	10.7 (1.34)	10.8 (1.50)	10.6 (1.32)	10.7 (1.40)	
Range	7–15	7–16	8–15	7–16	
Length at testing (cm)					
n	369	351	143	863	0.7787
Mean (StdDev)	81.1 (3.58)	80.9 (3.97)	80.8 (3.14)	81.0 (3.68)	
Range	71–92	67–91	72–91	67–92	
Head circumference at testing (cm)					
n	369	352	143	864	0.0807
Mean (StdDev)	47.1 (1.94)	46.8 (2.06)	47.1 (1.84)	47.0 (1.98)	
Range	36–54	36–55	44–54	36–55	
GMFCS 2: n (%)					
No	351/369 (95.1)	330/352 (93.8)	138/144 (95.8)	819/865 (94.7)	0.5692
Yes	18/369 (4.9)	22/352 (6.3)	6/144 (4.2)	46/865 (5.3)	
Blind: n (%)					

	White (N=369)	Black (N=352)	Hispanic-White (N=144)	Total (N=865)	P-value
No	368/369 (99.7)	347/352 (98.6)	142/144 (98.6)	857/865 (99.1)	0.2231
Yes	1/369 (0.3)	5/352 (1.4)	2/144 (1.4)	8/865 (0.9)	
Hearing Impaired: n (%)					
No	360/369 (97.6)	336/352 (95.5)	139/143 (97.2)	835/864 (96.6)	0.2690
Yes	9/369 (2.4)	16/352 (4.5)	4/143 (2.8)	29/864 (3.4)	

Table 3

Maternal/Primary Caretaker Characteristics For Study Population

	White (N=369)	Black (N=352)	Hispanic-White (N=144)	Total (N=865)	P-value
Maternal age (years)					
N	369	352	144	865	<.0001
Mean (StdDev)	28.5 (6.39)	26.0 (6.31)	27.8 (6.67)	27.4 (6.50)	
Range	16–48	12–43	16–42	12–48	
Primary caretaker education: n (%)					
< 7th grade	1/349 (0.3)	2/331 (0.6)	17/135 (12.6)	20/815 (2.5)	<.0001
7th to 9th grade	7/349 (2.0)	7/331 (2.1)	21/135 (15.6)	35/815 (4.3)	
10th to 12th grade	24/349 (6.9)	63/331 (19.0)	22/135 (16.3)	109/815 (13.4)	
High school degree	82/349 (23.5)	111/331 (33.5)	31/135 (23.0)	224/815 (27.5)	
Partial college	102/349 (29.2)	96/331 (29.0)	25/135 (18.5)	223/815 (27.4)	
College degree	89/349 (25.5)	39/331 (11.8)	9/135 (6.7)	137/815 (16.8)	
Graduate degree	43/349 (12.3)	10/331 (3.0)	6/135 (4.4)	59/815 (7.2)	
Unknown	1/349 (0.3)	3/331 (0.9)	4/135 (3.0)	8/815 (1.0)	
Primary language used in household: n (%)					
English	358/369 (97.0)	342/352 (97.2)	43/144 (29.9)	743/865 (85.9)	<.0001
Other	11/369 (3.0)	10/352 (2.8)	101/144 (70.1)	122/865 (14.1)	

Table 4

Association Between Race/Ethnicity and BSID III Score

	White (N=369)	Black (N=352)	Hispanic-White (N=144)	Total (N=865)	P-value [1]
BSID-III					
Cognitive					
Mean (StdDev)	91.9 (14.50)	88.2 (14.38)	88.2 (14.37)	89.8 (14.53)	0.0009
Range	54–140	54–130	54–120	54–140	
Adjusted Mean (StdErr)	68 (2.7)	66 (2.7)	65 (2.7)		0.1293
Language					
Mean (StdDev)	89.7 (17.54)	81.8 (16.08)	79.2 (16.88)	84.7 (17.39)	<.0001
Range	46–144	46–118	46–135	46–144	
Adjusted Mean (StdErr)	61 (3.5)	55 (3.4)	53 (3.4)		<.0001
Expressive					
Mean (StdDev)	8.3 (2.96)	7.4 (2.78)	6.9 (2.86)	7.7 (2.92)	<.0001
Range	1–17	1–14	1–16	1–17	
Adjusted Mean (StdErr)	6 (0.5)	5 (0.5)	4 (0.5)		0.0003
Receptive					
Mean (StdDev)	8.4 (3.04)	7.0 (2.50)	6.2 (3.01)	7.5 (2.95)	<.0001
Range	1–18	1–13	1–17	1–18	
Adjusted Mean (StdErr)	6 (0.5)	5 (0.5)	4 (0.5)		0.<0.0001

[1] P-values for 'Mean (StdDev)' rows obtained from an ANOVA model with the score of interest as the outcome and Race/Ethnicity as the explanatory variable. Adjusted means and the corresponding p-values obtained from an ANCOVA model with the score of interest as the outcome, Race/Ethnicity as the explanatory variable and controlling for medical and socioeconomic factors.