

Original citation:

Breeman, Linda D., Jaekel, Julia, Baumann, Nicole, Bartmann, Peter and Wolke, Dieter. (2015) Attention problems in very preterm children from childhood to adulthood: the Bavarian longitudinal study. Journal of Child Psychology and Psychiatry.

Permanent WRAP url:

http://wrap.warwick.ac.uk/72065

Copyright and reuse:

The Warwick Research Archive Portal (WRAP) makes this work by researchers of the University of Warwick available open access under the following conditions. Copyright © and all moral rights to the version of the paper presented here belong to the individual author(s) and/or other copyright owners. To the extent reasonable and practicable the material made available in WRAP has been checked for eligibility before being made available.

Copies of full items can be used for personal research or study, educational, or not-for profit purposes without prior permission or charge. Provided that the authors, title and full bibliographic details are credited, a hyperlink and/or URL is given for the original metadata page and the content is not changed in any way.

Publisher's statement:

"This is the peer reviewed version of the following article: Breeman, L. D., Jaekel, J., Baumann, N., Bartmann, P. and Wolke, D. (2015), Attention problems in very preterm children from childhood to adulthood: the Bavarian Longitudinal Study. Journal of Child Psychology and Psychiatry. doi: 10.1111/jcpp.12456, which has been published in final form at http://dx.doi.org/10.1111/jcpp.12456. This article may be used for non-commercial purposes in accordance with Wiley Terms and Conditions for Self-Archiving."

A note on versions:

The version presented here may differ from the published version or, version of record, if you wish to cite this item you are advised to consult the publisher's version. Please see the 'permanent WRAP url' above for details on accessing the published version and note that access may require a subscription.

For more information, please contact the WRAP Team at: publications@warwick.ac.uk



http://wrap.warwick.ac.uk

Attention Problems in Very Preterm Children from Childhood to Adulthood:

The Bavarian Longitudinal Study

Linda D. Breemana, Julia Jaekelab, Nicole Baumanna, Peter Bartmannc, Dieter Wolkead

Affiliations

^aDepartment of Psychology, University of Warwick, United Kingdom

^bDepartment of Developmental Psychology, Ruhr-University Bochum, Germany

^cDepartment of Neonatology, University Hospital Bonn, Germany

^dDivision of Mental Health and Wellbeing, Warwick Medical School, University of Warwick, United

Kingdom

Abbreviated title: Preterm children's attention problems into adulthood

Conflict of interest: The authors declare no conflict of interest

Word count: 5997

1

Abstract

Background: Very preterm (VP; gestational age <32 weeks) and very low birth weight (VLBW; <1500 grams) is related to attention problems in childhood and adulthood. The stability of these problems into adulthood is not known.

Methods: The Bavarian Longitudinal Study is a prospective cohort study that followed 260 VP/VLBW and 229 term-born individuals from birth to adulthood. Data on attention were collected at 6, 8, and 26 years of age, using parent reports, expert behavior observations, and clinical ADHD diagnoses.

Results: At each assessment, VP/VLBW individuals had significantly more attention problems, shorter attention span, and were more frequently diagnosed with ADHD than term-born comparisons. In both VP/VLBW and term-born individuals, overall, attention span increased and attention problems decreased from childhood to adulthood. Attention problems and attention span were more stable over time for VP/VLBW than term-born individuals. Similarly, ADHD diagnoses showed moderate stability from childhood to adulthood in VP/VLBW, but not in term-born individuals. However, when those with severe disabilities were excluded, differences between VP/VLBW and term-born individuals reduced.

Conclusions: Despite improvement in attention regulation from childhood to adulthood, children born very preterm remained at increased risk for attention problems in adulthood. In contrast, term-born children with clinical attention problems outgrew these by adulthood. As inattentive behavior of VP/VLBW children may be overlooked by teachers, it may be necessary to raise awareness for school intervention programs that reduce attention problems in VP/VLBW children.

Keywords: ADHD; prematurity; low birth weight; longitudinal studies; attention **Abbreviations**: VP – very preterm; VLBW – very low birth weight; CBCL – Child Behavior Checklist;

YABCL – Young Adult Behavior Checklist; TRCB – Tester's Rating of Child Behavior; TRAB –

Tester's Rating of Adult Behavior; ADHD-IA – ADHD predominantly inattention; ADHD-HI – ADHD predominantly hyperactive/impulsive; ADHD-C – ADHD combined type; GA – gestational age; SGA – small for gestational age

Introduction

Attention-deficit/hyperactivity disorder (ADHD) is associated with long-term functional impairments, such as impaired physical and mental health (Brook, Brook, Zhang, Seltzer, & Finch, 2013; Gjervan, Torgersen, Nordahl, & Rasmussen, 2012) and considerable costs for patients, their families, and society (Matza, Paramore, & Prasad, 2005). ADHD affects around 5-10% of school-aged children worldwide (Hechtman, 2011; Polanczyk, de Lima, Horta, Biederman, & Rohde, 2007). Although attention problems have been generally found to decrease into adulthood, the disorder may persist in 15-66% of individuals from childhood to adolescence and adulthood (Faraone, Biederman, & Mick, 2006). Because treating ADHD effectively in childhood is a public health priority (NICE, 2008), early identification of those at high risk is essential. Being born very preterm (VP; gestational age at birth <32 weeks) or with very low birth weight (VLBW; <1500 grams) significantly increases the risk of ADHD problems in childhood (Bhutta, Cleves, Casey, Cradock, & Anand, 2002; Johnson et al., 2010), adolescence (Indredavik et al., 2004; Johnson & Wolke, 2013), and adulthood (Strang-Karlsson et al., 2008; Van Lieshout, Boyle, Saigal, Morrison, & Schmidt, 2015). It has been noted that, compared to term-born children, these ADHD problems are more often of the inattentive rather than the hyperactive/impulsive subtype (Jaekel, Wolke, & Bartmann, 2013). Some suggested that VP/VLBW children may have a specific 'pure' form of ADHD due to neurological causes that specifically impacts attention regulation rather than motor hyperactivity/impulsivity (Indredavik et al., 2004). In addition to increased prevalence, the stability of attention problems from childhood to adulthood may be higher for VP/VLBW than term-born individuals. Preterm birth is related to complex alterations in brain development due to an amalgam of destructive and developmental mechanisms including inflammation of the brain and ischemia that cause brain injuries including white matter lesions, reduced white matter volume, ventricular dilation, and atrophy of the corpus callosum (Skranes et al., 2005). These brain injuries lead to long-term anatomical alterations and changes in intrinsic networks (Bäuml et al., 2014) which may limit the neural plasticity of the brain (Luciana, 2003). This in turn may affect a child's potential for functional adaptation (i.e., neurodevelopmental plasticity) as shown in less growth and higher stability of functions such as attention regulation from childhood to adulthood compared to term-born individuals.

There is a dearth of longitudinal studies comparing VP/VLBW and term-born individuals on attention problems into adulthood. This prospective study investigated a whole population-based

sample of VP/VLBW and term-born individuals from birth to adulthood. Attention was assessed using multiple measures and data sources including parent ratings, expert behavior observations, and clinical DSM-IV diagnoses of ADHD. We tested three hypotheses: First, do VP/VLBW individuals have more attention problems in childhood and adulthood than term-born individuals? Second, do attention problems reduce over time in both VP/VLBW and term-born individuals? Third, are attention problems more stable in VP/VLBW than in term-born individuals from childhood to adulthood?

Methods

Design

The Bavarian Longitudinal Study is a prospective study following a whole population sample of VP/VLBW children born in a geographically defined area of Southern Bavaria (Germany) in 1985-1986 who required admission to one of 16 children's hospitals within the first 10 days after birth. Healthy term-born comparisons (37-42 weeks gestation) were recruited in obstetric units in the same catchment area during the same period. Full details of this sample are given elsewhere (Wolke, Schmid, Schreier, & Meyer, 2009). In the present study, we report on data collected at 6, 8, and 26 years of age. The clinicians responsible for the assessments were blind to group membership and previous assessment results. Ethical approval of the original study was obtained from the University of Munich Children's Hospital and ethical approval for this follow-up study was granted by the Ethical Board of the University Hospital Bonn. Informed consent was provided by the parents within 48 hours of their child's birth and participating adults gave fully informed written consent in the follow-up study. In cases of severe impairment consent was provided by an assigned guardian.

Participants

This study assessed 682 VP/VLBW individuals. Of this cohort, 411 VP/VLBW were alive, living in Germany, and eligible for inclusion and 260 (63%) of these adults participated in the present study (flowchart: Figure S1 available online). Of the eligible healthy term-born children at 6 years, 350 were randomly selected within two stratification variables (sex and family SES) to be comparable to the VP/VLBW individuals. In adulthood, 308 individuals were eligible for inclusion and 229 (74%) participated at 26 years and are thus included in the present study.

Measures

The attention measures are briefly described below. More in-depth information can be found in Supplement 1 online.

Attention problems. Parents rated their children's attention problems at 6 years (6y) and 8 years (8y) using the well-studied and validated attention problems scale of the Child Behavior Checklist (CBCL; Achenbach, 1991; Arbeitsgruppe Deutsche Child Behavior Checklist, 1998). At 26 years (26y), parents rated their offspring's attention problems using the Young Adult Behavior Checklist (YABCL; Achenbach, 1997). Each item was rated on a scale from 0 (not true) to 2 (very/often true) and then summed into a total score with higher scores indicating more attention problems. Parent-rated attention problems scores were available for 217-238 (83-92%) VP/VLBW and 207-229 (90-100%) term-born individuals across the three time points.

Attention span. Psychologists rated the child's attention span using the Tester's Rating of Child Behavior (TRCB; Wolke, 1996) at 6y and 8y and the Tester's Rating of Adult Behavior (TRAB; Wolke, 2012) at 26y (Jaekel et al., 2013). Attention span was judged during a cognitive assessment and generally across all tasks during the assessment day. Psychologists scored the individual's attention on a scale from 1 (*very short attention span*) to 9 (*very long attention span*). Observer-rated attention span scores were available for 202-226 (78-87%) VP/VLBW and 197-229 (86-100%) termborn individuals.

ADHD diagnoses. ADHD diagnoses at 6y and 8y were made according to the structured and validated Mannheim Parent Interview (Esser, Blanz, Geisel, & Laucht, 1989) that allowed for a clinical DSM-IV diagnosis. The presence of ADHD symptoms at 26y were made with the DSM-IV based ADHD adult rating scale completed by parents (Kooij et al., 2005). This adult ADHD rating scale is considered a valid measure of ADHD and associated psychosocial impairment in adulthood (Kooij et al., 2005). According to guidelines by Kooij et al. (2005), adults exhibiting 4 out of 9 inattentive symptoms or 4 out of 9 hyperactivity/impulsivity symptoms 'often' or 'very often' are considered significantly impaired. They thus received a diagnosis of either predominantly inattention (ADHD-IA), predominantly hyperactive/impulsive (ADHD-HI) or ADHD combined type (ADHD-C). Data on ADHD diagnoses in childhood and the presence of ADHD symptoms in adulthood were available for 224-260 (86-100%) VP/VLBW and 206-229 (90-100%) term-born individuals.

Descriptives and confounders. Children with birth weights less than the sex specific 10th percentile for gestational age (GA) were classified as small for gestational age (SGA; Zander, Holzmann, & Selbmann, 1989). GA (weeks), birth weight (kilograms), SGA (number of children <10% criteria), sex, multiple births (twins or other multiples), and maternal age (years) were coded from the Bavarian perinatal survey forms at birth (Zander et al., 1989). So were pre-pregnancy complications (0-8 complications; e.g., prior disabled child, prior preterm birth), pregnancy complications (0-14 complications; e.g., nicotine addiction, anemia), birth complications (0-15 complications; e.g., no spontaneous labor, anesthesia), and neonatal complications (0-20 complications; e.g., nasogastric feeding, ventilation/intubation; Schmid, Schreier, Meyer, & Wolke, 2011). Family socioeconomic status (SES) at birth was computed as a weighted composite score of parents' education and occupation and grouped as low/middle/high (Bauer, 1988; Gutbrod, Wolke, Soehne, Ohrt, & Riegel, 2000). A dichotomous measure of disability status (coded 0=no disabilities and 1=disabled) was computed. Severe disability was determined in childhood according to the following criteria: IQ <-2 standard deviations as assessed with the Kaufman-Assessment Battery for Children (K-ABC; (Kaufman & Kaufman, 1983; Melchers & Preuss, 1991), suffering from grade 3 or 4 cerebral palsy, or blindness/deafness (insufficiently corrected).

Data Analysis

All analyses were performed in SPSS 22.0 or STATA 12.1. To test for differences between VP/VLBW and term-born individuals at birth, we performed one-way ANOVA's for continuous variables and χ^2 test for categorical variables. The outcomes of all further analyses were corrected for SES and statistical significance was set at p<.05. All tests were one-tailed (i.e., VP/VLBW have more attention problems).

First, differences between VP/VLBW and term-born individuals in attention problems and attention span means from childhood to adulthood were tested using ANCOVA's. Effect size is reported as Cohen's d of the adjusted estimated means (Cohen, 1988): 0.20=small, 0.50=medium, 0.80=large effects. In addition, SES adjusted relative risks (RR) of having ADHD in VP/VLBW compared to term-born individuals were calculated using Poisson regression with robust error variances. Second, changes in attention problems and attention span from childhood to adulthood were tested with repeated measure ANCOVA's. Effect sizes (partial eta squared (η_p^2)) were

interpreted: 0.02=small, 0.13=medium, 0.26=large effects. Third, to assess whether attention problems and attention span were more stable in VP/VLBW than term-born individuals, Pearson product moment correlations were examined. Correlations were converted to Fisher z-scores with 95% confidence intervals (CI) to compare VP/VLBW and term-born individuals with z-tests. Effect sizes for the difference in magnitude between population correlations (ES_{zr}) were calculated and interpreted: 0.10=small, 0.30=medium, 0.50=large effects. In addition, the stability of ADHD diagnoses was assessed by calculating the RR of having a stable ADHD diagnosis from childhood (at 6y/8y) to adulthood compared to receiving a first time adult ADHD diagnosis. Finally, all analyses were repeated excluding individuals with severe disabilities to examine whether the reported results would change.

Results

Sample Descriptives and Dropout

VP/VLBW individuals were more often small for gestational age, more often multiple births, and more complications were recorded for mother and child before pregnancy, during pregnancy, during birth, and the neonatal period. VP/VLBW adults more often had disabilities and had been born to more socioeconomically disadvantaged families than their term-born counterparts. The VP/VLBW and term-born individuals did not differ in terms of sex and maternal age (Table 1).

Moreover, the VP/VLBW adult participants did not differ from VP/VLBW dropouts (*n*=151) in terms of GA, SGA, birth weight, sex, multiple births, disabilities, and complications before pregnancy, during birth, and the neonatal period. However, dropouts had younger mothers, were more often socially disadvantaged, and their mothers had more complications during pregnancy. The participating term-born individuals did not differ from dropouts (*n*=79) in terms of GA, SGA, birth weight, sex, multiple births, disabilities, and mothers' complications before pregnancy, during birth, and the neonatal period. However, dropouts had younger mothers, were more often socially disadvantaged, and their mothers had more complications during pregnancy.

Do VP/VLBW Individuals Have More Attention Problems in Childhood and Adulthood?

Raw means with their 95%Cl of parent-rated attention problem scores and observer-rated attention span scores are presented in Figure 1 (see also Table S1 online). Although raw means differed

between males and females, the pattern of differences between VP/VLBW and their term-born counterparts was the same in both sexes. Both in childhood and in adulthood, VP/VLBW individuals had higher attention problem scores (6y: F(1,463)=32.84, p<.001; 8y: F(1,454)=20.65, p<.001; 26y: F(1,420)=39.45, p<.001) and lower attention span scores (6y: F(1,441)=52.40, p<.001; 8y: F(1,451)=50.08, p<.001; 26y: F(1,395)=16.34, p<.001) than term-born individuals. The effect sizes of the mean differences were in the medium range (attention problems: 0.42-0.61; attention span: 0.41-0.69).

Figure 2 shows the percentages of ADHD diagnoses in childhood (at either 6y/8y) and in adulthood (26y; see also Table S2 online). VP/VLBW individuals were more often diagnosed with ADHD in childhood (RR=2.01, *p*<.001, 95%Cl=1.44-2.80) and in adulthood (RR=3.29, *p*=.003, 95%Cl=1.39-7.81) than term-born individuals. In addition to more often having a diagnosis of any subtype of ADHD, VP/VLBW individuals more often had specific attention deficit disorder in childhood (ADHD-IA: RR=2.76, *p*=.001, 95%Cl=1.46-5.19; ADHD-C: RR=2.06, *p*=.010, 95%Cl=1.12-3.81), but not more often predominantly hyperactivity/impulsivity disorder (ADHD-HI: RR=1.25, *p*=.255, 95%Cl=0.64-2.46). In adulthood, there were too few diagnoses of ADHD-IA, ADHD-HI, and ADHD-C to compute reliable estimates for RR.

Do Attention Problems Reduce over Time?

Mean changes in attention scores are depicted in Figure 3. For attention problems, both a small linear $(F(1,393)=14.99, p<.001, \eta_p^2=.04)$ as well as a small quadratic time trend $(F(1,393)=36.62, p<.001, \eta_p^2=.09)$ were found. In general, attention problem scores decreased, yet more from 6y to 8y as there was an increase from 8y to 26y. In addition, we found a small main effect of group $(F(1,393)=16.04, p<.001, \eta_p^2=.04)$: individuals born VP/VLBW had higher attention problem scores than their term-born counterparts across all ages. We did not find a linear (F(1,393)=1.59, p=.105), but a small quadratic interaction of time and group $(F(1,393)=5.01, p=.013, \eta_p^2=.01)$: attention problems increased more from 8y to 26y in VP/VLBW than term-born individuals.

For attention span, a large linear (F(1,361)=363.26, p<.001, $\eta_p^2=.50$) as well as a small quadratic time trend (F(1,361)=11.32, p<.001, $\eta_p^2=.03$) were found. Attention span increased between 6y and 26y, yet this increase was larger from 8y to 26y. In addition, we found a small main effect of group (F(1,361)=15.06, p<.001, $\eta_p^2=.04$): individuals born VP/VLBW had lower attention span than

term-born individuals over time. Finally, a small linear interaction of time and group (F(1,361)=8.44, p=.002, $\eta_p^2=.02$) was found with VP/VLBW individuals showing an accelerated attention score increase over time compared to their term-born counterparts.

Are Attention Problems More Stable in VP/VLBW Individuals?

Correlations between attention problem scores from childhood to adulthood as measured with parent-ratings were larger for VP/VLBW (6-26y: r=.46; 8-26y: r=.47) than term-born individuals (6-26y: r=.11, z=3.80, p<.001; 8-26y: r=.17, z=3.36, p<.001). Similar results were found for observer-ratings of attention span: stability was higher for VP/VLBW (6-26y: r=.49; 8-26y: r=.31) than term-born individuals (6-26y: r=.25, z=2.64, p=.004; 8-26y: r=.10, z=2.16, p=.015). The effect sizes (ES $_{zr}$) were in the medium range (attention problems: 0.34-0.39; attention span: 0.23-0.28; Figure S2 online).

Figure 4A shows the results for the stability and change of ADHD diagnoses for VP/VLBW individuals. Relative risk analyses showed that VP/VLBW individuals diagnosed with ADHD in childhood were significantly more likely to still have ADHD in adulthood than those who did not have ADHD in childhood to develop ADHD by adulthood (RR = 2.54, p=.010, 95%Cl=1.15-5.58). The results for term-born individuals can be seen in Figure 4B. Term-born individuals diagnosed with ADHD in childhood were not more likely to still have ADHD in adulthood, than those who did not have ADHD in childhood to develop ADHD by adulthood (RR=2.51, p=.140, 95%Cl=0.47-13.31).

Excluding Individuals with Disabilities

Analyses were repeated excluding 54 individuals with severe disabilities (VP/VLBW: 50; term-born: 4). Most group differences in attention problems, attention span, and ADHD diagnoses remained, yet some changes were noted. While ADHD diagnoses remained more frequent in VP/VLBW in childhood, the prevalence of ADHD was not significantly different anymore between VP/VLBW and term-born individuals in adulthood (RR=1.94, *p*=.095; 95%Cl=0.72-5.21). Furthermore, removing those with severe neurodevelopmental disability led to similar attention span stability in VP/VLBW and term-born individuals (*6-26y*: *z*=0.58, *p*=.281; *8-26y*: *z*=0.39, *p*=.348). Similarly, VP/VLBW and term-born individuals without disabilities diagnosed with ADHD in childhood were not more likely to still have an ADHD diagnosis in adulthood, than those who did not have an ADHD diagnosis in childhood

to develop ADHD in adulthood (VP/VLBW: RR=1.50, p=.251, 95%Cl=0.46-4.85; term-born: RR=2.53, p=.136, 95%Cl=0.48-13.29). Full results are available online in Supplement 2.

Discussion

VP/VLBW individuals had significantly more attention problems, poorer attention span, and more often clinically significant ADHD symptoms than term-born individuals in childhood and in adulthood. In addition, attention was found to be more stable from childhood to adulthood in VP/VLBW than term-born comparisons. Nevertheless, VP/VLBW and term-born individuals' attention improved over time and most had outgrown clinically significant ADHD by adulthood. Many more VP/VLBW individuals had a severe disability of neurological or neurosensory origin. Once only those without any severe disability were considered, differences in prevalence of adult ADHD diagnoses disappeared: non-disabled VP/VLBW individuals showed similar neurodevelopmental plasticity (i.e., low stability) compared to term-born individuals.

More attention problems have been consistently reported in VP/VLBW children (Bhutta et al., 2002; Johnson et al., 2010), adolescents (Indredavik et al., 2004; Johnson & Wolke, 2013), and adults (Strang-Karlsson et al., 2008; Van Lieshout et al., 2015) compared to term-born individuals. Yet, as far as we are aware, this is the first prospective study report on attention development from childhood into adulthood on a whole population sample of VP/VLBW individuals. Consistent with previous research in general populations (Bongers, Koot, van der Ende, & Verhulst, 2003; Faraone et al., 2006), attention problems decreased over time in both VP/VLBW and in their term-born counterparts. However, compared to term-born individuals, VP/VLBW individuals had higher attention problems and lower attention span scores throughout childhood and into adulthood. The mean differences in adulthood attention remained at moderate effect size after adjusting for SES.

Furthermore, consistent with previous studies – both in childhood and adulthood – more VP/VLBW than term-born individuals were found to have a clinical diagnosis of ADHD (Indredavik et al., 2004; Johnson et al., 2010; Van Lieshout et al., 2015). These ADHD problems were predominantly of the inattentive (ADHD-IA) and combined (ADHD-C) subtypes consistent with previous reports of VP/VLBW children (Elgen, Sommerfelt, & Markestad, 2002). Specifically, previous studies reported a 15-23% prevalence of ADHD in VP/VLBW children (Elgen et al., 2002; Johnson et al., 2010) similar to the 21.9% prevalence of childhood ADHD in our VP/VLBW sample, which

equates to a 2-3 fold increased risk (Bhutta et al., 2002). Furthermore, the 7-23% prevalence of ADHD (Johnson & Wolke, 2013) in VLBW adolescents previously reported is fairly consistent with our VP/VLBW adult sample's 9.8% prevalence. In contrast, although 17.5% of term-born children had a diagnosis of ADHD in childhood, almost all (94%) had outgrown this diagnosis by adulthood. Meta-analyses estimate the prevalence of ADHD in adulthood in the general population at a 1.2-2.5% (Faraone et al., 2006; Simon, Czobor, Bálint, Mészáros, & Bitter, 2009), similar to our term-born adult's ADHD prevalence of 2.9%.

The persistence of ADHD from childhood into adolescence and adulthood in other prospective population studies is only around 15% (Faraone et al., 2006) and we found an even lower rate of 6% in our sample of term-born adults. In contrast, attention and ADHD were significantly more stable from childhood to adulthood in VP/VLBW individuals, especially when they also had a cognitive disability. Relatively enduring alterations in the brain associated with being born preterm (Bäuml et al., 2014; Skranes et al., 2005) may lead to these more persistent attention problems (Bora, Pritchard, Chen, Inder, & Woodward, 2014). This link between early brain trauma and attention problems has also been reported for children with acquired childhood brain trauma (Yeates et al., 2005). It is thus possible that attention problems are part of generally impaired functioning in multiple domains including cognitive function (Eryigit Madzwamuse, Baumann, Jaekel, Bartmann, & Wolke, 2014). However, it has been shown that attention problems are specific problems over and above intelligence (Jaekel et al., 2013; Wolke et al., 2015). As a consequence, persistence of attention problems may contribute to VP/VLBW individuals more often experiencing academic problems (Hack et al., 2002; Jaekel et al., 2013) and less full-time employment and wealth (Mathiasen, Hansen, Nybo Anderson, & Greisen, 2009). The hypothesis that alterations in brain development of VP/VLBW children place limits to their neurodevelopmental plasticity (Luciana, 2003) is supported by the finding that VP/VLBW individuals without a severe disability were not more likely than term-born individuals to still suffer clinically significant ADHD in adulthood. Those individuals without severe neurological or neurosensory disability, whether preterm or term-born, were more likely to change from childhood to adulthood, i.e., showed less stability and more neurodevelopmental plasticity. Alternatively, it is conceivable that gene-environment correlations are involved in a sense that parents are passing on the uterine adversity and the (potentially inheritable) factors that gave rise to it. However, a recent study that compared siblings found that the association of ADHD and gestation was independent of

any family effects (D'Onofrio et al., 2013). Nevertheless, future studies of preterm children would benefit from including siblings.

Strengths and Limitations

The strengths of this study are its prospective design from childhood into adulthood, using multiple measures and data sources in a large whole population sample of VP/VLBW and term-born individuals. There are also limitations. First, although 68% of the eligible VP/VLBW and term-born individuals assessed in childhood could be reached at 26 years, dropout was not random as VP/VLBW and term-born individuals at social disadvantage were less likely to continue participation. It is well known that social factors are a major reason for dropout in most longitudinal studies (Hille, Elbertse, Gravenhorst, Brand, & Verloove-Vanhorick, 2005). However, simulations have shown that even when dropout is selective and/or correlated with the outcome of interest, longitudinal regression estimates may change only marginally (Wolke, Waylen, et al., 2009). Second, missing data for individual measures at different time points ranged from 0-22%. Some were due to disabled individuals where attention regulation or ADHD diagnoses could not be assessed. Third, attention problems were assessed with parent reports, both in childhood and adulthood. Yet, only 38.5% of the VP/VLBW and 24.0% of the term-born adults still lived at home during the adult assessment, which may have impacted the reliability of these ratings. However, we used parent instead of self-ratings to be able to examine the stability of attention while avoiding rater bias. Fourth, information on clinical diagnoses of adulthood ADHD were obtained with the ADHD adult rating scale rather than clinical interviews as in childhood. However, external validity of this scale is good as ADHD diagnoses based on this assessment are related to adult's level of psychosocial impairment (Kooij et al., 2005).

Conclusion

VP/VLBW adults are more likely to have attention problems, poorer attention span, and ADHD than term-born adults. Moreover, these problems are more likely to persist into adulthood for VP/VLBW individuals – and in particular in those with disabilities – than their term-born counterparts. As VP/VLBW children are not impulsive and disruptive but find it difficult to concentrate, they may be overlooked by teachers and thus not receive special assistance enabling them to achieve in school (Johnson, Gilmore, Gallimore, Jaekel, & Wolke, 2015). It may therefore be necessary to raise

awareness for attention problems of VP/VLBW children and implement intervention programs that have been shown to reduce their attention problems (Grunewaldt, Løhaugen, Austeng, Brubakk, & Skranes, 2013).

Key Points

- Previous studies showed that VP/VLBW is related to attention problems.
- This study showed that although attention regulation improves over time, VP/VLBW
 individuals have more attention problems, poorer attention span, and are more likely to have
 an ADHD diagnosis than term-born individuals both in childhood and in adulthood.
- Attention problems are also more likely to persist into adulthood for VP/VLBW individuals than their term-born counterparts, yet this persistence is mainly carried by children with severe disabilities.
- These findings have implications for early interventions as preterm children may not outgrow their problems and require support for attention regulation into adulthood.

Acknowledgements

We would like to thank all current and former Bavarian Longitudinal Study group members, pediatricians, psychologists, and research nurses. Moreover, we would like to thank those who contributed to study organization, recruitment, data collection, and management at the 26 year assessment: Barbara Busch, Stephan Czeschka, Claudia Grünzinger, Christian Koch, Diana Kurze, Sonja Perk, Andrea Schreier, Antje Strasser, Julia Trummer, and Eva van Rossum. Special thanks are due to the study participants and their families. This study was supported by grants PKE24, JUG14, 01EP9504 and 01ER0801 from the German Federal Ministry of Education and Science.

Correspondence to

Dieter Wolke, Department of Psychology, University of Warwick, Coventry CV4 7AL, United Kingdom, +442476573217, D.Wolke@warwick.ac.uk

Figure Captions

Figure 1

Attention Problems and Attention Span Means at 6, 8 and 26 Years and their 95% Confidence Intervals for Males and Females Respectively.

Figure 2

Percentages of Any ADHD Diagnoses in Childhood and Adulthood, Divided into ADHD Predominantly Inattentive (ADHD-IA), ADHD Predominantly Hyperactive/Impulsive (ADHD-HI), and ADHD Combined (ADHD-C) Subtypes.

Figure 3

Development of Attention Problems (Higher Values Depict More Problems) and Attention Span (Higher Values Depict Better Attention Span) from Childhood to Adulthood.

Figure 4

Stability of ADHD Diagnoses from Childhood to Adulthood.

Figure S1

Flowchart of Participants.

Figure S2

Attention Problems and Attention Span Correlations from Childhood to Adulthood.

References

- Achenbach, T. M. (1991). *The manual for the Child Behavior Checklist 4-18 and 1991 Profile*.

 Burlington, VT: University of Vermont, Department of Psychiatry.
- Achenbach, T. M. (1997). Manual for the Young Adult Selt-Report and Young Adult Behavior

 Checklist. Burlington, VT: University of Vermont, Department of Psychiatry.
- Arbeitsgruppe Deutsche Child Behavior Checklist. (1998). Elternfragebogen über das verhalten von kindern und jugendlichen: Deutsche bearbeitung der Child Behavior Checklist (CBCL/4-18).

 Köln, Germany: Arbeitsgruppe Kinder-, Jugend- und Familiendiagnostik.
- Bauer, A. (1988). Ein verfahren zur messung des für das bildungsverhalten relevanten Status (BRSS). Frankfurt: Deutsches Institut für Internationale Pädagogische Forschung.
- Bäuml, J. G., Daamen, M., Meng, C., Neitzel, J., Scheef, L., Jaekel, J., . . . Sorg, C. (2014).
 Correspondence between aberrant intrinsic network connectivity and gray-matter volume in the ventral brain of preterm born adults. Cerebral Cortex, Epub ahead of print.
- Bhutta, A. T., Cleves, M. A., Casey, P. H., Cradock, M. M., & Anand, K. S. (2002). Cognitive and behavioral outcomes of school-aged children who were born preterm: A meta-analysis. *JAMA*, 288, 728-737.
- Bongers, I. L., Koot, H. M., van der Ende, J., & Verhulst, F. C. (2003). The normative development of child and adolescent problem behavior. *Journal of Abnormal Psychology*, *112*, 179-192.
- Bora, S., Pritchard, V. E., Chen, Z., Inder, T. E., & Woodward, L. J. (2014). Neonatal cerebral morphometry and later risk of persistent inattention/hyperactivity in children born very preterm. *Journal of Child Psychology and Psychiatry*, *55*, 828-838.
- Brook, J. S., Brook, D. W., Zhang, C., Seltzer, N., & Finch, S. J. (2013). Adolescent ADHD and adult physical and mental health, work performance, and financial stress. *Pediatrics*, *131*, 5-13.
- Cohen, J. (1988). Statistical power analysis for the behavioral sciences. Hillsdale, NJ: Erlbaum.
- D'Onofrio, B. M., Class, Q. A., Rickert, M. E., Larsson, H., Långström, N., & Lichtenstein, P. (2013).

 Preterm birth and mortality and morbidity: A population-based quasi-experimental study. *JAMA Psychiatry*, 70(11), 1231-1240.
- Elgen, I., Sommerfelt, K., & Markestad, T. (2002). Population based, controlled study of behavioural problems and psychiatric disorders in low birthweight children at 11 years of age. *Archives of Disease in Childhood Fetal and Neonatal Edition, 87*, F128-F132.

- Eryigit Madzwamuse, S., Baumann, N., Jaekel, J., Bartmann, P., & Wolke, D. (2014). Neuro-cognitive performance of very preterm or very low birth weight adults at 26 years. *Journal of Child Psychology and Psychiatry, Epub ahead of print*.
- Esser, G., Blanz, B., Geisel, B., & Laucht, M. (1989). *Mannheimer Elterninterview : Strukturiertes*interview zur erfassung von kinderpsychiatrischen auffalligkeiten. Beltz, Germany: Weinheim.
- Faraone, S. V., Biederman, J., & Mick, E. (2006). The age-dependent decline of attention deficit hyperactivity disorder: A meta-analysis of follow-up studies. *Psychological Medicine*, *36*, 159-165.
- Gjervan, B., Torgersen, T., Nordahl, H. M., & Rasmussen, K. (2012). Functional impairment and occupational outcome in adults with ADHD. *Journal of Attention Disorders*, *16*, 544-552.
- Grunewaldt, K. H., Løhaugen, G. C. C., Austeng, D., Brubakk, A.-M., & Skranes, J. (2013). Working Memory Training Improves Cognitive Function in VLBW Preschoolers. *Pediatrics*, *131*(3), e747-e754.
- Gutbrod, T., Wolke, D., Soehne, B., Ohrt, B., & Riegel, K. (2000). Effects of gestation and birth weight on the growth and development of very low birthweight small for gestational age infants: a matched group comparison. *Archives of Disease in Childhood Fetal and Neonatal Edition,* 82(3), F208-F214.
- Hack, M., Flannery, D. J., Schluchter, M., Cartar, L., Borawski, E., & Klein, N. (2002). Outcomes in young adulthood for very-low-birth-weight infants. *New England Journal of Medicine*, *346*(3), 149-157.
- Hechtman, L. (2011). Prospective follow-up studies of ADHD: Helping establish a valid diagnosis in adults. *Journal of the American Academy of Child and Adolescent Psychiatry*, *50*, 533-535.
- Hille, E. T. M., Elbertse, L., Gravenhorst, J. B., Brand, R., & Verloove-Vanhorick, S. P. (2005).Nonresponse bias in a follow-up study of 19-year-old adolescents born as preterm infants.Pediatrics, 116, e662-e666.
- Indredavik, M. S., Vik, T., Heyerdahl, S., Kulseng, S., Fayers, P., & Brubakk, A.-M. (2004). Psychiatric symptoms and disorders in adolescents with low birth weight. *Archives of Disease in Childhood Fetal and Neonatal Edition*, 89, F445-F450.

- Jaekel, J., Wolke, D., & Bartmann, P. (2013). Poor attention rather than hyperactivity/impulsivity predicts academic achievement in very preterm and full-term adolescents. *Psychological Medicine*, 43, 183-196.
- Johnson, S., Gilmore, C., Gallimore, I., Jaekel, J., & Wolke, D. (2015). The long-term consequences of preterm birth: what do teachers know? *Developmental Medicine and Child Neurology*, 57(6), 571-577.
- Johnson, S., Hollis, C., Kochhar, P., Hennessy, E., Wolke, D., & Marlow, N. (2010). Psychiatric disorders in extremely preterm children: Longitudinal finding at age 11 years in the EPICure study. *Journal of the American Academy of Child and Adolescent Psychiatry*, 49, 453-463.
- Johnson, S., & Wolke, D. (2013). Behavioural outcomes and psychopathology during adolescence. *Early Human Development, 89*, 199-207.
- Kaufman, A. S., & Kaufman, N. (1983). *Kaufman Assessment Battery for Children*. Circle Pines, MN: American Guidance Service.
- Kooij, J. J. S., Buitelaar, J. K., Van den Oord, E. J., Furer, J. W., Rijnders, C. A. T., & Hodiamont, P.
 P. G. (2005). Internal and external validity of Attention-Deficit Hyperactivity Disorder in a population-based sample of adults. *Psychological Medicine*, *35*, 817-827.
- Luciana, M. (2003). Cognitive development in children born preterm: Implications for theories of brain plasticity following early injury. *Development and Psychopathology*, *15*(4), 1017-1047.
- Mathiasen, R., Hansen, B. M., Nybo Anderson, A. M., & Greisen, G. (2009). Socio-economic achievements of individuals born very preterm at the age of 27 to 29 years: A nationwide cohort study. *Developmental Medicine and Child Neurology, 51*(11), 901-908.
- Matza, L., Paramore, C., & Prasad, M. (2005). A review of the economic burden of ADHD. *Cost Effectiveness and Resource Allocation*, 3, 5.
- Melchers, P., & Preuss, U. (1991). *Kaufman battery for children: Deutschsprachige fassung*. Frankfurt am Main, Germany: Swets & Zeitlinger.
- NICE. (2008). Attention deficit hyperactivity disorder: Diagnosis and management of ADHD in children, young people and adults. *NICE clinical guideline 72*.
- Polanczyk, G., de Lima, M. S., Horta, B. L., Biederman, J., & Rohde, L. A. (2007). The worldwide prevalence of ADHD: A systematic review and metaregression analysis. *American Journal of Psychiatry*, *164*, 942-948.

- Schmid, G., Schreier, A., Meyer, R., & Wolke, D. (2011). Predictors of crying, feeding and sleeping problems: a prospective study. *Child Care Health and Development*, *37*(4), 493-502.
- Simon, V., Czobor, P., Bálint, S., Mészáros, Á., & Bitter, I. (2009). Prevalence and correlates of adult attention-deficit hyperactivity disorder: Meta-analysis. *The British Journal of Psychiatry, 194*, 204-211.
- Skranes, J. S., Martinussen, M., Smevik, O., Myhr, G., Indredavik, M., Vik, T., & Brubakk, A.-M. (2005). Cerebral MRI findings in very-low-birth-weight and small-for-gestational-age children at 15 years of age. *Pediatric Radiology*, *35*, 758-765.
- Strang-Karlsson, S., Räikkönen, K., Pesonen, A. K., Kajantie, E., Paavonen, E. J., Lahti, J., . . .

 Andersson, S. (2008). Very Low Birth Weight and Behavioral Symptoms of Attention Deficit

 Hyperactivity Disorder in Young Adulthood: The Helsinki Study of Very-Low-Birth-Weight

 Adults. *American Journal of Psychiatry*, *165*(10), 1345-1353.
- Van Lieshout, R. J., Boyle, M. H., Saigal, S., Morrison, K., & Schmidt, L. A. (2015). Mental health of extremely low birth weight survivors in their 30s. *Pediatrics*, *135*(3), 452-459.
- Wolke, D. (1996). TRCB tester's rating of child behavior: Test construction and standardisation (in German). Available from author upon request.
- Wolke, D. (2012). TRAB tester's rating of adult behavior (in German): Available from author upon request.
- Wolke, D., Schmid, G., Schreier, A., & Meyer, R. (2009). Crying and feeding problems in infancy and cognitive outcome in preschool children born at risk: A prospective population study. *Journal of Developmental and Behavioral Pediatrics*, 30(3), 226-238.
- Wolke, D., Strauss, V. Y.-C., Johnson, S., Gilmore, C., Marlow, N., & Jaekel, J. (2015). Universal gestational age effects on cognitive and basic mathematic processing: 2 cohorts in 2 countries. *The Journal of Pediatrics, online first*.
- Wolke, D., Waylen, A., Samara, M., Steer, C., Goodman, R., Ford, T., & Lamberts, K. (2009).
 Selective drop-out in longitudinal studies and non-biased prediction of behaviour disorders.
 The British Journal of Psychiatry, 195(3), 249-256.
- Yeates, K. O., Armstrong, K., Janusz, J., Taylor, H. G., Wade, S., Stancin, T., & Drotar, D. (2005).

 Long-term attention problems in children with traumatic brain injury. *Journal of the American Academy of Child and Adolescent Psychiatry, 44*, 574-584.

Zander, J., Holzmann, K., & Selbmann, H. K. (1989). Materialien aus der bayerischen perinatalerhebung zur problematik der sectiofrequenz. *Geburtshilfe und Frauenheilkunde,* 49(4), 328-336.

Table 1. Demographics of Participating and Dropout VP/VLBW and Term-Born Individuals

	Participants			Dropouts			
	VP/VLBW	Control	p-	VP/VLBW	p-	Control	p-
	(N=260)	(N=229)	valueª	(N=151)	<i>value</i> ^b	(N=79)	value ^c
GA (weeks)	30.6 (2.2)	39.7 (1.2)	<.001	30.4 (2.4)	.491	39.6 (1.2)	.908
BW (kg)	1.32 (3.16)	3.36 (4.45)	<.001	1.27 (2.89)	.064	3.44 (4.46)	.191
SGA	108 (41.5%)	23 (10.0%)	<.001	68 (45.0%)	.490	8 (10.1%)	.983
Females	122 (46.9%)	122 (53.3%)	.161	77 (51.0%)	.426	32 (40.5%)	.050
Multiple births	69 (26.5%)	7 (3.1%)	<.001	34 (22.5%)	.364	5 (6.3%)	.195
Complications							
Pre-pregnancy	1.38 (0.82)	1.14 (0.80)	.001	1.27 (0.85)	.177	1.05 (0.77)	.414
Pregnancy	2.26 (1.20)	0.72 (0.87)	<.001	2.61 (1.26)	.005	1.06 (1.02)	.004
Birth	4.65 (1.42)	2.11 (1.49)	<.001	4.45 (1.40)	.164	2.16 (1.56)	.796
Neonatal	9.30 (2.69)	0.38 (0.64)	<.001	9.53 (2.71)	.408	0.39 (0.67)	.924
Disability	50 (19.2%)	4 (1.7%)	<.001	38 (25.2%)	.157	1 (1.3%)	.771
MA (years)	28.9 (4.7)	29.1 (4.6)	.611	27.8 (5.5)	.041	27.5 (5.3)	.011
SES							
SES-high	53 (20.5%)	77 (33.6%)	.001	28 (18.5%)	.638	15 (19.0%)	.014
SES-middle	122 (47.1%)	98 (42.8%)	.340	51 (33.8%)	.008	24 (30.4%)	.052
SES-low	84 (32.4%)	54 (23.6%)	.030	72 (47.7%)	.002	40 (50.6%)	<.001

GA = gestational age; BW = birth weight; SGA = small for gestational age; MA = maternal age; SES = socioeconomic status; reported values are either means and standard deviations or frequencies and percentages; ^a compares VP/VLBW and term-born; ^b compares participating and dropout VP/VLBW; ^c compares participating and dropout term-born.