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Systematic Assessment of Perinatal and Socio-demographic Factors Associated with IQ from Childhood to Adult Life Following Very Preterm Birth

Abstract

Objective: To construct a comprehensive model of predictors of IQ and its developmental trajectories in survivors of very preterm birth from childhood to adult life.

Methods: We examined trajectories of Full-scale, Verbal and Performance IQ from age 8 to 30 years in individuals who were born very preterm (< 32 weeks of gestation). Using linear mixed-effect modelling and model selection procedures, we systematically evaluated the impact of perinatal and socio-demographic factors on all IQ types and their trajectories.

Results: The association between all IQ subtypes and gestational age, socio-economic status and sex was stable over all studied time points. A linear association was demonstrated between IQ and gestational age when considering the full gestational age spectrum following removal of participants born during week 24 of gestation. For those individuals born between 25 to 33 weeks, every full gestational week was associated with 1.4 points increase in Full-scale IQ (95% confidence interval (CI): 0.64-2.15) and 1.3 points increase in IQ subtests (95% CI: 0.64-2.01). Younger gestational age was associated with lower Performance IQ to a greater extent than Verbal IQ. Low SES was associated with lower Full-scale IQ and males had higher Full-scale IQ than females.

Conclusion: Individuals who were born very preterm and especially those born at the lower end of the gestational age spectrum, continue to be at higher risk of cognitive impairment in adult life, with their Performance IQ being particularly affected.

Key Words: preterm, gestational age, IQ, trajectory

Introduction

Standardized intelligence quotient (IQ) is a commonly used measure thought to capture a wide range of cognitive abilities. These include non-verbal reasoning skills such as abstract thought and reasoning that estimate Performance IQ, which is often associated with executive function abilities (Roca et al., 2010). The second subscale, Verbal IQ, examines verbal skills, such as expressive vocabulary, and relies on acquired knowledge (Duncan, Emslie, Williams, Johnson, & Freer, 1996). In normative samples, Full-scale IQ remains fairly stable across the lifetime, with a gradual decline in later life (Bielak, Anstey, Christensen, & Windsor, 2012; Salthouse, 2016). Similarly, IQ subscales may follow distinct trajectories in typically developing individuals. Performance IQ develops increasingly until young adulthood and then gradually declines with age (Li et al., 2004), whereas Verbal IQ remains stable or increases with time (Salthouse, 2012).

These trajectories may vary in atypically developing populations including those born very preterm (< 32 weeks of gestation; Isaacs et al., 2004; Nosarti et al., 2008), who are also at high risk of long-term neurodevelopmental impairments (Breeman, Jaekel, Baumann, Bartmann, & Wolke, 2015; Mwaniki, Atieno, Lawn, & Newton, 2012). It has been widely demonstrated that very preterm born individuals are at a risk of exhibiting lower IQ scores in childhood (Bhutta, Cleves, Casey, Craddock, & Anand, 2002), adolescence (van der Pal-de Bruin, van der Pal, Verloove-Vanhorick, & Walther, 2015) and early adulthood (Linsell et al., 2018; Madzwamuse, Baumann, Jaekel, Bartmann, & Wolke, 2015; Nam, Castellanos, Simmons, Froudish-Walsh, et al., 2015) compared to full-term controls.

Nonetheless, preterm individuals are not a homogenous population and those at the lowest end of the gestational age spectrum may be at higher risk of cognitive impairments. This risk may be a result of a direct association between gestational age and cognition or may be due to perinatal complications, associated with low gestational age, such as low birthweight and neonatal brain injury (Anderson et al., 2017; Downie, Frisk, & Jakobson, 2005; Saigal, 2000). The relationship between gestational age and associated cognitive measures, including IQ, has been widely described and summarised in two recent meta-analyses (Brydges et al., 2018; Twilhaar et al., 2018). However, this association may be non-linear as very preterm individuals born at the lower end of the gestational age spectrum are at a

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disproportionally higher risk of impairment (Jaekel, Wolke, & Bartmann, 2013; Volpe, 2009).

Moreover, it has been shown that individuals born before 28 weeks' gestation, (e.g. extremely preterm), often display a substantially larger deficit on IQ tests compared to those born between 28 and 32 weeks, who often perform within the population norm (Johnson, 2007).

Currently, there is no consensus on which clinical and socio-demographic factors are associated with IQ directly or by interacting with one another. Some evidence suggests a lower IQ in preterm-born boys compared to preterm-born girls (Linsell et al., 2018). Perinatal risk factors, including the presence of periventricular haemorrhage and ventricular dilatation on cranial neonatal ultrasound, have also been associated with lower IQ after controlling for gestational age (Nosarti et al., 2011).

Other studies have reported interactive effects between clinical and environmental factors in very preterm or very low birth weight individuals, with younger gestational ages being particularly vulnerable to lower IQ when also belonging to lower socio-economic groups (Hack et al., 1992; Wolke & Meyer, 1999) and male sex (Marlow, Wolke, Bracewell, Samara, 2005). Conversely, a recent study showed a protective effect of higher childhood IQ against known risk factors affecting adults socioeconomic attainment, including socioeconomic disadvantage and psychiatric disorder (Dobson et al., 2017).

Due to a lack of longitudinal studies it remains unknown whether the association of these risk factors on IQ is stable or fluctuates as maturation progresses. The results of studies beyond the second decade of life are inconsistent, with some showing that very preterm participants continue to display cognitive deficits, including lower IQ scores (Breeman et al., 2015; Karolis et al., 2016) and others suggesting an improvement in specific cognitive functions, such as verbal abilities and working memory (Froudust-Walsh et al., 2015; Thuy Mai Luu, Ment, Allan, Schneider, & Vohr, 2011; Taylor, Minich, Klein, & Hack, 2004).

Although several studies suggest that very preterm individuals demonstrate a global, rather than a specific, cognitive deficit (Lohaugen et al., 2010; Wolke & Meyer, 1999) others have shown specific impairments in Performance IQ (Saavalainen et al., 2007) and in Verbal IQ, (Allin et al., 2008; Luu et al., 2009) including in the current cohort (Kroll et al., 2017; Nam, et al., 2015). Skills associated with Performance IQ, such as fine motor function and visuospatial abilities, may be distinctly compromised

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in very preterm populations (Geldof, van Wassenauer, de Kieviet, Kok, & Oosterlaan, 2012; Spittle et al., 2013). This may lead to a large discrepancy between Verbal IQ and Performance IQ (Allen, Cristofalo, & Kim, 2010). Furthermore, some investigators have reported no significant changes over time in Full-scale IQ, together with variations in functions that are used to estimate this scale (Ramsden et al., 2011). Such results indicate that a focus on general intellectual abilities may mask specific difficulties (Aylward, 2002).

Thus, further studies are required to determine the characteristics of IQ trajectories within preterm samples, including IQ subscales, spanning to individuals in their fourth decade of life.

The main objective of the current study was to systematically examine perinatal and socio-demographic factors associated with Full-scale, Performance and Verbal IQ and their developmental trajectories in survivors of very preterm birth from childhood to adult life. While the focus of the current paper is on gestational age, we systematically considered the independent contribution of several perinatal and environmental predictors of IQ trajectories. In this study, we modelled longitudinal trajectories using a linear mixed-effect modelling approach, an efficient method for dealing with unbalanced longitudinal designs, without the need for data imputation (Laird & Ware, 1982; Bernal-Rusiel et al, 2013). A robust model selection pipeline was implemented in order to build an optimal model whereby simple models contain few factors were incrementally expanded in order to include additional factors which would demonstrate statistically significant association with IQ and discard factors which did not. Thus the current paper addressed the following questions (1) What is the nature of the association between IQ and gestational age and does it fluctuate with time? (2) Do other perinatal and socioeconomic factors are associated with the differences in IQ or modulate its association with gestation age? (3) Do very preterm individuals demonstrate different Performance IQ and Verbal IQ trajectories?

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Methods

Study population

The study participants were part of a longitudinal follow-up study investigating the sequelae of very preterm birth. Participants were admitted to the neonatal unit at University College Hospital London, UK between 1979 and 1984. IQ assessments used in the current analyses were completed at age 8, 15, 19, 22 and 31 (Kroll et al., 2017; Nam, et al., 2015; Roth et al., 1994). All participants took part in the baseline assessment at age 8 (N=258) representing 74% of the total sample recruited at birth (N=348) and were included in the current study if they took part in at least one more follow-up assessment. Due to logistic reasons, a random sample stemming from the original population was examined at age 15 (N=161) and underwent a neurodevelopmental assessment. Similarly, at age 18 (N=158); 22 (N=66) and at age 30 (N=103) participants completed a comprehensive cognitive battery including IQ evaluation. During the last assessment (age 30), those who participated did not differ from those who did not in terms of their birth weight ($t=-1.73$, $df=447$, $p=.084$); however, those who were assessed were born at a slightly younger gestational age than those who were not ($t=-2.05$, $df=447$, $p=.040$). Ethical approval for the study was obtained from local ethical committees. Written informed consent was obtained from all participants and from an accompanying carer when participants were younger than 18.

Materials

Socio-demographic and perinatal details, including gestational age and birth weight, were collected for all participants at the time of birth and are described in Table 1. In addition, cranial ultrasonography was collected during the first week of life and qualitatively rated by a pediatric neuroradiologist. Severity of perinatal brain injury is summarized as a) normal, no-periventricular haemorrhage (no-PVH), b) uncomplicated periventricular haemorrhage without ventricular dilatation (PVH), and c) periventricular haemorrhage with ventricular dilatation (PVH+DIL; Nosarti et al., 2011). Parental occupation at birth was used to define participants' socio-economic status (SES) using Her Majesty's Stationary Office Occupational Classification criteria (Her Majesty's Stationary, 1991). Because of a small number of participants in some of SES categories, SES was collapsed into two

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groups for statistical modelling (as described below): a high SES category consisted of professional and managerial roles (levels 1-2); a low SES category comprised all other occupations (levels 3-5 and included missing variables).

IQ measures

At baseline (age 8) and at age 15 participants completed the Wechsler Intelligence Scale for Children – Revised (WISC – R; Wechsler, 1974) which consists of 12 subtests (Verbal IQ: General Information, Vocabulary, Similarities, Arithmetic, General Comprehension, Digit Span; Performance IQ: Picture Completion, Picture Arrangement, Block Design, , Object Assembly, Coding, and Mazes) that estimate Verbal, Performance and Full-Scale IQ scores. At age 18, 22 and 30 the Wechsler Abbreviated Scale of Intelligence (WASI; Wechsler, 1999) was administered. The WASI consists of four subtests: Vocabulary and Similarities which are used to estimate Verbal IQ and Block Design and Matrix Reasoning which are used to estimate Performance IQ. Scores on these widely used measures were standardised to age-appropriate norms. Individual subtest scores were generated to obtain Verbal IQ and Performance IQ subtest. A combination of the two subscales provides a Full-scale IQ score, which is thought to capture general intellectual abilities.

Statistical modelling

All analyses were performed in Matlab. Linear mixed-effect (LME) (Bernal-Rusiel, Greve, Reuter, Fischl, & Sabuncu, 2013; Curran, 2003; Laird & Ware, 1982) modelling with random intercept and a model selection procedure was implemented in order to systematically identify factors affecting IQ trajectories in very preterm individuals. The advantage of using LME is that it does not require filling missing data for a modelled variable (i.e, IQ for this study) and is particularly suitable for unbalanced longitudinal designs (Ghisletta & Lindenbergh, 2004). **Note that there were no missing data among predictor variables.** All models were fitted using maximum likelihood criterion. In order to determine which factors are associated with the differences in IQ, we constructed the model incrementally – starting by distinguishing between models containing a small set of predictors and then sequentially adding new predictors. This procedure avoids modelling the effect of all possible factors

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simultaneously, i.e., providing for a better control over the accuracy of model parameters' estimation. An optimal model was determined using 3-fold cross-validation, with model error calculated per participant (which represents a clustering variable in random intercept models), as described in (Fang, 2011), and then averaged across participants and folds. Time of assessment was included in all tested models as a categorical variable of no interest, as it is practically impossible to partial out a contribution of between-assessment differences in the used IQ scales from the main effect of time of assessment. For the Full-scale IQ analysis, we first compared the models containing gestational age as a predictor vs. containing log-transformed gestational age (with zero-coordinate shifted to 23 weeks). Having identified which of the two predictors best accounted for the data, we then tested new models by sequentially including new factors or their interactions and evaluating whether the inclusion of a factor resulted in a better fit. If it was the case, for example, a factor reduced the cross-validation error, the factor was retained in the model and used for further tests (Reunanen, 2003). The inclusion of the following factors was tested: 1) neonatal ultrasound classification, SES and sex; 2) two-way interactions between all possible pairwise combinations of the main factors (i.e., gestational age/birth weight, ultrasound results, SES and sex); 3) all two-way interactions between time of assessment and each main factor; 4) three-way interactions between time of assessment and all possible pairwise combinations of the main factors. After an optimal model for the dataset was identified, contrast tests for each main fixed effect and their interactions were applied to evaluate the significance of each predictor in the complete dataset. Due to the high covariance between gestational age and birth weight, the effect of the latter was not assessed in combination with gestation age. Instead we ran a separate model-selection pipeline, identical to the pipeline described above apart from substitution of gestation age with birth weight or log-transformed birth weight (with zero-coordinate shifted to 500 grams). The comparison of the best-fitting models for gestation age and birthweight was performed using Bayesian Information Criterion (BIC).

For analysis of IQ subtests, data for Verbal IQ and Performance IQ were concatenated. The model selection pipeline mimicked the procedure used for Full-scale IQ but included four additional sets of factors: 1) IQ subtest as a main factor; 2) the interaction between IQ subtest and time of assessment; 3)

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two-way interactions between IQ subtest and all other main factors; 4) three-way interactions between IQ subtest, time of assessment and all other main factors.

Results:

The results of the analyses are presented in three parts: the first section provides information on the association between predictors such as SES, sex, gestational age and IQ development; the second section focuses on the relationship between these predictors and Verbal and Performance IQ; the third section reports the results of a post-hoc analysis conducted following results in section one.

Perinatal, socio-demographic variables and IQ are presented in Table 1, for all assessment time points. Participants who were assessed at age 8 did not differ in terms of IQ scores, from those who were not assessed at later timepoints. A paired t-test revealed no significant difference, all $p > .074$ (uncorrected for multiple comparisons).

Table 1: Perinatal, socio-demographic data and IQ for the study participants

	Age 8 (<i>baseline</i>)	15	18	22	31
N	258	161	158	66	103
Age at assessment ¹	8.23 (0.35)	15.39 (0.47)	18.44 (0.83)	22.02 (1.18)	31.08 (2.27)
Gestational age (weeks) ¹	29.24 (2.18)	28.95 (2.31)	29.23 (2.06)	29.55 (2.01)	29.26 (2.10)
Birth weight (grams) ¹	1298 (347.84)	1286.6 (277.06)	1287.2 (325.35)	1322.5 (338.17)	1317.8 (255.93)
Low SES (%) ²	65	61	69	59	56
Gender (Males)	54	56	50	59	62
Neonatal Cranial Ultrasound Classification ³ (% no-PVH/PVH/PVH+DIL)	50/31/19	45/34/22	52/28/20	53/32/15	50/24/26
IQ¹					
Full-scale IQ	103.21 (16.35)	97.02 (17.2)	102.00 (14.88)	102.67 (11.85)	103.71 (14.26)
Performance IQ	98.92 (15.24)	97.75 (20.12)	103.07 (15.61)	107.23 (13.64)	105.16 (14.99)
Verbal IQ	106.49 (17.56)	96.57 (15.33)	101.91 (15.41)	98.08 (12.24)	101.53 (15.21)
Verbal minus Performance IQ	7.57 (15.37)	-1.18 (16.68)	-1.16 (15.21)	-9.15 (14.69)	-3.62 (16.19)

¹ Means and standard deviations are presented for age, gestational age, birth weight and IQ scores at each time of assessment.

² SES was collapsed into two groups; the percent of participants belonging to the low SES category (levels 3-5) is presented.

³ Ultrasound Classification: no-PVH: normal neonatal cranial ultrasound, PVH: uncomplicated periventricular haemorrhage, PVH+DIL: periventricular haemorrhage with ventricular dilatation.

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Section I: Model of Full-scale IQ

This section addresses the first and the second research question. The selection procedure identified an optimal model to explain Full-scale IQ, which included three factors: SES, sex and log-transformed gestational age (Table 2). There was no significant interaction between any of these factors and time of assessment. This indicates that Full-scale IQ did not change over the lifetime as a result of a modulatory effect of the examined variables. Low SES was associated with lower Full-scale IQ and males had higher Full-scale IQ compared to females. Very preterm individuals with lower gestational age demonstrated lower Full-scale IQ, with log-transformed gestational age fitting the data better than linearly scaled gestational age. Similar results were obtained for the best-fitting model that contained birth weight as a predictor instead of gestational age, with log-transformed birth weight outperforming linearly scaled birth weight. The birth weight model, however, provided a slightly worse fit to the data than the gestational age model (BIC = 5770 vs. 5767) and did not contain sex as a predictor. This may be attributed to a statistically significant interdependence between birth weight and sex, with males having a heavier birth weight than females, $t(740) = 5.51$, $p < .001$, $B = 137.7$, 95% CI = [88.7 186.7]. In contrast, sex differences in gestational age were not significant, $p = .87$. Considering this, and the fact that the current sample was selected on the basis of gestation age, not birth weight, further analyses were run using gestational age only.

Table 2: Significant predictors of Full-scale IQ

Factors	t (df =738)	β [95% CI]	P
SES	5.52	9.25 [5.96 12.54]	<.001
Sex	2.23	3.58 [0.42 6.74]	.026
Gestational Age	5.67	9.81 [6.41 13.20]	<.001

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Section II: Model of Verbal and Performance IQ

The following findings refer to our third research question. The optimal model for Verbal and Performance IQ contained SES, sex and log gestational age as main factors (Table 3), as was also the case for Full-scale IQ.

Table 3: Significant predictors of Verbal and Performance IQ.

Factors	F	df	B [95% CI]	p
SES	14.93	1, 1475	6.08 [2.97 9.19]	<.001
Sex	4.99	1, 1475	3.24 [.40 6.09]	.026
Gestational Age	33.38	1, 1475	10.55 [7.27 13.83]	<.001
IQ subtest: Time	22.02	4, 1475	NA*	<.001
IQ subtest: SES: Time	5.64	4, 1475	NA*	<.001

* No single B exists because the factor is coded by more than one column in the design matrix.

Two significant interactions were also identified. The first interaction was between IQ subtest and time. At age 8 there was a relatively high discrepancy between Verbal and Performance IQ (with a Verbal IQ advantage) compared to subsequent time-points, with 34% of the total sample demonstrating a clinically defined discrepancy (15 points or more (Blackburn et al., 2007)). This discrepancy diminished by the age of 15 onwards. The second interaction was three-way: among IQ subtest, SES and time. High SES was associated with relatively higher Verbal than Performance IQ (i.e. a larger discrepancy between IQ subtests) at all ages except age 15.

Section III: Post-Hoc Analysis

The logarithmic functions fitting scores for Full-scale IQ and IQ subtests are shown in Figure 1, which suggests that the trend may be driven by individuals who were born at 24 weeks' gestational age. In order to verify this, we utilised the models that were identified as best-fitting in previous analyses (Table 2 and Table 3) and tested whether log gestational age still outperformed linear gestational age in a reduced sample, after removing participants born at 24 weeks' gestational age.

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Results showed that this was no longer the case for both Full-scale IQ and IQ subtests, with models using linear gestational age marginally outperforming those using log gestational age (BIC for Full-scale IQ: 5640 vs. 5639, respectively; BIC for IQ subtests: 11645 vs. 11644, respectively). In both analyses, the effect of linear gestational age was significant (Full-scale IQ: $B = 1.39 [0.64-2.15]$, $t(723) = 3.61$, $p < .001$; IQ subtests: $B = 1.30 [0.61-1.98]$, $t(1446) = 3.72$, $p < .001$), as well as the effect of sex ($\beta = 2.84 [0.02-5.67]$, $t(1446) = 1.97$, $p = .049$) and SES ($B = 6.69 [3.60-9.78]$, $t(1446) = 4.25$, $p < .001$). For those individuals born between 25 to 33 weeks, every full gestational week was associated with 1.4 points increase in Full-scale IQ and 1.3 points increase in IQ subtests. In the analysis of IQ subtests, the interaction between IQ subtest and time and the three-way interaction between SES, time and IQ subtest remained significant ($F(4,1446) = 22.22$, $p < .001$, and $F(4,1446) = 6.98$, $p < .001$).

Figure 1: The log functions fitting each type of IQ separately.

Figure 1: The log functions fitting Full-scale, Verbal and Performance IQ separately.

Discussion

The main objective of this study was to determine a comprehensive model of perinatal and socio-demographic factors associated with IQ and its developmental trajectories in very preterm individuals from childhood to adult life. The resulting models for all IQ types contained socio-economic status, sex and gestational age as significant predictors and their association with IQ was mostly stable over all studied time points. Specifically, younger gestational age and low SES were associated with lower IQ scores, and males had higher IQ scores compared to females. A logarithmic association was

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demonstrated between IQ and gestational age; however, after removing those individuals who were born at the further end of the gestational age spectrum, i.e., at 24 weeks, a linear association between IQ and gestational age was found, with every full gestational week being associated with 1.4 points increase in Full-scale IQ and 1.3 points increase in IQ subtests. When modelling Performance and Verbal IQ, we also found that gestational age exerted a greater influence on Performance IQ compared to Verbal IQ, but again this held only when participants born at 24 weeks were included. Furthermore, we found a Verbal IQ advantage at age 8 compared to Performance IQ, which disappeared by age 15. Finally, high SES was associated with relatively higher Verbal than Performance IQ (but not at age 15).

Our observation of a linear association between gestational age and IQ is in line with the results of previous investigations (Clark, Woodward, Horwood, & Moor, 2008; Kerr-Wilson, Mackay, Smith, & Pell, 2012). However, other studies focusing on specific aspects of cognition, rather than general intellectual abilities, found a disproportionate risk of cognitive deficits at the lower end of the gestational age spectrum (Jaekel et al., 2013; Moster, Lie, & Markestad, 2008; Quigley et al., 2012; Wolke et al., 2015). One possible explanation for the association between gestational age, IQ and other aspects of cognition may be that the immature brain is vulnerable to endogenous and exogenous injury (Volpe, 2009). Gestational age has in fact been linearly associated with a higher prevalence of focal and widespread structural brain alterations that are also thought to underlie cognitive performance (Ball et al., 2013; Nosarti et al., 2014). Furthermore, weeks 24–32 of gestation are critical for the development of thalamocortical connections, which are crucial for behavioural flexibility (Makinson & Huguenard, 2015), and executive functions (Eisenberg & Berman, 2010). Therefore, an implication of the current findings is that every additional week of gestation, has important consequences for individuals' life-long general intellectual skills.

Our results contrast with several findings reported in literature. For instance, in a study of extremely premature children it was demonstrated that boys have a lower IQ than girls (Linsell et al., 2018), whereas in the current sample, in those individuals born at less than 26 weeks of gestation males had a higher IQ than females. Given that boys had a higher birth weight than girls, the current result may suggest that weight is a protective factor in very preterm individuals. Moreover, the same study demonstrated a negative impact of neonatal brain injury, whereas we found no evidence for this in the

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current sample. Even though it has been speculated that brain injury is likely to pose constraints on the plasticity of the very preterm brain (Breeman et al., 2015), and therefore affect the development of cognitive abilities, our own neuroimaging work suggests that the very preterm brain has a sufficient ability to re-organise its structural and functional networks in the presence of brain injury or loss of grey and white matter resources (Karolis et al., 2016; 2017; Froudish-Walsh et al., 2015) and therefore the presence of brain injury is not necessarily a decisive factor. Taken together, the contrast with the results of Linsell et al.'s (2018) study suggest that the same factors may differentially affect the cognitive profile of the very preterm and extreme preterm individuals.

We found no evidence that the effects of socio-demographic and perinatal factors fluctuated over time. This could be attributed to a lack of power to detect them, although our study analysed one of the largest available datasets of preterm-born individuals. On the other hand, these negative findings may reflect a difficulty of identifying a single factor associated with cognitive improvement in the very preterm individuals. Whereas some studies report an improvement either in some cognitive domains (Thuy Mai Luu et al., 2011) or in a subgroup of very preterm individuals (Taylor, Minich, Bangert, Filipek, & Hack, 2004), the literature on this topic remains inconclusive. This is not mitigated by the fact that the majority of studies to date have examined participants who were substantially younger than those currently investigated (Aarnoudse-Moens, 2009; Lohaugen et al., 2010; Nosarti et al., 2002). A meta-analysis examining IQ changes in very preterm individuals between childhood and adolescence did not find evidence of an IQ improvement over time (Kerr-Wilson et al., 2012), although another study reported that the influence of perinatal factors on cognitive outcomes diminished with time (Kormos, Wilkinson, Davey, & Cunningham, 2014), suggesting that study participants' age may, in part, explain the inconsistent results. A recent investigation which examined very preterm individuals of comparable age to the current sample (26 years old) also did not report IQ improvement over time (Breeman et al., 2015; Madzwamuse et al., 2015).

34% of our participants displayed a specific IQ deficit at age 8 indicated by a large difference (15 points) between verbal and performance subtests (Blackburn et al., 2007). This finding has been previously demonstrated in very preterm children (Gabrielson et al., 2002), in autism (Bucaille et al., 2016), epilepsy (Blackburn et al., 2007) and traumatic brain injury (Gao, Jiang, Wang, & Chen, 2000),

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but is novel in adults who were born very preterm. Large IQ discrepancies are rarely found in healthy populations and they have been interpreted as representing cerebral alterations (Kim, Yi, Son, & Kim, 2003), as changes in IQ subtests are associated with changes in brain development (Ramsden et al., 2011). Considering that the very preterm brain often follows an atypical developmental trajectory (Nam, Castellanos, Simmons, Froudish Walsh, et al., 2015) examination of the neural correlates of IQ subtype is needed to clarify how atypical development can influence cognition.

Our results further showed that IQ subtype significantly interacted with time, with the greatest discrepancies between Verbal and Performance IQ occurring in childhood and disappearing by adult life; and that socio-economic factors particularly influenced Verbal IQ both in childhood and in adult life. Such findings could help to identify the role that potentially protective environmental factors may play in shaping intellectual abilities, and to critical periods during which cognition-enhancing interventions may be most beneficial (Jolles & Crone, 2012).

The current study has several limitations. Throughout the years, different cognitive measures were administered; this was necessary for age-specific testing. However, this limitation should not have a significant impact on data quality because we were primarily interested in delineating the cognitive trajectories of a heterogeneous group of very preterm individuals; any test bias would have affected all trajectories in a similar manner. In addition, several pre- and perinatal complications, that were not examined, such as necrotizing enterocolitis, bronchopulmonary dysplasia and maternal smoking may contribute to IQ development (Rees, Pierro, & Eaton, 2007; Short et al., 2007; Waldie et al., 2014). Nonetheless, the risk factors chosen in the current analyses have been widely studied as directly affecting IQ development in younger preterm cohorts including the current one (Nosarti et al., 2011; Wolke et al., 2015). Finally, as rates of attrition are common in longitudinal studies, with evidence that those most vulnerable do not return (Wolke et al., 2009), the findings presented may be more relevant for well-functioning individuals who were born very preterm.

Conclusion

Our study shows that every full gestational week contributes a higher IQ in individuals who were born very preterm. IQ is thought to predict important life outcomes, such as educational achievement, employability, and cognitive decline in late adulthood (Bourne, Fox, Deary, & Whalley, 2007; Staff, Hogan, & Whalley, 2014). The malleability of IQ is of great debate; for instance, it remains unclear whether working memory training may transfer to fluid intelligence (Au et al., 2015; Jaeggi, Buschkuhl, Jonides, & Perrig, 2008; Melby-Lervåg & Hulme, 2013). **Thus far, there is little evidence to suggest that cognitive training extends beyond targeted area (Kassai, Futo, Demetrovics, & Takacs, 2019).** However, continuous efforts to improve training programmes may one day yield results, which may extend to ‘real-life’ achievements such as academic attainment (Goldin et al., 2014). Similarly, protective environmental factors such as high SES may also contribute significantly to IQ growth and stability (von Stumm & Plomin, 2015). These findings are encouraging as they suggest that IQ could potentially be improved with appropriate interventions. Future efforts should be directed at utilising protective factors to target and intervene in those at highest risk.

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