Introduction

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Our understanding and management of brain-behavior relationships over the lifespan has advanced significantly since we published our first book on this topic in 2007 (Donders & Hunter, 2007) and a similar text that was published by others six years later (Baron & Rey-Casserly, 2013). In this volume, we wanted to provide an updated account of the most common neuropsychological conditions that most clinicians may encounter in their practice. Whenever possible, we aspired to include within the same chapter descriptions of the different manifestations across the lifespan, although understandably some conditions (e.g., low birth weight, dementia) are unique to the extremes of the age spectrum.

It was our goal that each chapter in this volume provide a concise but sufficiently in-depth review of the clinical manifestations of the condition at hand, with particular attention paid to the role of neuropsychological assessment and intervention, culminating in pragmatic suggestions for clinical practice as well as future research. Each chapter was written by contributors who have considerable clinical as well as empirical expertise with the condition being discussed. We hope that this book serves as an updated reference point for our current understanding of a wide range of commonly encountered neuropsychological conditions across the lifespan. We anticipate that it will be of interest to not only neuropsychologists but also to professionals in rehabilitation, neurology, and a variety of related health professions.

References

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Chapter 1

Preterm and Low-Birth-Weight Birth

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Introduction

Two of the most significant risk factors for long-term developmental outcomes are preterm birth (<37 weeks gestational age [GA]) and low birth weight (<2,500 g). Prematurity is the leading cause of infant mortality and long-term morbidity (March of Dimes, PMNCH, Save the Children, & WHO, 2012). According to the World Health Organization (WHO), about 15 million babies worldwide (>10% of all births) are born preterm every year, and nearly 22 million infants (16%) have low birth weight (Blanc & Wardlaw, 2005). In addition, prematurity is associated with intrauterine growth restriction and small for gestational age (SGA) birth, commonly defined as birth weight below the 10th percentile for GA according to national sex-specific norms. Based on recent findings on a progressive impact of prematurity on long-term outcomes with increased prematurity (Lipkind, Slopen, Pfeiffer, & McVeigh, 2012; MacKay, Smith, Dobbie, & Pell, 2010; Poulsen et al., 2013; Quigley et al., 2012), fine-grained definitions for groups of preterm and low-birth-weight children have been established (see Table 1.1 and abbreviations therein). Accordingly, in this chapter we refer to the highest risk groups of premature infants as VP/VLBW and EP/ELBW.

Clinical Manifestation

Epidemiology and Pathophysiology

The etiology of preterm birth can be differentiated into spontaneous and medically indicated, often as a result of intrauterine growth restriction and maternal conditions such as preeclampsia. A number of diverse risk factors for preterm birth have been identified (e.g., infection/inflammation, social adversity, Black ethnicity, maternal stress, and preconception and prenatal smoking); however, the precise mechanisms and majority of variance remain unexplained (Goldenberg, Culhane, Iams, & Romero, 2008; Raisanen, Gissler, Saari, Kramer, & Heinonen, 2013). The preterm birth rate in the United States is now 9.6% (March of Dimes, 2016). The preterm birth rate has increased in most countries in the last two decades due to changing demographics (e.g., older mothers), increased fertility treatment leading to increased multiple births, which are often preterm, and the increased use of elective cesarean sections, which often occur early in the term (Cheong & Doyle, 2012; Goldenberg et al., 2008). However, the preterm live birth weight peaked in 2006 and has declined or remained relatively stable from year to year since then (March of Dimes, 2016). This decline has been attributed to improved medical

Table 1.1 Classification of Premature Children According to Birth Weight and Gestational Age Groups and Their Overall Percentage Among All Live Births in the United States (CDC, 2016)

Birth Weight (BW) Groups (%)	BW (g)	Preterm Birth in GA Groups (%)	GA (weeks)
Extremely low BW (ELBW), 0.7	<1,000	Extremely preterm (EP), 0.7	<28
Very low BW (VLBW), 0.7	1,000–1,499	Very preterm (VP), 0.9	28–31
		Moderately preterm, 1.5	32–33
Low BW (LBW), 6.6	1,500–2,499	Late preterm (LP), 6.8	34–36
		Early term, 24.8	37–38
Normal BW (NBW), 92	>2,499	Full term, 58.7	>38

interventions as well as changes in clinical practice around LP birth. With increasing recognition of risks associated with LP birth, delivery before 39 weeks' gestation is now discouraged unless there is a clear medical rationale (ACOG Committee, 2008; Ashton, 2010).

Due to continuous advances in neonatal care (i.e., early surfactant administration and less-invasive treatment), more EP/ELBW infants are surviving (Gopel et al., 2011; Halliday, 2008). Although medical advances have improved the survival rate and decreased the rates of severe medical and neurodevelopmental complications, the prevalence of cognitive problems in preterm populations has not changed with these improvements in viability (Moore et al., 2012). In addition, although significant deficits have been clearly documented in individuals with a history of EP/ELBW, specific patterns of neurocognitive weakness have been identified in LP groups as well (Baron, Litman, Ahronovich, & Baker, 2012).

Neurodevelopmental and Medical Complications

In addition to cognitive outcomes discussed in greater detail in the section on Cognition, there are a number of significant medical and neurodevelopmental challenges with EP/ELBW and VP/VLBW infants. EP/ELBW birth means that these infants are born with immature organs, including their lungs and brains, and they often experience organ complications (e.g., bleeding into the brain). Severe neurological injuries such as periventricular leukomalacia (PVL) have become rare today, but diffuse white matter injuries remain common and can be used to predict neurodevelopmental outcomes (Woodward, Anderson, Austin, Howard, & Inder, 2006; Woodward, Clark, Bora, & Inder, 2012). A number of factors have been identified that are associated with PVL and intraventricular and cerebellar hemorrhage in VP/VLBW infants, including low Apgar scores, necrotizing enterocolitis, inotropic support, and patent ductus arteriosus (Kidokoro et al., 2014). Moreover, PVL is often associated with neuronal/axonal disease in a destructive amalgam termed encephalopathy of prematurity, affecting cerebral white matter and cortex, the thalamus, basal ganglia, the brain stem, and the cerebellum (Volpe, 2009). Research has also documented that an important cellular mechanism for explaining changes to the preterm brain is the developing oligodendrocyte (Volpe, Kinney, Jensen, & Rosenberg, 2011) and the timing of its exposure to oxygen (Felderhoff-Müser et al., 2004; Prager et al., 2013).

In terms of broader neurodevelopmental outcomes, rates of cerebral palsy (CP) in preterm children are variable in the literature. A 2008 meta-analysis of 26 studies indicated that the prevalence of CP increases with lower GA; <1% of children born between 32 and 36 weeks GA have CP, and the numbers increase to 6% at 28–31 weeks GA and to 14% at 22–27 weeks GA (Himpens, Van den Broeck, Oostra, Calders, & Vanhaesebrouck, 2008). Moreover, developmental coordination disorder is common in VP/VLBW children, with highly variable rates in the literature that range from 9.5% to 51% when compared with a 6% rate of occurrence in the general population (Arpino et al., 2010). Children born preterm also have higher rates of vision impairments, including retinopathy of prematurity (occurring in up to 56% of EP/ELBW), strabismus, and low visual acuity, and of hearing deficits (occurring in up to 3% of EP/ELBW) (Arpino et al., 2010). It is notable that despite these frequent problems, parents and teachers of preterm children often expect developmental catch-up before school entry; however, patterns of developmental difficulties are relatively stable from age 2 years onward (Breeman, Jaekel, Baumann, Bartmann, & Wolke, 2015). In fact, specific developmental problems often become more apparent during primary school because of the larger demands on differential abilities such as mathematics.

Prevention

As described in the section on Epidemiology and Pathophysiology, up to 78% of the variation in preterm birth remains unexplained. This is found even when looking at data from large whole-population studies (Goldenberg et al., 2008; Raisanen et al., 2013). Thus, although there are techniques to delay birth under some conditions, with variable success, it is currently not possible to identify women who are at risk for preterm birth and to prevent preterm birth (Rubens et al., 2014). In addition, research in this area is complicated by a lack of standardization and consistency in primary outcomes used to measure prevention of preterm birth in randomized controlled studies and systematic reviews (Meher & Alfirevic, 2014).

Long-Term Neuropsychological Outcomes

When reviewing literature on outcomes of VP/VLBW and EP/ELBW children, it is important to be careful about generalizing results of outcome research from older birth cohorts to more recent cohorts born after 2000. Although the outcome data regarding neuropsychological impairment are fairly consistent across studies, Table 1.2 indicates a large range of effects when compared across the available literature. Given the significant advances in neonatal care implemented since 1980, there have been substantial changes in the mortality and disability rates in these populations, a fact that has likely contributed to significant differences in cohorts across time. In addition, significant research methodology changes in the 1990s, including a shift toward longitudinal analyses and the use of neuropsychological measures to examine neurodevelopmental profiles beyond broad cognitive outcomes, led to vast differences in the information available for these different cohorts (Baron & Rey-Casserly, 2010). Beyond these methodological and cohort differences, researchers have often interpreted findings about temporal change or stability in developmental outcomes differently, contributing to continued variability in rates and profiles of impact.

Table 1.2 Overall Rates of Neuropsychological and Related Problems After VP/VLBW Birth

Outcome Area Affected by VP/VLBW Birth	Range of Problems Reported in the Literature (%)
General cognitive impairment	20–30
Attention problems, attention-deficit/hyperactivity disorder	10–25
Executive function deficits	10–70
Visual-motor skills	30–60
Mathematics deficiencies	10–25
Reading/language deficiencies	24–34
Special educational needs	20–45
Below average attainment	40–48
Emotional problems	10–40
Social relationship difficulties	10–30
Autism spectrum disorder	3–8

Research on brain development in VP/VLBW children suggests that their brains grow more slowly and differently than the brains of children born at full term (Ball et al., 2012; Kapellou et al., 2006; Woodward et al., 2012). As a result, VP/VLBW children are at highly increased risk for a range of neurodevelopmental, cognitive, attention, mental health, and social relationship difficulties (Farooqi, Hagglof, Sedin, Gothefors, & Serenius, 2007). VP/VLBW children more often struggle in school and have persistent difficulties throughout adolescence (Johnson & Wolke, 2013). In adulthood, preterm individuals, across periods of prematurity, have lower academic attainment and income, increased reliance on social benefits, and increased risk of psychiatric problems, and these individuals report poorer interpersonal relationships and less satisfaction with their lives (Darlow, Horwood, Pere-Bracken, & Woodward, 2013a; D'Onofrio et al., 2013; Hack, 2009, 2013; Heinonen et al., 2013; Johnson & Marlow, 2014; Moster, Lie, & Markestad, 2008).

Cognition

Recent studies suggest that delivery at any gestation other than full term may confer an insult to brain development, rendering survivors at risk for adverse neurocognitive outcomes (MacKay et al., 2010; Quigley et al., 2012). Depending on the timing and severity of gestational insults, reorganization of cortical structures is still detectable throughout childhood and adolescence in multiple regions (Nosarti, Murray, & Hack, 2010; Peterson, 2003). As neuroimaging techniques have advanced, widespread brain changes in preterm infants, adolescents, and adults have been demonstrated (Ball et al., 2012; Kapellou et al., 2006; Nosarti, 2013; Nosarti et al., 2010; Peterson, 2003). For example, effects of preterm birth on the brain's large-scale intrinsic networks with related changes of intrinsic connectivity and gray matter structure in the ventral brain of preterm adults have been documented at 26 years of age (Bäuml et al., 2014). Across development, cortical changes are prospectively related to academic achievement because they functionally manifest in poor attention (Woodward et al., 2012) and slower processing speed (Mulder, Pitchford, & Marlow, 2010). Attention, for example, is an important prerequisite for learning in the classroom but preterm children's attention problems make it hard for them to profit from teaching input in school.

General Cognitive Ability. A number of meta-analyses and systematic reviews have examined general cognitive ability (otherwise discussed as IQ) in preterm children, beginning with the earliest cohorts studied systematically. One seminal meta-analysis of children born between 1975 and 1988 found a weighted mean difference of 10.9 IQ points in favor of term controls (Bhutta, Cleves, Casey, Cradock, & Anand, 2002). In a more recent meta-analysis of studies examining cognitive outcomes in preterm children born between 1975 and 2000, the mean IQ score difference was 11.9 points in favor of term controls (Kerr-Wilson, Mackay, Smith, & Pell, 2012). In both studies, IQ was associated with GA, and there was an increasing difference in IQ scores between preterm and term-matched controls with lower GA, indicating a nonlinear quadratic trend (Jaekel, Baumann, & Wolke, 2013).

Both meta-analyses included studies of preterm birth cohorts from different eras of neonatal care, which limits the generalizability of these findings to more recent birth cohorts. Nevertheless, results of cognitive deficits seem to remain consistent. In a large cohort of children born in Australia in the 1990s, ELBW children also performed significantly below NBW controls with a mean Full Scale IQ difference on the Wechsler Intelligence Scale for Children-III of 9.4 points (Anderson, Doyle, & Victorian Infant Collaborative Study Group, 2003). Although significant mean differences were identified across test indices, the most significant group differences were found for the following IQ indices: perceptual organization (9.9 points) and freedom from distractibility (8.1 points), whereas the verbal comprehension (6.8 points) and processing speed (6.7 points) indices indicated a less significant discrepancy in the favor of NBW controls. Similarly, in a 2001–2003 birth cohort, cognitive deficits were three to six times higher at 6 years of age in an EP/ELBW cohort as compared with term controls (Orchinik et al., 2011). In a recent large multisite study of EP children's neurocognitive outcomes at age 10 years, the distribution of test scores was significantly shifted, situated below normative expectations on the Differential Ability Scale, 2nd ed. In this US cohort, 17% of the EP group demonstrated Verbal Cluster scores that were more than 2 SD below the population mean and 19% fell between 1 and 2 SD below the mean (Joseph et al., 2016). On the Nonverbal Cluster of the same scale, 15% of the EP group demonstrated scores that were more than 2 SD below the population mean and 24% fell between 1 and 2 SD below the mean (Joseph et al., 2016). Although there was no term control group available, these rates of cognitive impairment are significantly greater than expected based on normative data.

Attention and Executive Functioning. Attention regulation is often compromised in VP/VLBW individuals (please see the section on attention-deficit/hyperactivity disorder [ADHD] for more details on this condition). Research has investigated the underlying mechanisms that may explain the association between different markers of prematurity (i.e., low GA, low BW, SGA birth) and attention problems (Hall, Jaekel, & Wolke, 2012) and found specific developmental pathways; for example, SGA affected attention problems at age 6 years in response to reduced brain volume, and preterm birth impacted attention problems in response to altered brain function (Hall et al., 2012). Moreover, although boys in general are more often found to have attention problems, attention problems after preterm birth are more apparent in girls. This finding has important implications for clinical practice, such that regular childhood follow-up assessments of preterm children are more sensitive to potential gender differences in potential challenges.

With regard to the neural mechanisms underlying attention in VP/VLBW, it is not clear which specific attentional submechanisms are affected and how they relate to broader unfolding brain circuitry. There is recent evidence for selectively changed attention mechanisms in relation to preterm adults' altered intrinsic brain networks (Finke et al., 2015). Intrinsic functional connectivity is organized by brain networks that are defined by synchronous ongoing activity (i.e., circuits). One such brain circuit is the attentional network that is involved in alerting, orienting, and executive control. Anatomically, this includes the anterior cingulate and anterior insula as well as areas of the prefrontal cortex (for inhibition of dominant responses) (Petersen & Posner, 2012). The computational theory of visual attention further separates components for the assessment of specific attention submechanisms including visual perceptual processing speed, visual short-term memory storage capacity, efficiency of top-down control, and spatial laterality of attention. When comparing preterm and term-born adults, Finke and colleagues (2015) found specific impairments in visual short-term memory storage capacity that was predicted by the degree of neonatal medical complications. Most importantly, patterns of changed connectivity in preterm versus full term adults were systematically associated with short-term storage capacity (i.e., the more connectivity differences the better preterm adults' storage capacity) (Finke et al., 2015). This suggests that changes in intrinsic functional connectivity patterns may have the potential to compensate adverse developmental consequences of prematurity on visual short-term memory capacity.

In a meta-analysis of attention and executive functioning (EF) outcomes in EP/ELBW, deficits in a number of specific domains of attention were identified, i.e., selective attention, sustained attention, response inhibition, working memory, verbal fluency, planning and shifting (Mulder, Pitchford, Hagger, & Marlow, 2009). Results across individual studies of selective attention have gleaned variable results in the EP literature. In the preterm population, development of selective attention is impacted by sex, socioeconomic status, chronological age, and gestational age. In the EP group, studies demonstrated a moderate effect of prematurity on selective attention (0.58), which was relatively stable over time. In preterm children born later than 26 weeks GA a large effect size was identified in the preschool years, but this appeared to decline over time with preterm children catching up to term controls in their later school-age years (Mulder et al., 2009).

Across studies of sustained attention, there was variability in findings. As part of the meta-analysis, studies were split based on GA. For studies that examined sustained attention in an EP cohort, a moderate to large effect size (0.67) was identified with a significant relationship between the effect size and GA (Mulder et al., 2009). Across analyses of EF, Mulder and colleagues also demonstrated a number of areas of impact in preterm children compared with term controls. Given the interaction between GA and task performance, studies were again split by GA, revealing a moderate effect size for studies of children born before 26 weeks GA. There were not enough studies with similar assessments to measure working memory, although results indicated that spatial working memory was impacted in preterm children when compared with term controls, whereas performances on nonspatial working memory tasks were not different. On verbal fluency tasks, both semantic and phonemic verbal fluency skills were affected in preterm children with small to moderate effect size. On studies of planning on a tower test, the mean effect size was moderated by GA. When examining studies of children born less than 26 weeks GA the mean effect size was moderate to large, but the effect size became nonsignificant when focusing on studies of preterm children born more than 26 weeks GA. Finally, studies assessing shifting abilities (Trail Making Test part B) revealed a moderate mean effect size. Overall, results support a pattern of less effective attention and EF skills in preterm children compared with term controls (Mulder et al., 2009).

In a large Australian EP/ELBW cohort, specific aspects of attention and EF were examined compared with term controls at 8 years of age (Anderson et al., 2011). The EP/ELBW performed significantly below the term control group across assessments of selective attention, sustained attention, attention encoding, shifting, and divided attention. In addition, the EP/ELBW group demonstrated significantly higher ADHD symptoms. In contrast to many of the findings from the meta-analysis by Mulder et al. (2009), the authors did not find a significant interaction with GA.

A number of studies have identified EF deficits across the lifespan in preterm populations. Significantly higher rates of deficits across measures of response inhibition, cognitive set-shifting, and working memory were identified in a geographical cohort of kindergarten-age EP/ELBW children compared with term controls (Orchinik et al., 2011). These differences remained significant even when controlling for verbal knowledge (Orchinik et al., 2011). Parent and teacher reports of ADHD symptoms and impaired self-regulation were associated with deficits on tests of EF in this EP/ELBW cohort (Scott et al., 2012). These results indicate that differences in the development of EF skills are present early in life in preterm children and impact functioning in daily life. When examining early EF skills in ELBW, late-preterm, and term-born preschoolers, ELBW children performed significantly poorer than term-born controls on assessments of working memory and inhibition as well as sustained attention (Baron, Kerns, Muller, Abronovich, & Litman, 2012). Importantly, LP preschoolers performed significantly poorer than term controls on assessments of working memory, indicating subtle neurocognitive weaknesses in this group often considered to be at low risk for negative neurocognitive outcomes.

EF deficits appear to remain throughout adolescence and young adulthood. In a meta-analysis of neurobehavioral outcomes in VP/VLBW children, Aarnoudse-Moens, Weisglas-Kuperus, van Goudoever, and Oosterlaan (2009) examined EF outcomes in 12 studies of VP/VLBW outcomes with mean participants ages ranging from 7.5 to 23.2 years. Results of this meta-analysis indicated that VP/VLBW children performed significantly poorer than controls across assessments of verbal fluency, working memory, and cognitive flexibility, with small to medium effect sizes ranging from −0.36 to −0.57 across these domains of EF (Aarnoudse-Moens et al., 2009). Adolescents born very prematurely demonstrated deficits in numerous domains of EF including verbal fluency, inhibition, cognitive flexibility, planning/organization, and working memory when compared with term controls (Luu, Ment, Allan, Schneider, & Vohr, 2011). These results remained significant when controlling for intellectual impairment. Consistent with performance on neuropsychological assessments, VP adolescents were rated by their parents as exhibiting more difficulties with EF in daily life, with elevated scores on the Metacognition Index and Global Executive Composite of the Behavior Rating Inventory of Executive Function. Finally, in addition to EF, VP subjects demonstrated more difficulty with verbal and visuospatial memory. These results suggest that deficits in EF may impact academic functioning including learning and memory.

Several studies have identified potential neuroanatomical correlates of EF deficits. White matter abnormalities on neonatal magnetic resonance imaging have been identified as a predictors of poorer outcomes at 4 and 6 years of age on assessments of general intelligence, language, and executive function, with more severe white matter abnormalities associated with poorer cognitive outcomes (Woodward, Clark, Pritchard, Anderson, & Inder, 2011; Woodward et al., 2012). When examining the associations between brain abnormalities and neurocognitive outcomes in VLBW adolescents, Taylor and colleagues (2011) identified smaller brain volumes, larger lateral ventricles, and smaller surface area of the corpus callosum in the VLBW group compared with NBW controls. Additional findings included white matter abnormalities as well as differences in subcortical gray matter and the cerebellum. Reduced performance on one or more measures of cognitive functioning (e.g., IQ, language, memory, perceptual-motor organization, EF) was associated with greater reductions in whole brain volume, cerebral white matter, subcortical gray matter nuclei, cerebellar white and gray matter, brain stem, and corpus callosum (Taylor et al., 2011).

Visual Motor Skills. Previous studies of extremely premature samples have identified significant deficits in visuomotor integration that are present beyond the generalized cognitive weaknesses seen in this population. Visual motor skills are influenced by different cognitive processes, such as fine motor, visual, proprioceptive, and tactile skills as well as working memory. Studies report lower proprioceptive and tactile skills in preterm compared with full-term children, but their validity may be limited due to a lack of internationally standardized assessments. A recent meta-analysis of 32 case-control studies of VP children with standardized assessments of visual perception and visual-motor integration published from 1985 to 2010 demonstrated lower performance of preterm compared with full-term children (Geldof, van Wassenaer, de Kieviet, Kok, & Oosterlaan, 2012). In a review of 12 studies of fine motor skills in preterm infants published between 1997 and 2012, the prevalence of deficits ranged from 40% to 60% (Bos et al., 2013).

Academic Outcomes and Learning Disabilities. Research has consistently identified poorer educational outcomes in preterm children. As in many other domains, a GA or BW gradient is observed in educational outcomes, with the EP/ELBW infants at the greatest risk for academic underachievement when compared with full-term and normal-birth-weight peers. In a meta-analysis of neurobehavioral outcomes in VP/VLBW children, 14 studies assessing academic outcomes were included to examine outcomes from school age to adulthood with the mean age ranging from 8.0 to 20.0 across these studies (Aarnoudse-Moens et al., 2009). Results indicated that VP/VLBW children performed significantly more poorly across assessments of reading, spelling, and mathematics in comparison with term control groups. Combined effect sizes were medium to large with effect sizes of −0.48 for reading, −0.60 for mathematics, and −0.76 for spelling.

Difficulties in educational progress have been identified in EP children at the time of school entry (Taylor et al., 2011). EP children had significantly lower mean scores on standardized assessments of mathematics and spelling achievement compared with term controls and higher rates of teacher report of poor academic progress in written language and mathematics in kindergarten. These group differences remained when controlling for neurosensory impairment and low cognitive functioning (Taylor et al., 2011). Deficits persist into the school-age years. In a large geographic cohort of EP/ELBW children, assessments of academic achievement revealed that 8-year-old EP/ELBW participants performed significantly lower than the control group on standardized assessments of reading, spelling, and math with the group differences falling between 0.5 SD for reading and spelling and 0.6 SD for mathematics (Hutchinson, De Luca, Doyle, Roberts, & Anderson, 2013). In the EPICure cohort of EP children, Johnson and colleagues (Johnson, Hennessy, et al., 2009) found that at 11 years of age, EP children had significantly lower scores on assessments of reading (−18 points) and mathematics (−27 points) than term peers. These differences remained significant when controlling for cognitive ability. In addition, teachers rated half of the EP population as having poor educational attainment as compared with 5% of their term peers (Johnson, Hennessy, et al., 2009).

As has been found in a number of other studies, EP/ELBW children also require higher utilization of special education services (Aarnoudse-Moens et al., 2011; Anderson et al., 2003; Buck, Msall, Shisterman, Lyon, & Rogers, 2000). ELBW adolescents had significantly lower academic achievement than normal-birth-weight peers on assessments of academic achievement in reading and mathematics (Litt et al., 2012). Higher rates of mathematics learning disabilities, as defined by a low achievement scores in cognitively average teens, were found in the EP group, with 50% of EP adolescents versus 28% of term controls meeting criteria. Rates of special education involvement at age 14 were also significantly higher in the EP group (OR = 11.78) (Litt et al., 2012).

Studies consistently show that EP/ELBW individuals are at high risk for learning disabilities, and these are often comorbid with intellectual impairments (Johnson et al., 2016). In addition to general cognitive and attention problems, neurodevelopmental deficits of VP/VLBW individuals profoundly affect their ability to perceive, integrate, and process stimuli simultaneously; thus their mathematical performance appears particularly compromised (Taylor, Espy, & Anderson, 2009). Some have suggested that VP/VLBW children's mathematic deficits are specific and not explained by global cognitive function (Johnson, Wolke, Hennessy, & Marlow, 2011; Litt et al., 2012; Simms, Cragg, Gilmore, Marlow, & Johnson, 2013). However, comparing different diagnosis alternatives (fixed cutoff scores vs. discrepancy-based residual scores), others have shown that although the risk for general cognitive and mathematic impairments increases with lower GA, preterm children have no increased risk of dyscalculia after statistically adjusting for gender, family socioeconomic status, and SGA birth (Jaekel & Wolke, 2014).

To tailor specific educational support and develop effective interventions we need to understand the underlying mechanisms that explain preterm children's long-term problems. One such example is a cognitive workload model that may help explain the association between cognitive task complexity and incremental performance deficits: cognitive performance of preterm children decreases as the cognitive workload of tasks increases (Jaekel, Baumann, et al., 2013). Current studies point to a possibly universal effect of GA on later mathematics attainment (Johnson, Hennessy, et al., 2009; Lipkind et al., 2012; Quigley et al., 2012; Saigal et al., 2003), but there is uncertainty about the specific shape and magnitude of this effect. Study populations are heterogeneous and may be affected by a number of confounding factors such as socioeconomic, cultural, and health-care standards, as well as opportunities available within education systems. One study has investigated whether the effects of GA on IQ and mathematic abilities that were found in the Bavarian Longitudinal Study (Jaekel, Baumann, et al., 2013; Jaekel & Wolke, 2014) are universal (e.g., whether similar associations are found across cohorts assessed in different countries and during different eras of neonatal care). Prematurity had significant adverse effects on IQ and basic mathematic processing following birth at all gestations <36 weeks and on IQ <34 weeks GA (Wolke, Strauss, et al., 2015). These prediction functions then accurately predicted IQ and mathematic processing in the EPICure Study of 171 children born <26 weeks GA in the United Kingdom in 1995. Thus, despite significant improvements in neonatal intensive care, there is considerable temporal and cross-national consistency in long-term cognitive abilities as evidenced in IQ and basic numerical processing (Wolke, Strauss, et al., 2015). The ability to predict long-term outcomes from one cohort to another suggests that neurodevelopmental rather than environmental factors explain the long-term effects of gestation at birth.

Behavior

Premature birth is associated with a specific cluster of behavioral problems including attention, emotional, and sociocommunication difficulties (Farooqi et al., 2007; Hille et al., 2001). This preterm behavioral phenotype manifests in a high prevalence of internalizing disorders, autism, and ADHD (D'Onofrio et al., 2013; Johnson & Marlow, 2011; Johnson & Wolke, 2013) and is evident in studies using behavioral screening measures as well as diagnostic psychiatric interviews. Recently, generally increased risks for non–substance use disorders (Van Lieshout, Boyle, Saigal, Morrison, & Schmidt, 2015), low self-esteem, and the need for social assistance have been reported for ELBW adults (Saigal et al., 2016). However, most studies report that differences between groups disappear when individuals with neurosensory or neurodevelopmental impairments (percentages range from 5% to 40% depending on the degree of neonatal risk and sampling criteria in different populations) are excluded from analyses.

ADHD. This condition is one of the psychiatric disorders most consistently associated with the preterm behavioral phenotype (Aarnoudse-Moens et al., 2009; Bhutta et al., 2002; Hack et al., 2009; Hille et al., 2001). Prevalence rates of up to 25% have been reported for preterm children and adolescents (Johnson & Marlow, 2011; Johnson & Wolke, 2013), and a meta-analysis of VP/VLBW compared with full-term children found a pooled relative ADHD risk of 2.6 (Bhutta et al., 2002). In a study examining behavior outcomes at school entry in ELBW compared with classroom-matched NBW control children, rates of ADHD combined subtype assessed with psychiatric interviews were about twice as high for the ELBW group. The ELBW group also had much higher rates of teacher-identified deficits in attention, self-regulation (Behavior Rating Inventory of Executive Function), and social functioning. ADHD and impaired behavioral self-regulation were associated with deficits on tests of EF but not with global cognitive impairment (Scott et al., 2012).

Recent studies have shown that the increased risk for ADHD may be specific to attention problems without hyperactivity/impulsivity and stable across childhood and adulthood in preterm individuals (i.e., ADHD inattentive subtype) (Breeman, Jaekel, Baumann, Bartmann, & Wolke, 2016; Jaekel, Wolke, & Bartmann, 2013). Moreover, in the general population ADHD is often comorbid with conduct disorder/oppositional defiant disorder (Biederman et al., 2008), whereas ADHD in preterm children is not accompanied by comorbid conduct problems (Hack et al., 2009; Samara, Marlow, & Wolke, 2008). Together, these findings suggest a predominantly neurodevelopmental etiology for ADHD in preterm populations.

Social Difficulties and Autism Spectrum Disorder. There is increasing evidence that VP/VLBW individuals are at an increased risk of autism spectrum disorders (ASD) than term-born peers, with a prevalence of up to 8% compared with a median prevalence of 0.6% in the general population (Elsabbagh et al., 2012). In a recent study of EP children, prevalence rates of ASD were assessed using gold standard assessment measures, the Autism Diagnostic Interview-Revised (Rutter, LeCouteur, & Lord, 2003, 2008) and Autism Diagnostic Observation Schedule, 2nd Edition (Lord et al., 2012). In a large, national EP cohort assessed at 10 years of age, 7.1% of the cohort met criteria for ASD (Joseph et al., 2017). However, general problems with social interaction and cognitive impairment may explain VP/VLBW children's elevated risk for an ASD diagnosis (Johnson et al., 2010a, 2010b; Pinto-Martin et al., 2011). VP/VLBW children more often experience peer relationship difficulties and tend to be socially isolated (Bora, Pritchard, Moor, Austin, & Woodward, 2011; Hutchinson et al., 2013; Jones, Champion, & Woodward, 2013; Larroque et al., 2011; Ritchie, Bora, & Woodward, 2015). It has been postulated that these social difficulties may be due to VP/VLBW children's cognitive and neurosensory deficits (Delobel-Ayoub et al., 2009), potentially resulting in difficulties processing complex social stimuli (Jaekel, Baumann, et al., 2013; Johnson & Wolke, 2013); however, differences in social adjustment usually remain significant even after statistically adjusting for neurodevelopmental impairment (Eryigit-Madzwamuse, Strauss, Baumann, Bartmann, & Wolke, 2015; Samara et al., 2008; Scott et al., 2012). Growing evidence also suggests that VP/VLBW children are more often targets of bullying and victimization than their full-term peers (Day et al., 2015; Wolke, Baumann, Strauss, Johnson, & Marlow, 2015). With survivors of some of the best-documented VP/VLBW cohorts entering adulthood, more research has emerged on self-reports of young adults' social relationships and friendships, with all studies consistently reporting very limited social support from friends and romantic partners (Darlow, Horwood, Pere-Bracken, & Woodward, 2013b; Lund et al., 2012; Mannisto et al., 2015; Wolke, Chernova, et al., 2013).

Emotional Problems. Studies have shown mixed results in relation to the risk for internalizing symptoms (i.e., anxiety and depression) in preterm cohorts (Bhutta et al., 2002; Hille et al., 2001; Samara et al., 2008), but meta-analyses have consistently shown that preterm adolescents are at a 2- to 3-fold increased risk for emotional disorders (Burnett et al., 2011; Somhovd, Hansen, Brok, Esbjorn, & Greisen, 2012). In general, VP/VLBW individuals present a higher rate of anxiety problems and are more often diagnosed with anxiety disorders in childhood, adolescence, and adulthood (Johnson & Wolke, 2013; Lund, Vik, Skranes, Brubakk, & Indredavik, 2011). Evidence for depression has been mixed, depending on the age at assessment, number of participants, inclusion criteria for preterm and term comparison groups, type of assessment instrument (e.g., dimensional measures vs. psychiatric diagnoses), and sources of information (e.g., self-report vs. parent rating) (Jaekel, Baumann, Bartmann, & Wolke, 2018; Johnson & Marlow, 2011; Johnson & Wolke, 2013; Nosarti et al., 2012; Westrupp, Northam, Doyle, Callanan, & Anderson, 2011). Inconsistencies between studies may also partly be explained by the fact that mood disorders, in general, show a rise in onset in adolescence and early adulthood but most studies of those born VP/VLBW were limited to cross-sectional childhood data. Overall, the clinical risk after VP/VLBW birth seems to be higher for anxiety rather than depression (Johnson et al., 2010b; Treyvaud et al., 2013). It has also been suggested that emotional problems may be more stable over time in VP/VLBW compared with full-term children and adolescents (Hall & Wolke, 2012), resulting in a greater relative risk for morbidity in adulthood among preterm individuals (Van Lieshout et al., 2015).

Personality. Recent studies have shown that the described VP/VLBW behavioral phenotype in adults may not be limited to certain behaviors such as shyness and low risk-taking but may include a more general socially withdrawn personality tendency. This VP/VLBW personality has been described as being easily worried, rigid in communication, minimally socially engaged, and not interested in physical or social risks that underlie novel, complex, or sensation-seeking experiences (Eryigit-Madzwamuse, Strauss, et al., 2015; Waxman, Van Lieshout, Saigal, Boyle, & Schmidt, 2013). Overall, VP/VLBW birth increases the risk for behavioral and socioemotional difficulties that may adversely affect long-term developmental outcomes, including life satisfaction, social support, wealth, and health. Not surprisingly, VP/VLBW adults consistently report lower quality of life than their term-born peers (Wolke, 2016). Early identification and treatment of behavioral, social, and emotional problems may not only help reduce the individual lifelong burden of the sequelae of preterm birth but also increase overall life satisfaction and happiness.

Neuropsychological Assessment

There are a number of considerations to address when using normative data with preterm and LBW populations. In research studies, use of test norms is believed to lead to underestimations of impairment when compared with using a local term control group. In clinical practice, care should be taken to consider the sociodemographic characteristics of the standardization sample and how they may differ from the characteristics of a VP/VLBW or EP/ELBW sample. Given the rates of neurosensory impairment, specifically visual perceptual abnormalities, careful test selection should consider the potential impact of deficits in visual acuity and tracking on test performance beyond the domain of visual perception. Finally, given high rates of CP and developmental coordination disorder, providers and researchers should consider the negative impact of motor deficits on assessments of domains outside the strictly motor, including measures of attention, processing speed, visual memory, and academic achievement, which may negatively impact test performance and lead to an underestimate of functioning.

During early developmental evaluations, "corrected age" (chronological age minus the numbers of weeks born before full term, or 40 weeks' gestation) is often used for preterm infants to account or control for delays in neurological maturation related to preterm birth. Standard practice has often been to use age-corrected norms until 24–30 months of age (Baron & Rey-Casserly, 2010), although some researchers have advocated for extending the use of age-corrected norms, given that more infants are