

# The Role of Executive and General Cognitive Functioning in the Attention Problems of Very and Extremely Preterm Adults

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**ABSTRACT:** *Objective:* To determine whether the attention problems in adults born very preterm/very low birth weight (VP/VLBW; <32 weeks' gestation/<1500 g) or extremely preterm (EP; <26 weeks' gestation) are associated with specific executive or general cognitive deficits. *Method:* Cohorts of VP/VLBW (the Bavarian Longitudinal Study [BLS]) and EP (the EPICure Study) participants were followed from birth to early adulthood, each also following a respective control group. Adult attention deficit hyperactivity disorder (ADHD) symptoms were assessed via self-report in both cohorts and additionally by parent report in the BLS. Participants in both cohorts also had their attention span rated by trained observers. Performed separately in each cohort, hierarchical regression analyses were used to assess whether the association between preterm birth status and attention problems remained after accounting for executive functioning (inhibitory control and working memory) in adulthood, childhood intelligence score (IQ), or sex. *Results:* In the discovery cohort of the BLS, significant differences were found between VP/VLBW adults and controls for parent-rated inattention ( $p < 0.001$ ). However, for self-reported measures of ADHD, no significant differences were found in the BLS or in the EPICure replication cohort. In both cohorts, observer-rated attention spans were lower for VP/VLBW and EP participants in comparison to their respective control groups ( $p < 0.001$ ). In final models for the BLS, inhibitory control and childhood IQ were significantly associated with parent-rated inattention symptoms ( $p < 0.006$ ), whereas working memory and childhood IQ were significantly associated with observer-rated attention span ( $p < 0.001$ ). The effect of childhood IQ on observer-rated attention span was replicated in EPICure. *Conclusion:* VP/VLBW and EP adults are at increased risk of observer-rated attention problems. These problems were predominantly associated with poorer general cognitive ability in early childhood and somewhat with adult executive functioning.

(*J Dev Behav Pediatr* 00:1–9, 2020) **Index Terms:** attention-deficit/hyperactivity disorder, preterm, attention, executive functioning, intelligence.

In comparison to term-born controls, those born very preterm or at very low birth weight (VP/VLBW; <32 weeks' gestation or <1500 g) have been found to have

greater attention problems.<sup>1</sup> In childhood, this has been found when assessed via parent report,<sup>2</sup> teacher rating,<sup>3</sup> and observer rating of attention span.<sup>4</sup> VP/VLBW individuals are also at increased risk of attention deficit hyperactivity disorder (ADHD) diagnosis in childhood<sup>1</sup> and adulthood.<sup>4</sup> In particular, a preterm-specific phenotype of ADHD, consisting of more inattention symptoms (ADHD-I) with relatively few problems of hyperactivity/impulsivity (ADHD-H),<sup>2</sup> has been proposed. Although men are more likely to have ADHD symptoms or diagnosis in the general population, this sex difference has not been consistently found within the VP/VLBW groups.<sup>1</sup>

Attention problems have been primarily associated with deficits in executive functioning, a set of higher-order neurocognitive processes required for decision-making and goal orienting.<sup>5</sup> Although there is discussion over which behaviors and tasks best measure executive functioning, Diamond's<sup>6</sup> framework states that 2 main components are the ability to hold and manipulate information in mind—working memory—and the ability to selectively attend and suppress attention to stimuli—inhibitory control. In comparison to controls, VP/VLBW children and adolescents show deficits on a range of

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executive functioning tasks,<sup>7</sup> which may explain the attention problems seen in VP/VLBW children. For example, working memory has been found to mediate the relationship between VP/VLBW birth and teacher-rated inattention.<sup>3</sup> Similarly, impulse control, a component of inhibitory control, has been associated with attention scores in VP/VLBW children and controls.<sup>8</sup> Thus, the greater childhood attention problems seen in VP/VLBW when compared with term-born individuals may be partly explained by executive functioning. However, whether these specific executive functions explain the differences in adulthood has not yet been explored.

Alternatively, it has been suggested that the differences in attention between VP/VLBW individuals and term-born controls may be explained by VP/VLBW individuals having, on average, lower intelligence scores (IQs).<sup>2</sup> However, scores on tests of IQ and executive function are correlated with poor executive functioning being partially responsible for poor IQ scores.<sup>9</sup> This is especially true for adult IQ tests that have working memory as a subtest for the calculation of full-scale IQ, meaning the 2 constructs are not independent. To reduce this issue, childhood IQ can be used to control for general cognitive ability while being less correlated with current abilities in executive function. Overall, if adult inattention is primarily because of specifically poor executive function, then concurrent measures of executive function should provide the best ability to explain the differences in attention between the groups, over and above the effect of childhood IQ scores.

The aim of this study was to investigate whether the greater attention problems seen in VP/VLBW as compared to term-born adults are best explained by specific executive functioning deficits, general cognitive abilities, or sex. The discovery sample is the Bavarian Longitudinal Study (BLS), and replication was conducted in the EPICure study of extremely preterm participants (EP, <26 weeks' gestation). It was hypothesized that the poorer attention seen in VP/VLBW and EP adults would be significantly associated with poor executive functioning, as measured by inhibitory control and working memory, and that these effects would remain after controlling for other potential risk factors of low childhood IQ and male sex.

## METHOD

### Participants

#### Bavarian Longitudinal Study

Details of the design of the Bavarian Longitudinal Study (BLS) have been previously reported,<sup>10</sup> as have the details of the assessments at 26 years of age.<sup>11</sup> Briefly, of 682 very preterm/very low birth weight (VP/VLBW) infants born alive between January 1985 and March 1986 in Southern Bavaria, Germany, and who required admission to a children's hospital within the first 10 days after birth, 411 were alive and eligible for the 26-year follow-up assessment. In total, 260 participated (63%) with 194 (47%) completing measures of self-reported ADHD and experimental measures of executive functioning. Three hundred

fifty eligible healthy term-born controls born in the same hospitals, matched for sex and socioeconomic status, served as controls and were also followed from birth. In adulthood, 308 controls were eligible for inclusion, and 229 (74%) participated, with 197 (64%) completing self-reported ADHD and executive functioning measures at 26 years and thus being included in this study. Of the 194 VP/VLBW participants and 197 controls, 172 (89%) and 181 (93%) also had data available for parent-reported ADHD symptoms at 26 years of age. The participant flow chart for the BLS is presented in Supplemental Digital Content 1, <http://links.lww.com/JDBP/A256>. Informed consent was obtained from parents and participants; ethical approval was obtained from the University Hospital Bonn Ethical Committee.

#### EPICure

Details of the design of EPICure have been previously reported,<sup>12</sup> as have the details of the assessments at 19 years of age.<sup>13</sup> Briefly, EPICure included EP infants who were born in the United Kingdom and Ireland from March through December 1995. Of the 315 alive at hospital discharge, 306 EP participants were eligible for the 19-year follow-up assessment, of which 129 (42%) participated. Of these, 107 (35%) completed the measures of self-reported ADHD symptoms and tests of executive functioning. A stratified comparison group of 160 children were initially recruited at age 6, with 43 further recruited at 11 years. Of the full-term control group at 11 years (N: 153), 65 (42%) took part at 19 years of age, with 60 (39%) completing measures of self-reported ADHD symptoms and tests of executive functioning. The participant flow chart for EPICure is presented in Supplemental Digital Content 1, <http://links.lww.com/JDBP/A256>. Informed consent was obtained from participants; ethical approval was obtained from the South Central—Hampshire A Research Ethics Committee.

## Measures

### Adult Attention Deficit Hyperactivity Disorder Symptoms

Both EPICure and BLS participants completed the Kooij DSM-IV-based ADHD adult rating scale.<sup>14</sup> This 23 item scale is considered a valid and reliable measure of ADHD in adulthood.<sup>14</sup> The scale determines a participant as having a symptom if the participant responds "often" or "very often" to items such as "I fail to give close attention to details in work." Two subscores assessing 9 ADHD-I symptoms and 9 ADHD-H symptoms, ranging from 0 (no ADHD sub score symptoms present) to 9 (maximum number of ADHD sub score symptoms present), are calculated with the combined ADHD symptoms (ADHD-C) calculated by totaling the 2 subscores. In both cohorts, the self-reported ADHD scales had good internal reliability (BLS:  $\alpha = 0.75$ , EPICure:  $\alpha = 0.85$ ). In the BLS cohort only, parents also assessed their child's ADHD symptoms using the same questionnaire, with a similarly good internal reliability ( $\alpha = 0.88$ ). All ADHD-I, ADHD-H, and

ADHD-C symptom scores were then converted into Z scores based on the mean and SD of each cohort's respective control group.

### **Tester Rating of Adult Behaviour—Attention Span**

In both cohorts, psychologists rated the individual's attention on a scale from 1 (very short attention span) to 9 (very long attention span).<sup>15</sup> Assessments were made 3 times across the assessment day: (1) during the cognitive assessment, (2) during the afternoon session, and (3) at the end of the assessment day. The means of these 3 time points were then combined to produce an overall assessment of attention span, which were then converted into Z scores based upon the mean and SD of each cohort's respective control group. Within the BLS, Tester Rating of Adult Behaviour—Attention Span (TRAB-AS) showed moderate inter-rater reliability ( $Kappa = 0.67$ ). For EPICure, all assessments were made by a single psychologist.

### **Adult Executive Functioning: Inhibitory Control**

Inhibitory control was measured using the Attention Network Task (ANT).<sup>16</sup> The ANT measures alerting, orienting, and executive control. For this study, executive control was of interest as a measure of inhibitory control. Consisting of 128 trials, the ANT requires participants to determine the direction of a central target arrow as accurately and as quickly as possible while ignoring the flanker arrows. Inhibitory control was calculated by taking the mean reaction time on trials when the flanker arrows were incongruent and subtracting the mean reaction time when the flanker arrows were congruent. The scores were measured in milliseconds, with a larger inhibitory control score indicating greater difficulty with inhibiting extraneous stimuli. See Supplemental Digital Content 2, <http://links.lww.com/JDBP/A256> for a diagram demonstrating the sequence of events in an ANT trial and a detailed description of how the ANT was performed in both cohorts using identical procedure.

### **Adult Executive Functioning: Working Memory**

For BLS participants, the working memory assessment comprised a Letter-Number Sequencing task, a subtest of Wechsler Adult Intelligence Scale III.<sup>17</sup> Participants heard sequences of numbers and letters and then repeated back the numbers in ascending order and the letters in alphabetical order. EPICure participants partook in a different verbal working memory assessment, the backwards digit recall task, which is a subtest of Wechsler<sup>18</sup> Adult Intelligence Scale IV. Participants listened to the sequences of numbers and then repeated them back in the reverse order, a working memory assessment found to be closely related to the Letter-Number Sequencing task.<sup>19</sup> The scores in both the cohorts were standardized based on each cohort's respective control group with a mean of 100 and an SD of 15.

### **Childhood Intelligence Score**

At 6 years of age, the IQ of participants was assessed with the Kaufman Assessment Battery for Children Mental Processing Component, comprising 8 subtests, 5 subtests

to measure simultaneous processing and 3 subtests to measure sequential processing.<sup>20–22</sup> The scores in both the cohorts were standardized based on each cohort's respective control group with a mean of 100 and an SD of 15. If IQ data were missing at 6 years, IQ scores from the next available cognitive assessment at either 8 years (BLS) or 11 years (EPICure) were used (N: 41%, 7% of all participants).

### **Statistical Analysis**

SPSS version 24 (IBM Corp., Armonk, NY) and R version 3.4.2 were used to analyze the data. The comparison of demographic data in VP/VLBW or EP and control samples was assessed using  $\chi^2$  tests in both cohorts. Participants with complete data for measures of executive functioning, self-reported ADHD symptoms, and TRAB-AS were included for the analysis. All analyses were performed separately for each cohort, first in the BLS and then subsequently replicated in EPICure, allowing for the robustness of the findings to be explored.

To test for differences between the VP/VLBW participants or EP participants and controls, independent samples *t* tests were first used to compare self-reported ADHD symptoms, parent-reported ADHD symptoms (BLS only), TRAB-AS, inhibitory control, working memory, and IQ at 6 years for each cohort. Adjustment for multiple comparisons was made using the procedure by Hochberg<sup>23</sup>. The effect sizes are reported as Cohen's<sup>24</sup> *d*: 0.20 = small, 0.50 = medium, and 0.80 = large.

When significant differences in attention problems were found between VP/VLBW or EP participants and controls, hierarchical regressions were performed to identify which factors reduced and explained these differences. This was performed first in the discovery sample of the BLS and replicated when possible in EPICure. Hierarchical regressions were used to determine whether deficits in executive function explained the greater attention problems in VP/VLBW and EP individuals, above and beyond the effect of IQ or sex. Each hierarchical regression added at step 1 the binary variable of birth group (VP/VLBW or control for BLS, EP or control for EPICure). At step 2, the measures of executive function were added. IQ at 6 years was added at step 3, whereas male sex, a common risk factor for attention problems, was added at step 4. At each step in the hierarchical regression, the importance of each variable was assessed in 2 ways: first, by the  $R^2$  change of the overall model fit for the ADHD-I symptoms or the TRAB-AS outcome, determining how each step improves the prediction of attention problems in adulthood. At step 4, the final model was assessed to determine the predictive ability of each variable on consideration of all other variables in the model and the total variance explained. In addition, the estimated adjusted means for VP/VLBW (or EP) and controls were calculated at each step in the hierarchical regression. This assessed the importance of inhibitory control, working memory, IQ at 6 years, and sex by their effect on the differences in means between the VP/VLBW (or EP) groups and their

respective controls. If for example, the reason for poor attention in VP/VLBW and EP adults was because of poor executive functioning, then the adding of executive functioning measures at step 2 should cause the difference in estimated adjusted means between VP/VLBW and controls to diminish, becoming no longer statistically significant.

## RESULTS

### Demographic Data and Dropout Analysis

Information regarding demographic data and loss to follow up into adulthood has been reported previously for the Bavarian Longitudinal Study (BLS)<sup>11</sup> and in EPICure.<sup>13</sup> Very preterm/very low birth weight (VP/VLBW) and extremely preterm (EP) participants in both cohorts were more likely to be of higher socioeconomic status than dropouts from their respective cohorts ( $p = 0.003$  in BLS,  $p = 0.004$  in EPICure). Participating EP individuals were also more likely to be women than EP participants lost to follow up ( $p = 0.039$ ). The only significant difference within both cohorts comparing demographic data of VP/VLBW and EP to controls was that BLS controls were more likely to have higher socioeconomic status than BLS VP/VLBW individuals ( $p = 0.030$ ).

### Differences Between Extremely Preterm/Very Preterm/Very Low Birth Weight Adults and Controls in Attention Deficit Hyperactivity Disorder Symptoms, Executive Function, and Intelligence Score

Between-group differences in attention deficit hyperactivity disorder (ADHD) symptoms, attention span, executive function, and intelligence score (IQ) are shown in Table 1. In the discovery sample, the BLS, VP/VLBW participants did not self-report significantly higher ADHD-I, ADHD-H, or ADHD-C symptoms than controls. Similarly, after adjustments for multiple comparisons were made,<sup>23</sup> there were no significant differences in self-reported ADHD between EP and controls in the replication sample of EPICure. Parents of the BLS VP/VLBW participants reported their adult children as having significantly higher ADHD-C symptoms than controls, which was primarily because of the differences in ADHD-I symptoms rather than ADHD-H symptoms. Finally, in the BLS, VP/VLBW participants were found to have considerably shorter attention spans than controls when rated by observers using the Tester Rating of Adult Behaviour—Attention Span (TRAB-AS), which was replicated in EPICure (Table 1).

For executive function, BLS's VP/VLBW participants demonstrated poorer performance in both domains, with larger response times for inhibitory control and lower working memory scores in comparison to controls. On the measure of IQ at 6 years of age, VP/VLBW participants scored considerably lower than their respective control group. In the replication sample of EPICure, a robustly similar set of findings regarding executive and general cognitive functions were found.

However, the magnitude of difference between the EP participants and controls was slightly larger than the difference found between the VP/VLBW and controls in the BLS (Table 1). A correlation matrix for attention measures, executive functioning, and general cognitive functioning is also provided in Supplementary Digital Content 3, <http://links.lww.com/JDBP/A256>.

### Hierarchical Regressions Explaining Tester Rating of Adult Behaviour—Attention Span and Attention Deficit Hyperactivity Disorder Inattention Symptoms Differences in Very Preterm/Very Low Birth Weight or Extremely Preterm Adults and Controls

For TRAB-AS in the BLS, the estimated adjusted means between groups at each hierarchical step are shown in Figure 1. Initially at step 1, the VP/VLBW groups' attention span ratings were  $z = -0.48$  ( $-0.70, -0.25$ ) lower than controls. At step 2, both inhibitory control and working memory were found to be significantly associated with TRAB-AS rating, with the difference in adjusted means between groups reducing to  $z = -0.21$  ( $-0.43, 0.01$ ) and no longer statistically significant. At step 3, IQ at 6 years old was also found to be significantly associated with TRAB-AS rating, further reducing the estimated adjusted means to a difference of  $z = -0.04$  ( $-0.26, 0.19$ ). Although at step 1, the difference in estimated adjusted means between VP/VLBW and controls was found to be 0.48, this reduced to 0.04 at step 4 (Fig. 2). The final model for predicting TRAB-AS in the BLS explained 23% of the variance with working memory and IQ at 6 years old, the only factors remaining significantly associated with attention span rating (Table 2).

For TRAB-AS in EPICure, the estimated adjusted means between the groups at each hierarchical step are shown in Figure 1. Initially at step 1, the EP groups' attention span ratings were  $z = -1.14$  ( $-1.73, -0.55$ ) lower than controls. At step 2, working memory and inhibitory controls significantly diminished the effect of birth group on attention span rating to  $z = -0.58$  ( $-1.21, 0.06$ ). At step 3, adding the measure of IQ at 6 years old, both executive functioning variables were no longer statistically significant and resulted in controls having an adjusted attention span of  $z = 0.14$  ( $-0.55, 0.83$ ) lower than EP participants. Although at step 1, the estimated difference in adjusted means found the EP group to have a deficit of  $z = -1.14$ , at step 4, with sex also introduced, the difference had switched to controls having a deficit of  $z = 0.11$  (Fig. 2). The final model for TRAB-AS in EPICure explained 26% of the variance, with IQ at 6 years of age being the only remaining significant predictor (Table 2).

For BLS parent-reported ADHD-I symptoms, the estimated adjusted means for VP/VLBW and controls at each hierarchical step are shown in Figure 2. Initially, at step 1, the VP/VLBW group had an ADHD-I symptom  $z$  score 0.95 greater than the controls, 95% confidence interval 0.49 to 1.41. When inhibitory control and working memory were entered at step 2, both executive functioning measures

**Table 1.** Univariate Differences Between VP/VLBW or EP Participants and Controls

	BLS				EPICure			
	Mean Difference (VP/VLBW-Control)	Mean Difference 95% CI	Adjusted <i>p</i>	Cohen's <i>d</i> (EP-Control)	Mean Difference	Mean Difference 95% CI	Adjusted <i>p</i>	Cohen's <i>d</i>
ADHD-inattention self-reported symptoms—Z scored	0.12	[−0.09, 0.34]	0.522	0.11	0.39	[0.03, 0.75]	0.084	0.34
ADHD-hyperactivity/impulsivity self-reported—Z scored	−0.16	[−0.36, 0.03]	0.340	−0.17	−0.06	[−0.40, 0.29]	0.739	−0.05
ADHD-combined self-reported—Z scored	−0.05	[−0.26, 0.15]	0.597	−0.05	0.19	[−0.16, 0.54]	0.543	0.17
ADHD-inattention parent reported—Z scored	0.95	[0.49, 1.41]	<0.001	0.44	—	—	—	—
ADHD-hyperactivity/impulsivity parent reported—Z scored	0.20	[−0.05, 0.44]	0.34	0.17	—	—	—	—
ADHD-combined parent reported—Z scored	0.51	[0.19, 0.84]	0.01	0.33	—	—	—	—
Observer rating of attention span (TRAB-AS)—Z scored	−0.48	[−0.70, −0.25]	<0.001	−0.42	−1.14	[−1.73, −0.55]	0.001	−0.62
Inhibitory control (ms)	27.53	[17.04, 38.01]	<0.001	0.52	41.86	[22.4, 61.33]	<0.001	0.69
Working memory	−8.98	[−12.72, −5.24]	<0.001	−0.48	−10.37	[−14.77, −5.96]	<0.001	−0.75
IQ at 6 yr	−16.49	[−19.81, −13.17]	<0.001	−0.99	−26.24	[−31.69, −20.79]	<0.001	−1.54

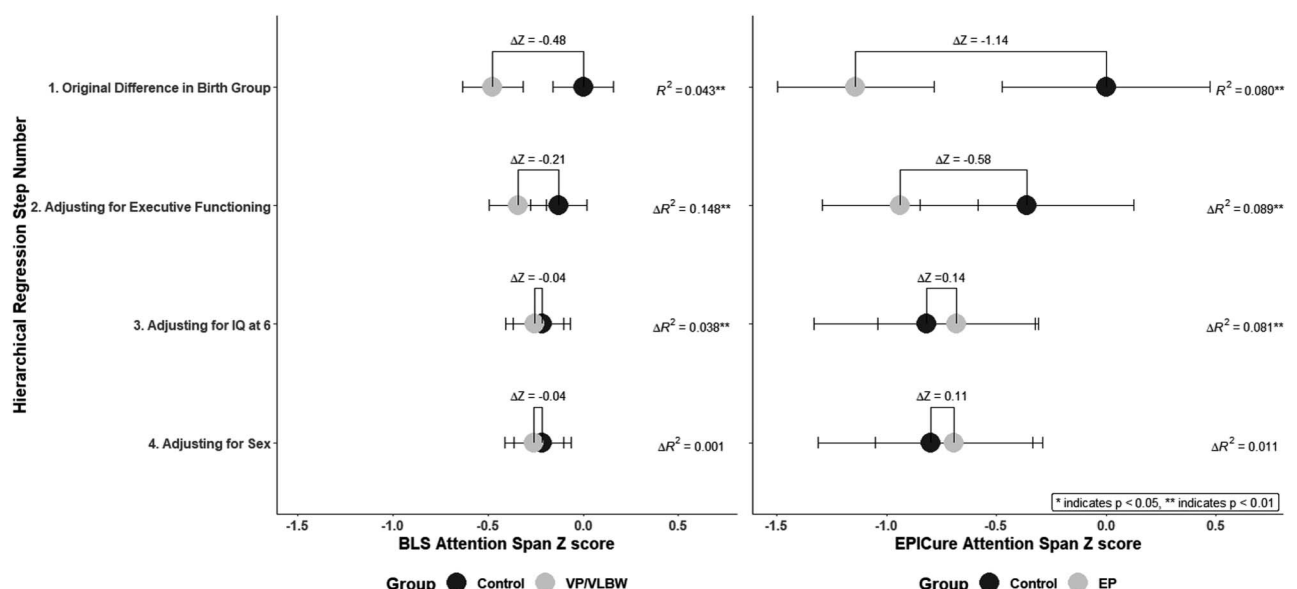
Inhibitory control as measured by the Attention Network Task. Working memory as measured by the letter-number sequencing task in the BLS and backward digit recall task in EPICure. IQ at 6 years as measured by the K-ABC task. *p* Values are adjusted using Hochberg's correction. Z-scored indicates that raw scores are standardized based on the mean and SD of the respective control group. ADHD, attention deficit hyperactivity disorder; BLS, Bavarian Longitudinal Study; EP, extremely preterm; IQ, intelligence score; K-ABC, Kaufman Assessment Battery for Children; TRAB-AS, Tester Rating of Adult Behaviour—Attention Span VP/VLBW, very preterm/very low birth weight.

were significantly associated with ADHD-I symptoms, with the difference in estimated adjusted means between VP/VLBW and controls reducing to  $z = 0.50$  (0.04, 0.95). It was not until step 3, when IQ at age 6 years was added, that the estimated mean differences between groups became statistically insignificant, reducing to a difference of  $z = 0.03$  (−0.43, 0.50). At step 4, the variable of sex did not significantly increase  $R^2$  and only minimally influenced the estimated adjusted means 0.01 (−0.46, 0.48). From the initial differences between VP/VLBW and controls at step 1 being  $z = 0.95$ , the difference in estimated

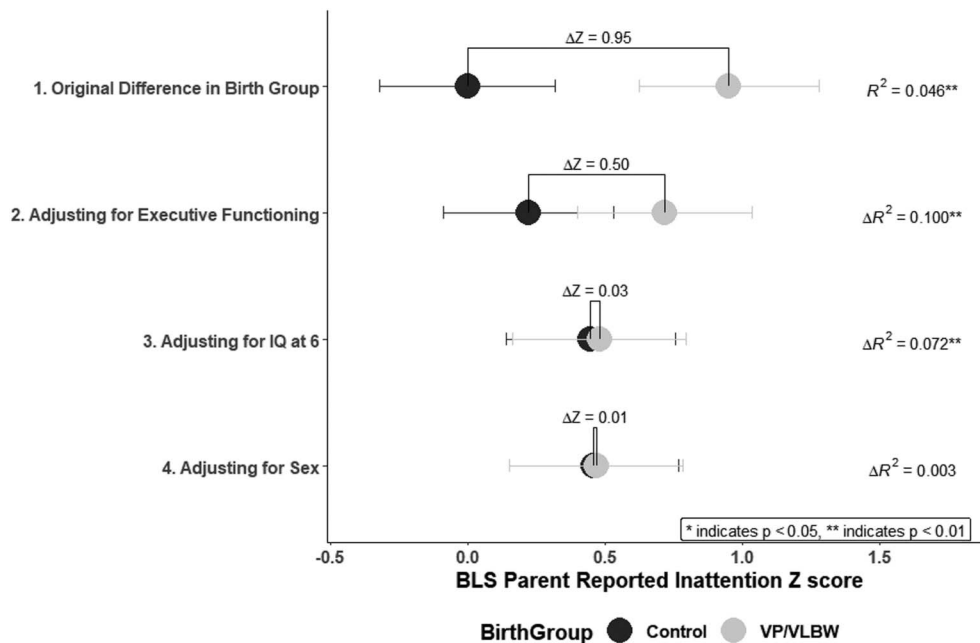
adjusted means between VP/VLBW and controls in the final model was reduced to a difference of  $z = 0.01$ . The final model for BLS parent-reported ADHD-I symptoms explained 22% of the variance and was predominantly explained by IQ at 6 years of age and inhibitory control in adulthood (Table 2).

## DISCUSSION

In the discovery sample of the Bavarian Longitudinal Study (BLS), we observed evidence of greater attention



**Figure 1.** Differences in TRAB-AS between VP/VLBW and EP individuals with their respective control group at each step of the hierarchical regression for the BLS and EPICure. Error bars represent 95% confidence intervals. BLS, Bavarian Longitudinal Study; EP, extremely preterm; IQ, intelligence score; TRAB-AS, Tester Rating of Adult Behaviour—Attention Span; VP/VLBW, very preterm/very low birth weight.



**Figure 2.** Differences in parent-reported ADHD-inattention symptomatology between VP/VLBW and controls at each step of the hierarchical regression for the BLS. Error bars represent 95% confidence intervals. ADHD, attention deficit hyperactive disorder; BLS, Bavarian Longitudinal Study; IQ, intelligence score; VP/VLBW, very preterm/very low birth weight.

problems for very preterm/very low birth weight (VP/VLBW) adults, as demonstrated by poorer observed attention span in comparison to controls, further validated by greater parent-reported attention deficit hyperactivity disorder-inattention (ADHD-I) symptoms. By contrast, we found no self-reported difference in ADHD between VP/VLBW and controls. These results were found to be robust, being replicated in the EPICure sample in which extremely preterm (EP) adults had shorter observer-rated attention span, but no self-reported differences in ADHD, either. Our hypothesis, that differences in attention would be explained by executive functioning, was only partially supported. In the BLS, measures of inhibitory control and working memory in adulthood partially explained the effect of VP/VLBW birth. However, after childhood intelligence score (IQ) was accounted for, inhibitory control only remained significantly associated with parent-reported ADHD-I symptoms, whereas work-

ing memory only remained significantly associated with Tester Rating of Adult Behaviour—AttentionSpan (TRAB-AS) ratings. For EPICure, although the effect of EP birth on TRAB-AS rating was explained by inhibitory control and working memory, neither factor remained significant after accounting for childhood IQ. The results from both cohorts indicate that while specific executive functioning measures can aid in explaining why VP/VLBW or EP adults show more attention problems than controls, childhood IQ explains a larger amount of the difference between groups.

The pattern of results from adulthood is largely in concordance with past research looking at attention problems in preterm children, suggesting specific problems of inattention rather than hyperactivity/impulsivity. In addition, the greater relative differences found between EP and controls in EPICure than between the VP/VLBW and controls in the BLS may

**Table 2.** Final Multiple Regression Models (Step 4) Predicting Standardized Parent-Reported ADHD-I Symptoms and TRAB-AS Ratings in the BLS and EPICure

Predictor	BLS ADHD-I PR		BLS TRAB-AS		EPICure TRAB-AS	
	Beta	p	Beta	p	Beta	p
Birth group (0 = control, 1 = EP/VP/VLBW)	0.00	0.971	-0.02	0.712	0.03	0.759
Inhibitory control	0.14	0.006	-0.07	0.149	-0.11	0.114
Working memory	-0.07	0.213	0.24	<0.001	0.12	0.165
IQ at 6 yr	-0.35	<0.001	0.26	<0.001	0.39	<0.001
Sex (0 = female, 1 = male)	0.06	0.218	0.03	0.566	-0.11	0.119
Total R <sup>2</sup>	0.22		0.23		0.26	

Inhibitory control as measured by the Attention Network Task, working memory as measured by the letter number sequencing task in the BLS and backward digit memory task in EPICure. IQ at 6 years as measured by the K-ABC task. ADHD-I PR, parent reported ADHD-inattention symptoms; BLS, Bavarian Longitudinal Study; EP, extremely preterm; IQ, intelligence score; TRAB-AS, observer rating of attention span; VP/VLBW, very preterm/very low birth weight.

result from a “gestational gradient,” whereby the risk of attention problems increases as gestational age at birth decreases.<sup>1</sup> The EPICure EP group were born on average 6 weeks more preterm than the BLS VP/VLBW group. Also consistent with this interpretation is the relatively poorer performances on the measures of executive functioning and the larger deficits in general cognitive ability between EPICure’s EP adults and controls than between BLS’s VP/VLBW adults and controls. Alternatively, or additionally, year of birth (1985 vs 1995) and age of assessment (26 vs 19 year old) differed between the discovery sample (BLS) and the replication sample (EPICure). Regarding era of birth, previous studies<sup>25,26</sup> found that although survival of very-preterm-born babies has increased, there is little evidence of improved cognitive outcome across eras. Age of assessment may also be important if deficits in executive function and attention are due to developmental delay that may narrow with age. Because the BLS’ VP/VLBW participants were older than EPICure’s EP participants, they may have had more time to “catch up” in comparison to their respective control group. Nevertheless, our results were remarkably similar across cohorts despite differences in degree of prematurity and age of assessment, indicating generalizability of findings.

Within the general population and in VP/VLBW children, attention problems have been primarily associated with deficits in executive functioning;<sup>5,8,27</sup> however, we found inconsistent evidence for this after we controlled for childhood IQ. Our results are in line with the postulation by Willcutt et al.<sup>5</sup> that deficits in executive function are important but are not the sole factor causing ADHD symptoms. Alternatively, as our VP/VLBW and EP participants demonstrated a behaviorally distinct phenotype, primarily comprising inattention rather than hyperactivity/impulsivity, it may be that this phenotype has a different primary factor. The attention problems of VP/VLBW and EP adults, as shown here, would appear to be due to a general cognitive deficit rather than the specific executive functioning deficit seen in the general population. However, if inattention is because of a specific executive functioning deficit, it is also possible that our measures were not sensitive to those specific deficits. In childhood, inattention within the general population, but also in VP/VLBW and EP participants, has been found to be more closely related to visuospatial working memory rather than verbal working memory.<sup>27-29</sup> As our measures of working memory were verbal, it may be that we failed to assess the correct specific measures of executive functioning. Although future studies should look to address this, the current results are in line with recent research suggesting the limited efficacy of working memory interventions on attention and working memory performance itself for VP/VLBW children.<sup>30</sup> If verbal working memory is both impervious to intervention and only partially related to inattention in VP/VLBW and EP adults, it suggests that interventions for VP/VLBW and EP children may be focused elsewhere.

The fact that childhood IQ was significantly related to attention problems in adulthood in both cohorts, regardless of how attention was assessed, and partially explained the effect of being born VP/VLBW or EP is pertinent. Intelligence is unlikely to be assessed independent of executive function in childhood. For example, the IQ test used (the K-ABC) has some tasks that are related to executive functioning. However, the K-ABC is strongly correlated with the widely used Wechsler Intelligence Scale for Children, at  $r = 0.79$  and  $0.70$  throughout childhood.<sup>20,31</sup> Thus, our results are unlikely to differ depending on the child IQ test used. Regardless, failing to control for general cognitive ability might lead to the potentially erroneous conclusion that a specific executive functioning is responsible for attention problems when it is instead part of a more general cognitive deficit. If early identification of VP/VLBW or EP children at risk of long-term attention problems is of primary importance, then IQ testing seems a relatively straightforward approach to do so. VP/VLBW and EP individuals have been found to be at increased risk of brain injury, such as reduced cholinergic basal forebrain integrity and decreased white and gray matter, which has been found to mediate the relationship between preterm birth and poorer IQ.<sup>32,33</sup> It may be that IQ scores in childhood act as an indicator of overall poor brain growth. This poor brain growth may result in long term behavioral deficits in domains such as inattention, but less so for behaviors regarding hyperactivity and impulsivity. The finding of a strong association between general cognitive ability and inattention is consistent with evidence from EPICure in childhood<sup>2</sup> and other research finding strong links between general cognitive performance and behavioral difficulties for VP/VLBW children.<sup>8,34</sup>

Another important finding is that the method for assessing attention problems is key, with nonsignificant differences by self-report but larger differences when assessed through parent report or observer rating. When BLS VP/VLBW behavior was rated by their parents or observer, more attention problems were found, but this was not found for self-report. In EPICure, parent report was unavailable, but the results found a similar disparity between self-report and observer ratings. Overall, our results support other research into attention in extremely low birth weight adults and controls, finding no significant difference for self-reported ADHD of any subtype.<sup>35,36</sup> We can speculate that the VP/VLBW group’s reporting of fewer symptoms as compared with parents is compatible with Festinger’s<sup>37</sup> theory of social comparison. VP/VLBW and EP adults have been found to have a lower educational level and are more likely to be in manual employment.<sup>38</sup> An individual’s primary comparison is with those they socialize with the most, i.e., peers. Compared with peers in their social circle, VP/VLBW and EP adults may not consider themselves to have attention problems. By contrast, parents are more likely to compare their offspring to their birth cohort (i.e., all adults) and, thus, use a different

comparison level and report more attention problems, similar to the observation measures of attention. Regardless of why EP and VP/VLBW adults under-report their own symptoms, these results are in concordance with studies in the general population. In both childhood and into adulthood, there is substantial evidence that individuals with attention problems report fewer symptoms than their parents or independent observers do.<sup>39,40</sup> Overall, self-report measures of ADHD may underestimate symptoms in VP/VLBW and EP adults, and as such, multiple informants should be assessed.

There are clear strengths to this study. These include the use of 2 prospectively studied cohorts allowing for the replication of findings. The use of identical measures for ADHD symptoms, observer rating of attention span, inhibitory control, and child IQ in both cohorts reduces the influence of methodological issues in interpreting the results. However, there are also limitations. First, the rate of attrition was moderate to high, with the remaining participants found to be of higher socioeconomic status in both cohorts. This potential bias is unlikely to have had an impact on our results because regressions models may be only marginally affected by selective dropout<sup>41</sup>; nevertheless, bias cannot be excluded. The lack of parent report in EPICure and the difference in working memory assessments limited direct replication of some of the findings from the BLS. Although the 2 measures of verbal working memory have been found to be closely related,<sup>19</sup> the letter-number sequencing task may be more associated with attention ratings because of its greater complexity.<sup>42</sup> Future research should look to address the importance of task complexity as well as assessing visuo-spatial working memory, which, as previously noted, may be more linked to attention deficits. Finally, although our study was able to assess multiple possible predictors of inattention, it had the limitation that we were unable to directly assess other important cognitive factors such as processing speed equivalently for both cohorts because it has been noted as a core deficit for inattention in the general population and VP/VLBW children.<sup>28,43</sup> Although working memory performance is thought to be at least partially reliant on processing speed,<sup>44</sup> directly testing whether this lower-level ability is key to adult inattention could be pivotal for future interventions.

To conclude, this study provides further evidence for specific attention problems in early adulthood for VP/VLBW and EP in comparison to controls, replicating findings from childhood. Although we found that adult executive functioning measures were associated with attention problems in adulthood, childhood IQ was a stronger and more consistent predictor in both the discovery and replication sample. Early assessment of cognitive ability would allow for the early identification of VP/VLBW and EP children at risk for long-term attention problems.

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