The Relationship of Maternal Prepregnancy Body Mass Index and Pregnancy Weight Gain to Neurocognitive Function at Age 10 Years among Children Born Extremely Preterm

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Objective To assess the association between maternal prepregnancy body mass index and adequacy of pregnancy weight gain in relation to neurocognitive function in school-aged children born extremely preterm.

Study design Study participants were 535 ten-year-old children enrolled previously in the prospective multicenter Extremely Low Gestational Age Newborns cohort study who were products of singleton pregnancies. Soon after delivery, mothers provided information about prepregnancy weight. Prepregnancy body mass index and adequacy of weight gain were characterized based on this information. Children underwent a neurocognitive evaluation at 10 years of age.

Results Maternal prepregnancy obesity was associated with increased odds of a lower score for Differential Ability Scales-II Verbal IQ, for Developmental Neuropsychological Assessment-II measures of processing speed and visual fine motor control, and for Wechsler Individual Achievement Test-III Spelling. Children born to mothers who gained an excessive amount of weight were at increased odds of a low score on the Oral and Written Language Scales Oral Expression assessment. Conversely, children whose mother did not gain an adequate amount of weight were at increased odds of a lower score on the Oral and Written Language Scales Oral Expression and Wechsler Individual Achievement Test-III Word Reading assessments.

Conclusion In this cohort of infants born extremely preterm, maternal obesity was associated with poorer performance on some assessments of neurocognitive function. Our findings are consistent with the observational and experimental literature and suggest that opportunities may exist to mitigate risk through education and behavioral intervention before pregnancy. *(J Pediatr 2017;■■:■■-■■).*

See editorial, p •••

More than one-third of all women of childbearing age in the US are obese (body mass index [BMI] ≥ 30 kg/m^2).[1] The relationship between maternal obesity and neurocognitive function in children has been studied extensively, and a majority of studies associate impaired neurocognitive function with maternal obesity, although conclusions differ as to whether this association arises from a state of obesity before pregnancy, from excess weight gain during pregnancy, or both. Some studies evaluated preschool children,[2-5] at ages when assessments of neurocognitive function are less reliable or stable than at older ages,[6] which is pertinent especially to studies of children born preterm.[7,8]

Children born premature are at increased risk for neurocognitive impairment,[9,10] with the greatest risk occurring among extremely preterm births (<28 weeks' gestation).[11] Although the long-term neurodevelopmental and cognitive outcomes of children born preterm generally are well-described, less is known about antecedents and modifiers of this association. We are not aware of any study that assessed the relationship between the mother's adiposity and her child's neurocognitive function at age 10 years. Identification of such a relationship would

BMI	Body mass index
DAS-II	Differential Ability Scales-II
NEPSY-II	Developmental Neuropsychological Assessment-II
OWLS	Oral and Written Language Scales
WIAT-III	Wechsler Individual Achievement Test-III

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strengthen the justification to develop strategies for weight management among women who are planning to conceive and women at risk of having a preterm delivery.

Previously, in a cohort of children born extremely preterm (<28 weeks), the Extremely Low Gestational Age Newborns study, we described an association between maternal prepregnancy obesity and developmental delay at 2 years adjusted age.[12] In the present study, we extend this line of research by evaluating the relationship of both prepregnancy BMI and pregnancy weight gain to neurocognitive and academic outcomes at 10 years of age. We hypothesized that maternal obesity and excessive pregnancy weight gain are associated with less favorable neurocognitive and academic outcomes at school age.

Methods

The Extremely Low Gestational Age Newborns study is a multicenter prospective, observational study of the risk of structural and functional neurologic disorders in infants born extremely preterm.[13] A total of 1506 infants born before the 28th week of gestation were enrolled during the years 2002-2004 and 1200 survived to 2 years, when 1102 returned for a developmental assessment.[14] At age 10 years, 889 (92%) of 966 children who were recruited actively for follow-up (because of the availability of data on inflammation-related proteins in blood samples from their first postnatal month) returned for an assessment of cognitive skills and academic achievement. Of the 889 children, the mothers of 32 did not provide measures necessary for calculating BMI, and an additional 12 did not provide information necessary for calculating adequacy of pregnancy weight gain. Among these 845 children were 535 singletons. We excluded all multiple births. The institutional review boards of all participating institutions approved enrollment and consent procedures for this follow-up study.

After delivery, a trained research nurse interviewed each mother using a structured data collection form and defined procedures for the interview process. Following the mother's discharge, the research nurse reviewed the maternal chart using a second structured data collection form. The medical record was the source of information about events during the mother's and infant's hospitalization. Gestational age estimates were based on a hierarchy of the quality of available information. Most desirable were estimates based on the dates of embryo retrieval or intrauterine insemination or fetal ultrasound before the 14th week (413/535 = 77%). When these were not available, reliance was placed sequentially on a fetal ultrasound at ≥14 weeks (105/535 = 20%), last menstrual period without fetal ultrasound (16/535 = 3%), and gestational age recorded in the log of the neonatal intensive care unit (1/535 = 0/.2%).

Each mother was asked to provide her height and her prepregnancy weight. These were used to calculate her prepregnancy BMI. BMI was characterized as underweight (<18.5 kg/m^2), normal weight (18.5-24.9 kg/m^2), overweight (25.0-29.9 kg/m^2), and obese (≥30.0 kg/m^2).[15] Adequacy of pregnancy weight gain at delivery (insufficient, adequate, more than adequate) was characterized by comparing the maternal weight at delivery with the adequacy of weight gain as defined by the Institute of Medicine, based on prepregnancy BMI status (underweight, overweight, or obese, as defined previously) (**Table I**; available at www.jpeds.com).[16]

Participating families were scheduled for a single visit, during which all of the measures reported in the present study were administered. Assessments of both children and their mothers were completed. For mothers, the Kaufman Brief Intelligence Test-2[17] was administered. Assessments of children were completed in 3-4 hours, including breaks. The assessments were selected to provide the most comprehensive information about neurocognitive and academic function in a single testing session. The tests administered were well-validated and provided recently normed standard scores, thus allowing comparison with US population norms. The test measures and outcomes of interest for the children are described briefly to follow.[18]

General Cognitive Ability (IQ)

General cognitive ability (IQ) was assessed with the School-Age Differential Ability Scales-II (DAS-II) Verbal and Nonverbal Reasoning scales.[19]

Language

Expressive and receptive language skills were evaluated with the Oral and Written Language Scales (OWLS), which assess semantic, morphologic, syntactic, and pragmatic production and comprehension of elaborated sentences.[20]

Executive Function

Executive function was assessed with both the DAS-II Working Memory scale[19] and the NEPSY-II (Developmental Neuropsychological Assessment-II).[21] The DAS-II Recall of Digits Backward and Recall of Sequential Order subtests measure verbal working memory, whereas the NEPSY-II Auditory Attention and Response Set measures auditory attention, set switching, and inhibition. NEPSY-II Inhibition Inhibition and Inhibition Switching measure simple inhibition and inhibition in the context of set shifting, respectively, and Animal Sorting measures visual concept formation and set shifting.

Processing Speed, Visual Perception, and Visual-Motor Function

Speed of processing was assessed with the NEPSY-II Inhibition Naming task, which provides a baseline measure of processing speed and has no inhibitory component. Visual perception was assessed with NEPSY-II Arrows and Geometric Puzzles tasks, whereas visual fine motor function was measured with the NEPSY-II Visuomotor Precision task.

Academic Achievement

Wechsler Individual Achievement Test-III (WIAT-III) subtests administered included Word Reading (speed and accuracy of word recognition), Pseudoword Decoding (single-word decoding), Spelling (written spelling of single words), and Numerical Operations (written math calculation skills).[22]

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