

## RESEARCH LETTERS

### Prenatal and Perinatal Risk Factors for Attention-Deficit/Hyperactivity Disorder

**A**ttention-deficit/hyperactivity disorder (ADHD), a highly persistent and prevalent pediatric disorder, constitutes substantial burden to affected patients, their families, and society.<sup>1</sup> Apart from genetics, environmental risk factors relevantly contribute to the etiology of ADHD.<sup>1</sup> With great interest, we read the article by Nomura et al<sup>2</sup> recently published in the *Archives* suggesting that the combination of maternal gestational diabetes mellitus (GDM) and low socioeconomic position (SEP) is a strong risk factor for childhood ADHD. Limitations of this study are the selected study base and the relatively small sample size.<sup>2</sup> We aimed to replicate the findings in a large population-based sample.

**Methods.** The German Health Interview and Examination Survey for Children and Adolescents (KiGGS) is a nationwide representative survey on the health status of German children and adolescents in 2003 to 2006 (N=17 642; aged 0-17 years).<sup>3</sup> We used the public use file of KiGGS, which does not contain any personal identifiers; thus, ethical approval was not required. Data from

all participants aged 3 to 17 years (n=13 488) were included. The outcome of interest was lifetime diagnosis of ADHD on the basis of medical or psychological examination as reported in standardized parental interviews conducted by trained interviewers.<sup>3</sup> In Germany, ADHD is generally diagnosed according to the *International Statistical Classification of Diseases, 10th Revision* criteria of "hyperkinetic disorder" that largely correspond with the criteria of the *Diagnostic and Statistical Manual of Mental Disorders* (Fourth Edition, Text Revision) definition of ADHD combined subtype.<sup>1</sup> Primary exposures of interest were self-reported physician-diagnosed GDM (absent/present) and SEP classified as low, medium, or high based on parental education, professional qualification, professional status, and family net income.<sup>4</sup> Additionally, age, sex, and a broad set of environmental exposures in the prenatal/perinatal period and in infancy such as breastfeeding (ever vs never fully breastfed); postnatal health problems including breathing problems, maladaptation, infections, jaundice, low birth weight and/or premature delivery, and inpatient treatment (present/absent); maternal smoking/drinking during pregnancy (ever/never); and physician-diagnosed atopic eczema<sup>5</sup> (ever/never) were considered as competing risk factors in multivariate logistic regression models based on 11 222 observations without missing data. Additive and multiplicative interaction was explored by combining SEP and GDM into 1 variable (reference: no GDM, high SEP). To assess the mode of interaction (additive or multiplicative), we compared the expected odds ratios (ORs) on the basis of single exposures with the ob-

**Table. Sample Characteristics and Risk Factors of ADHD in Children and Adolescents**

Characteristic/Exposure (Reference for Regression Analyses)	Sample Characteristics, No. (%) <sup>a</sup>		Logistic Regression Analysis, OR (95% CI)	
	Children With ADHD (n = 660)	Children Without ADHD (n = 12 828)	Bivariable (Unadjusted) Analysis	Multivariable (Adjusted) Analysis <sup>b</sup>
Sex (reference: female)	133 (20.2)	6604 (51.5)	4.20 (3.47-5.10)	4.42 (3.56-5.49)
Age, y, mean (SD)	9.8 (4.3)	11.3 (3.4)	1.08 (1.06-1.11)	1.09 (1.07-1.11)
Socioeconomic position <sup>c</sup>				
Upper class (reference)	114 (17.4)	3486 (27.3)	1 [Reference]	1 [Reference]
Middle class	325 (49.5)	6087 (47.7)	1.63 (1.31-2.03)	1.57 (1.23-2.00)
Lower class	218 (33.2)	3202 (25.1)	2.08 (1.65-2.62)	2.04 (1.56-2.68)
Maternal gestational diabetes mellitus (reference: absent)	24 (4.1)	256 (2.2)	1.93 (1.26-2.95)	1.91 (1.21-3.01)
Maternal smoking during pregnancy (reference: never)	158 (24.6)	2081 (16.4)	1.66 (1.38-2.00)	1.48 (1.19-1.84)
Maternal alcohol consumption during pregnancy (reference: never)	96 (14.8)	1775 (14.0)	1.07 (0.86-1.34)	1.02 (0.79-1.33)
Perinatal health problems (reference: absent) <sup>d</sup>	235 (36.2)	2955 (23.2)	1.88 (1.60-2.22)	1.69 (1.40-2.03)
Breastfeeding (ever vs never fully breastfeeding)	345 (56.7)	7943 (67.5)	0.63 (0.54-0.74)	0.83 (0.69-0.996)
Atopic eczema (ever vs never)	132 (20.2)	1820 (14.4)	1.51 (1.24-1.84)	1.62 (1.30-2.02)

Abbreviations: ADHD, attention-deficit/hyperactivity disorder; OR, odds ratio.

<sup>a</sup>Numbers represent number (proportion) of children per exposed for discrete variables and means (SD) for continuous variables.

<sup>b</sup>Adjusted for all exposures listed in the Table; analysis based on 11 222 observations without any missing data.

<sup>c</sup>Classified based on parental education, professional qualification, professional status, and family net income according to Winkler and Stolzenberg.<sup>4</sup>

<sup>d</sup>Breathing problems, maladaptation, infections, icterus, low birth weight/premature delivery, and/or inpatient treatment.

served OR of combined exposure to GDM and SEP.<sup>6</sup> Data were analyzed using Stata (StataCorp).

**Results.** Mean participant age was 9.9 years; 50.1% (n=6751) were female. The prevalence of ADHD, GDM, and low SEP was 4.9% (n=660), 2.3% (n=280), and 25.5% (n=3420), respectively. Both maternal GDM and low SEP were significantly related to ADHD (**Table**). Multivariate regression modeling indicated that not only GDM (OR, 1.91; 95% CI, 1.21-3.01) and low SEP (OR, 2.04; 95% CI, 1.56-2.68) but also perinatal health problems, maternal smoking during pregnancy, and atopic eczema are independent risk factors for ADHD, whereas fully breastfeeding appears to be protective (irrespective of the duration of breastfeeding; data not shown). Further analyses indicated the presence of additive interaction between maternal GDM and SEP on the risk of ADHD (observed OR for middle-class children exposed to GDM: 3.47; expected OR: 2.93; observed OR for lower-class children exposed to GDM: 3.68; expected OR: 3.56).

**Comment.** Our study confirms the previously reported<sup>2</sup> association between low SEP, maternal GDM, and ADHD and their additive interaction as risk factors for ADHD in a large population-based sample. Extending previous research, our study indicates that fully breastfeeding may have protective effects on childhood ADHD. Exposure to maternal smoking in pregnancy and perinatal health problems do seem to increase the risk for ADHD. Modification of these environmental risk factors by evidence-based prevention programs may help to decrease the burden of ADHD.

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**Published Online:** September 10, 2012. doi:10.1001/archpediatrics.2012.1078

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**Author Contributions:** *Study concept and design:* Schmitt and Romanos. *Analysis and interpretation of data:* Schmitt and Romanos. *Drafting of the manuscript:* Schmitt and Romanos. *Critical revision of the manuscript for important intellectual content:* Romanos. *Statistical analysis:* Schmitt. *Administrative, technical, and material support:* Schmitt.

**Financial Disclosure:** None reported.

**Additional Contributions:** We thank the Robert Koch Institute for making the data of the KiGGS study available and all participants for their time and information.

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## Agreement Between Bayley Scales Second and Third Edition Assessments of Very Low-Birth-Weight Infants

The Bayley Scales of Infant Development (BSID) are the most widely used assessments to identify children with developmental delay. Between 1993 and 2006, the BSID-Second Edition (BSID-II)<sup>1</sup> was used; in 2006, a third edition (BSID-III)<sup>2</sup> was published.

Rather than the 2-factor model of the BSID-II that described mental and psychomotor development, the BSID-III purports to assess 5 separate areas: cognition, language, motor, social-emotional, and adaptive. The aim of this study was to compare the BSID-II Mental and Motor scale scores and the BSID-III Motor, Cognitive, and Language scale scores in a cohort of very low-birth-weight preterm infants.

**Methods.** This study was approved by our institutional ethics committee, and informed consent was obtained for all participants.

We enrolled preterm infants with a birth weight less than 1500 g and gestational age less than 32 weeks, who were born in the Hospital de Clínicas de Porto Alegre, a level 3 referral center for high-risk neonates in southern Brazil, and survived to 24 months of age. We excluded infants with major congenital malformations, inborn errors, or chromosomal anomalies, congenital infections, severe hearing loss, blindness, or severe cerebral palsy.

**Neurodevelopmental Assessments.** The BSID-II was administered at 22 to 24 months' corrected age, immediately before a follow-up visit to our Follow-up Clinic. The BSID-II yields a Mental Development Index and Psychomotor Development Index. Within 2 months after the assessment with the BSID-II, study participants were assessed using the BSID-III, which yields Cognitive, Language, and Motor scale scores. A single psychologist (G.R.F.) administered the BSID-II and BSID-III in Portuguese.

**Statistical Analyses.** Comparison between groups was performed with a 2-tailed  $\chi^2$  test or Fisher exact test for categorical variables and a *t* test or Mann-Whitney test for continuous variables.

**Results.** During the study period, 60 children met inclusion criteria and underwent BSID-II and BSID-III assessments at 22 to 24 months' corrected age. The mean