Learning disabilities among extremely preterm children without neurosensory impairment: Comorbidity, neuropsychological profiles and scholastic outcomes

Learning disabilities among extremely preterm children without neurosensory impairment: Comorbidity, neuropsychological profiles and scholastic outcomes

Authors: Samantha Johnson[a], PhD, CPsychol, AFBPsS; Victoria Strauss[b], PhD; Camilla Gilmore[c], DPhil, CPsychol, AFBPsS; Julia Jaekel[d, e, f], PhD; Neil Marlow[g], DM, FMedSci; Dieter Wolke[f], PhD, CPsychol, AFBPsS.

Affiliations: [a]Department of Health Sciences, University of Leicester, Leicester, UK; [b] Centre for Statistics in Medicine, Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, University of Oxford, Oxford, UK; [c]Mathematics Education Centre, Loughborough University, Epinal Way, Loughborough, Leicestershire, LE11 3TU, UK; [d]Department of Child and Family Studies, College of Education, Health, and Human Sciences, The University of Tennessee Knoxville, 1215 West Cumberland Ave., Knoxville, TN 37996 , USA; [e] Department of Developmental Psychology, Ruhr-University Bochum, Universitätsstr. 150, 44801 Bochum, Germany; [f]Department of Psychology and Health Sciences Research Institute and Division of Mental Health and Wellbeing, Warwick Medical School, University of Warwick, Coventry, UK; [g]Institute for Women's Health, University College London, 74 Huntley Street, London, WC1E 6AU, UK;

Corresponding author (address for reprints): Dr Samantha Johnson, Senior Research Fellow, Department of Health Sciences, 22-28 Princess Road West, Leicester LE1 6TP United Kingdom. Tel: 0116 252 5798; Fax: 0116 252 3272; Email: sjj19@le.ac.uk

Running head: Learning disabilities in extremely preterm children

Conflicts of interest: None.

Abbreviations: ELBW Extremely low birthweight (<1000g); EP extremely preterm; ID Intellectual Disability; LD Learning disability; MLD Mathematics learning disability; MPC Mental Processing Composite; RLD Reading learning disability; SEN Special Educational Needs.

Source of funding: The EPICure Studies were funded by the Medical Research Council (MRC) UK and the work conducted for this manuscript was supported by a project grant from The Nuffield Foundation (EDU/40442). Neil Marlow receives a proportion of funding from the Department of Health's NIHR Biomedical Research Centres funding scheme at UCLH/UCL. Dr Gilmore is supported by a Royal Society Dorothy Hodgkin Fellowship.

.

ABSTRACT

Background: Children born extremely preterm are at high risk for intellectual impairment, learning disabilities, executive dysfunction and special educational needs, but little is understood about the comorbidity of intellectual and learning disorders in this population.

Aims: This study explored comorbidity in intellectual disability (ID) and learning disabilities (LD) in children born extremely preterm (EP; $<26^{+0}$ weeks' gestation).

Subjects and study design: A UK national cohort of 161 EP children and 153 term-born controls without neurosensory impairments was assessed at 11 years of age (the EPICure Study).

Outcome measures: IQ, mathematics and reading attainment, executive function, visuospatial processing and sensorimotor skills were assessed using standardised tests, and curriculum-based attainment and special educational needs (SEN) using teacher reports.

Results: Overall, 75 (47%) EP children and 7 (4.6%) controls had ID or LD (RR 10.12; 95% CI 4.81, 21.27). Comorbidity in ID/LD was more common among EP children than controls (24% vs. 0%). EP children with comorbid ID/LD had significantly poorer neuropsychological abilities and curriculum-based attainment than EP children with isolated or no disabilities. LD were associated with a 3 times increased risk for SEN. However, EP children with ID alone had poorer neuropsychological abilities and curriculum-based attainment than children with no disabilities, yet there was no increase in SEN provision among this group.

Conclusions: EP children are at high risk for comorbid intellectual and learning disabilities. Education professionals should be aware of the complex nature of EP children's difficulties and the need for multi-domain assessments to guide intervention.

Keywords: extremely preterm; learning disabilities; reading; mathematics; special educational needs; academic attainment.

INTRODUCTION

Extremely preterm birth (EP; $<26^{+0}$ weeks' gestation) places children at high risk for neurodevelopmental disability and intellectual impairment later in life, and there is growing interest in educational outcomes as key predictors of an individual's life chances. Amongst all preterm children, the poorest scholastic outcomes are observed among those born EP [1-3], with up to two thirds having special educational needs (SEN) [4, 5]. Moreover, SEN are not confined only to EP children with severe disabilities [5-9].

Studies using low attainment definitions have shown an increased risk for learning difficulties (LD) in EP or extremely low birthweight (ELBW;<1000g) children compared with term-born peers [5, 7, 10-13]. There is also evidence of an increased risk for *specific* LD in these populations where discrepancy based definitions are applied, the most frequent of which are mathematics learning difficulties (MLD) [7, 8, 10, 13]. In contrast to reading and literacy, group differences in mathematics attainment are frequently not accounted for by low IQ [5, 6, 10, 14]. Other neuropsychological processes such as attention, executive function, sensori-motor and visuo-spatial skills contribute to scholastic attainment in typically developing and preterm children [7, 10, 15-18] and may be core cognitive deficits in this population [19-21].

Previous studies have also shown that EP/ELBW children are more likely to have impairments in multiple neurodevelopmental domains, such as in neurological, motor, cognitive and behavioural function, than children born at term [12, 22]. However, comorbidity among intellectual and learning disabilities is poorly understood. Where studies have been conducted, a greater frequency of comorbid intellectual disability (ID) and LD has been observed in very preterm preschoolers (<32 weeks' gestation) compared with term-born controls [23, 24]. At school age, ELBW has been associated with an increased risk for comorbidity of LD in mathematics and reading [7], but this study included only a small sample of ELBW children without ID and the children were born in the 1970s, before the dawn of modern neonatal care. More recently, children born <34 weeks' gestation have been shown to have comorbid LD at early school age [8].

As yet, we are not aware of any studies that have explored patterns of comorbidity in ID and LD in a contemporary EP population, or the underlying neuropsychological profiles of children with isolated versus multiple deficits. Such investigations are important for elucidating the mechanisms underlying academic difficulties, identifying the educational needs of children with different comorbidities and informing the provision of intervention strategies.

In a national, population-based cohort of EP children without neurosensory impairments who were born in the 1990s, we explored the prevalence and comorbidity of ID and LD in both reading and mathematics. The aims of the present study were to (1) describe the rates of ID and LD and explore the extent to which these are comorbid among EP children, (2) explore the neuropsychological profiles of EP children with specific and comorbid disabilities and (3) investigate the impact of specific versus comorbid disabilities on scholastic outcomes.

Given the high risk for poor general cognitive processing observed in this population, we hypothesised that EP children without neurosensory impairments would have significantly higher rates of ID and LD and a greater risk for comorbid ID/LD than children born at term. We also hypothesised that ID and LD would be associated with poor neuropsychological abilities and that EP children with comorbid ID/LD would have the poorest performance on tests of executive function, sensori-motor and visuo-spatial skills and a significantly greater reliance on SEN provision.

MATERIAL AND METHODS

Participants

Participants were members of the UK EPICure Study cohort. From 1st March through 31st December 1995, all babies born $<26^{+0}$ weeks' gestational age and admitted for neonatal intensive care in the whole of the UK and Ireland were identified (n=811) and surviving children (n=314) were invited to participate in follow-up assessments. For the first two assessment waves, response rates were 90% (n=283) at two years of age [25] and 78% (n=241) at six years of age [26]. Data for the present report relate to the results of the 11 year outcome evaluation carried out when children were in the final year of primary school. At this age, 219 of 307 (71%) survivors were assessed [27].

A contemporaneous reference group of 153 children born at term (≥ 37 weeks' gestation) was also assessed at 11 years of age. These children were selected from the classmates of EP children in mainstream schools at either the 6 or 11 year follow-up, and were matched for age, sex and ethnicity, to their EP classmate. Although controls could not be selected for every EP child, including those in special schools, there were no significant differences in age, sex and ethnicity between EP children and classmates assessed at 11 years of age (see [27] for a detailed description of the cohort).

Of the 219 EP children assessed at 11 years, 50 (23%) had neurosensory impairment (moderate/severe vision, hearing impairment or gross motor impairment) and were excluded from the present analyses in order to explore outcomes among those free of major neurological sequelae. A further eight (4%) EP children with incomplete data on the 11 year outcome measures were excluded as neuropsychological profiles could not be explored for these children. In the term control group, there were no children with neurosensory impairments, but 1 (1%) child did not complete the outcome assessments. As such, the final sample for the present report comprised 161 EP children and 152 term-born controls without neurosensory impairment; this represents 74% and 99% of the total EP and control sample assessed at 11 years (Figure 1). Table 1 shows the characteristics of the final sample. There were no significant differences in age, sex and socio-economic status (SES) between EP children and term-born controls. However, EP children had significantly poorer IQ and neuropsychological skills and were more likely to have SEN than term-born controls (Table 1).

<<FIGURE 1>> << TABLE 1>>

Procedure

Parents provided informed consent for their child's participation and the study was approved by the Southampton and South West Hampshire Research Ethics Committee. Children were initially offered an assessment at school, however in cases in which a school assessment was not possible or where the parents preferred their child to be assessed out of school hours, a home or clinic based assessment was offered to maximise response rates. In total, 193 (88%) EP children were assessed at school, 22 (10%)

at home and 4 (2%) at a clinic. Among the term-born controls, 151 (99%) were assessed at school and the remaining 2 (1%) were assessed at home. The assessment protocol was identical in each setting.

Standardised tests

The Kaufman Assessment Battery for Children (K-ABC)[28] was used to assess children's general cognitive ability, from which an age standardised Mental Processing Composite score (MPC) score, equivalent to IQ, was derived (*Mean* 100; *SD* 15; *range* 40-160). Intellectual disability (ID) was defined as MPC scores < -2 SD using the mean and SD of the term control group (i.e.,MPC <82). The use of contemporaneous reference data for defining disability is recommended to account for the Flynn Effect, the secular upward drift in IQ scores over time [27, 29, 30].

Academic attainment was assessed using the Wechsler Individual Achievement Test-II^{UK} (WIAT-II^{UK}) [31] from which age standardised composite scores were derived for proficiency in reading and mathematics (*Mean* 100; *SD* 15; *range* 40-160). LD were classified using standardised scores < -2 SD of the term control group (Reading standardised score <74; Mathematics standardised score <69) [32]. To explore how neurodevelopmental sequelae manifest in this population, we investigated comorbidity in ID and LD, such that LD could occur in isolation or co-exist with ID. As such, LD were classified as *specific* if the LD occurred in the absence of ID (i.e., where attainment was < -2SD and IQ was ≥ -2 SD of the mean of the control group).

Neuropsychological abilities commonly affected by EP birth were assessed using the NEPSY Developmental Neuropsychological Test [33] from which age standardised scores (*Mean* 100; *SD* 15; *range* 50-150) were derived for the three core domains of (1) Attention/Executive Function (derived from the Tower, Auditory Attention and Response Set, and Visual Attention subtests administered to assess planning, shifting, sustained and selective attention), (2) Sensorimotor Skills (derived from the Fingertip Tapping, Imitating Hand Positions and Visuo-motor Precision subtests administered to assess manual dexterity and fine motor skills) and (3) Visuo-Spatial Processing (derived from the Design Copying and Arrows subtests to assess visuo-motor integration and judgement of line orientation). Assessments were carried out by one of three psychologists blind to the children's

clinical history and study group allocation. Prior to commencing data collection, the psychologists simultaneously scored tests during assessments carried out with non-study participants and excellent inter-rater reliability was achieved (>95% agreement across individual test items on all measures).

Teacher report

Curriculum-based attainment of children in mainstream schools was assessed using the Teacher Academic Attainment Scale (TAAS) for which the child's main class teacher rated his or her performance in relation to the national average expected for his/her age across seven subjects. Ratings were on a five point likert scale and ranged from one (very below average) to five (very above average). The TAAS has excellent validity when compared with results on gold standard achievement tests [34]. Teachers were also asked to specify whether the child had SEN, defined in the UK as a learning difficulty or disability which calls for special educational provision to be made, or the child has a disability which prevents or hinders him or her from making use of educational facilities of a kind generally provided for other children of the same age in mainstream schools [35].

Parent report

Parents completed a questionnaire to provide socio-demographic information, from which family SES was coded into three categories corresponding to high, medium and low SES using national statistics relating to parental occupation [36].

Statistical analyses

Statistical analyses were undertaken using Stata version 13·0 (StataCorp, College Station, TX). For each outcome measure, between group differences were assessed using independent samples t-tests for continuous outcomes and chi-square tests for categorical outcomes. To determine whether there were differences in the neuropsychological profiles of children with different patterns of ID and/or LD (i.e. no disabilities, ID alone, specific LD, ID+LD), three tests were used to assess differences in NEPSY standardised scores for each sub-group. For each score, differences between sub-groups were analysed

using ANOVA with Bonferroni correction to adjust for multiple comparisons. For each sub-group, the equality of the three NEPSY scores was tested using MANOVA (i.e., flatness test of each sub-group's profile). Again, a MANOVA was used to determine whether the profiles of attainment in the four sub-groups differed significantly (i.e., parallelism tests). For t-tests and ANOVAs, analyses confirmed that the assumptions of normality and homogeneity of variance were met for all outcome measures. In addition, for MANOVA tests, the assumptions of linearity between outcome measures, absence of multicollinearity and equality of covariance matrices were also confirmed for all outcome measures. Finally, to examine the impact of specific versus comorbid disabilities on the prevalence of SEN, generalized linear models with Poisson distribution were used to compute relative risks with 95% Confidence Intervals (CI) for the risk of SEN, before and after adjustment for sex, age at assessment and SES.

RESULTS

Prevalence of learning disabilities

The prevalence and comorbidity of LD are shown in Table 2. In total, 86 (53%) of EP children and 145 (95%) of controls had no disability. Thus adverse outcomes were significantly more common among EP children, with a total of 75 (47%) EP children having either ID or LD compared with 7 (4.6%) controls (RR 10.12; 95% CI 4.81 to 21.27). Fifteen (9%) EP children and 2 (1%) controls had ID alone (RR 12.65; 95% CI 2.82 to 56.67). Adding together those with specific LD (i.e., LD without ID), 22 (14%) EP children and 5 (3%) controls had specific LD (i.e., RR 7.42; 95% CI 2.71 to 20.31). (See Table 2 for the prevalence of specific RLD and MLD).

<< TABLE 2>>

Comorbidity was more common among EP children than controls. Of two control children with ID, neither had LD. Among EP children, 38 (24%) had comorbid ID and LD (Table 2). The majority of these (n=23, 14% of the total sample) had IQ, reading *and* mathematics scores < -2SD. Twenty-two EP children without ID had specific LD: 3 (2%) had RLD, 11 (7%) MLD, and 8 (5%) both RLD and MLD. Of the controls, 5 (3%) had specific RLD or MLD (Table 2). The prevalence of comorbidity

increased with increasing severity of ID. Of 108 EP children with no ID, 8 (16%) had comorbid LD; of 43 with moderate ID (IQ -2 to -3 SD), 18 (42%) had comorbid LD; and 5 (50%) of 10 EP children with severe ID (IQ < -3 SD) had comorbid LD.

Overall, mathematics difficulties were more common than reading difficulties among EP children. In total, 56 (35%) EP children had MLD, either specific or comorbid with ID or RLD, compared with just 2 (1%) controls; in contrast, 35 (22%) of EP children had RLD, either specific or comorbid with ID or MLD, compared with 3 (2%) of controls. Whilst the rates of specific MLD were higher in EP children than controls (7% vs. 1%), the rate of specific RLD was similar between groups (2% vs. 2%).

MPC (IQ) scores are shown in Table 3. The mean MPC score for EP children without ID was 97.4 (SD 9.2) compared with 104.8 (SD 10.4) in controls, thus a deficit of 7 IQ points among EP children without ID compared with their term-born classmates. EP children with specific RLD and MLD had lower MPC scores than EP without LD, and MPC scores were lowest for those with comorbid ID and LD (see Table 3). The small number of children in each sub-group precluded statistical analysis.

<<TABLE 3>>

Neuropsychological profiles of EP children

Figure 2 shows the neuropsychological profiles of sub-groups of EP children with ID and/or LD, and the pairwise comparisons of mean scores adjusted for multiple comparisons are shown in Appendix A. Profile analysis indicated that the profiles of the 4 groups were significantly different ($p<0.01$). As shown in Figure 2, EP children with comorbid ID and LD had the poorest neuropsychological abilities with significantly lower scores in all domains than EP children who had no disabilities. They also had significantly poorer executive function than children with ID alone and, additionally, poorer visuo-spatial processing than children with specific LD. Compared with EP children with no disability, EP children with specific LD had poorer scores for tests of executive function, and those with ID alone had poorer scores on test of executive function and visuo-spatial processing. There were no significant differences in any test scores between children with ID and specific LD.

<<FIGURE 2>>

Impact of cognitive and learning disabilities on EP children's scholastic outcomes

Teacher rated attainment for 156 EP children in mainstream schools is shown in Figure 3, and pairwise comparisons of mean scores by disability sub-group in Appendix B. Profile analysis indicated that the attainment profiles of the four sub-groups were significantly different ($p<0.01$). As expected, EP children with LD, either specific or comorbid, had the poorest attainment with significantly lower ratings across all school subjects compared with EP children with no LD or ID. Children with comorbid ID and LD also had significantly lower attainment in all but one subject (design/technology) than children with ID alone, but their outcomes were not significantly different to children with specific LD. Those with ID alone had significantly poorer teacher-rated attainment in reading, mathematics, science and design/technology than children with no disabilities.

<<FIGURE 3>>

The risk of being identified with SEN among EP children in mainstream schools is shown in Table 4. EP children with LD were at 3 times increased risk for SEN and this remained significant after adjustment for confounders. The adjusted RR for SEN was similar between children with specific LD (RR 3.43; 95% CI 2.36 to 5.00) and comorbid ID and LD (RR 3.31; 95% CI 2.28 to 4.79). ID alone was not associated with an increased risk for being identified with SEN compared with EP children who had no disabilities.

<<TABLE 4>>

DISCUSSION

In this national cohort study we found that of the 47% of EP children with cognitive or learning deficits, the vast majority had comorbid difficulties, and that half of those with comorbid difficulties had ID, RLD *and* MLD. Isolated cognitive or learning deficits were therefore uncommon among EP children. This highlights the complex nature of learning difficulties and disabilities following EP birth and the pervasive impact of extreme prematurity across multiple developmental domains.

These results are consistent with previous studies of comorbidity in neurodevelopmental sequelae [22-24] and of LD [7, 8] in children born very or extremely preterm/ELBW. EP birth confers both destructive influences to brain development via focal brain injuries sustained during the neonatal period, and disturbances to normal neurodevelopment that result in diffuse alterations in brain size, architecture, complexity and connectivity [37]. These have wide ranging and pervasive effects on neurological development leaving survivors at risk for multiple developmental disorders and generalised cognitive impairments. Such impairments comprise deficits in IQ and in domain-general cognitive processes including attention, executive function, visuospatial processing and visuo-motor integration [19, 20, 38].

Notably we found that difficulties with mathematics were far more common than difficulties with reading among EP children. Among the 22 EP children with specific LD, only 3 had RLD yet 19 had MLD, either isolated or with RLD, and whilst rates of specific MLD were much higher among EP children than controls (12% vs. 1%), the rates of specific RLD were similar (2% vs. 2%). Similarly, among the 38 EP children with comorbid ID and LD, all but 1 child had MLD. These results are commensurate with previous studies which show that mathematics difficulties are especially common among children born preterm.[14, 39] The excess of mathematics difficulties in this population has been associated with domain-general cognitive deficits, in particular with deficits in working memory, executive function and visuo-spatial processing.[16, 40]

Indeed visuo-spatial processing, sensori-motor integration and executive function were significantly poorer in EP children with ID or LD than those with IQ and attainment in the average range. Notably, children with comorbid ID and LD had the poorest neuropsychological abilities with significantly lower scores in all core domains compared with children with no disability. Moreover, these children had poorer executive function than children with ID alone and poorer executive function and visuo-spatial processing than children with specific LD. The importance of executive functions and visuo-spatial processing for academic success in preterm children has been highlighted in previous studies [10, 16, 40]. From the present study, we are unable to ascertain whether these poor neuropsychological abilities are causal factors leading to lowered overall performance or whether they are outcomes of

poor performance. However, other longitudinal studies have identified the importance of early executive functions and visual-spatial skills for long-term success at school in both preterm [41] and typically developing children [42, 43] suggesting a causal role of deficits in general cognitive processing in the development of learning difficulties at school. These therefore represent potential targets for intervention for improving outcomes in children born EP.

We also explored the impact of comorbid difficulties on attainment at school. Children with LD, either specific or comorbid, had the poorest scholastic outcomes. Those with LD had generally poorer attainment in most school subjects than children with ID alone and were at 3 times increased risk for SEN than EP children without LD/ID. These results would be expected given the definition of LD and indicate that these children clearly have the greatest need for special educational support. However, we also found that ID alone did not place EP children at higher risk for SEN, yet these children had significantly poorer attainment in the core subjects of literacy, mathematics and science and poorer neuropsychological skills than EP children without ID/LD and term-born peers. This suggests that EP children who have cognitive difficulties but academic attainment within the broadly average range may have unmet needs and may benefit from additional support in the classroom. Previous studies have noted that preterm children with LD may fail to receive SEN support [9, 44] and our study suggests that even those without significant LD might also benefit from additional help in school.

Problems in multiple developmental domains may increasingly limit children's learning opportunities with cascading effects on development over time [22]. The assessment of functioning in separate domains or areas of learning is therefore likely to underestimate the true extent of a child's functional needs [45] underscoring the need for long-term multi-domain assessments in this population [38]. Education professionals lack knowledge of the outcomes of children born preterm and feel ill equipped to support their learning in the classroom [46], yet it is important for teaching staff, educational psychologists and specialists in SEN provision to recognise the need to assess a wide range of outcomes in preterm children. These results also have far reaching societal and economic implications. Since the greatest costs associated with very preterm birth after neonatal care lie within

education [47], reducing the prevalence of learning disabilities in preterm populations represents a key focus of current research and a growing challenge for clinicians and educators alike.

The focus of the present paper, as of the vast majority of research in this field, is on the group of EP children with long-term problems and on the mechanisms underlying those difficulties. The strengths of this study lie in the exploration of outcomes in a sample drawn from a national population-based cohort of EP children. Neuropsychological and academic outcomes were assessed using gold standard psychometric tests carried out by psychologists who achieved excellent inter-rater reliability and were blind to children's group allocation. However, only 71% of the surviving EP cohort was assessed at 11 years of age. We have previously reported that those lost to follow-up were at greater risk for neurodevelopmental and intellectual disabilities [27]. This analysis may therefore underestimate the prevalence of disability at a population level and the pattern of comorbidity msay differ had the total cohort been assessed. We also recognise that few controls had ID and LD; however the focus of the paper was largely on within-group differences and patterns of impairments among the EP children. In this study, global domain scores for executive function, visuo-spatial processing and sensori-motor skills were used to explore the impact of neuropsychological abilities on LD. Future studies should attempt to explore the role of other important cognitive processes such as language and memory in the development of learning difficulties in this population, and to identify the role of specific components of executive function in the development of LD as potential targets for intervention.

In summary, EP children without neurosensory impairments are at high risk for multiple intellectual and learning disabilities which impact on their school performance. Even those without significant learning disabilities may have poor neuropsychological skills that impact on performance at school. Improving executive functions and visuospatial skills following EP birth represents a potential target for intervention. Education professionals should be aware of the complex nature of cognitive and learning difficulties in children born preterm in order to provide appropriate academic support.

Acknowledgements

The authors are indebted to the EPICure Study Group, which included paediatricians in 276 maternity units in the United Kingdom and Ireland who identified the original cohort, contributed data to the study and whose help was invaluable. We are also indebted to the schools and teachers who supported study assessments throughout this follow-up, and to the many children and parents for their continued participation in the EPICure Studies. Co-investigators for the 11 year evaluation of the cohort were Neil Marlow (Chief Investigator), Kate Costeloe, Enid Hennessy, Janet Stocks and Elizabeth Draper. Psychological assessments were performed by Rebecca Trikic, Rebecca Smith, & Samantha Johnson. Heather Palmer was the Study Manager.

Contributors' statements

Samantha Johnson contributed to study design and management, data collection, wrote the first draft of the manuscript, critically revised it and approved it for submission. Victoria Strauss conducted data analyses, reviewed and critically revised the manuscript and approved it for submission. Camilla Gilmore and Julia Jaekel reviewed and critically revised the manuscript and approved it for submission. Neil Marlow, chief investigator of the EPICure Study, led the study design, management and data collection, reviewed and critically revised the manuscript and approved it for submission. Dieter Wolke, co-investigator for the EPICure Study, contributed to study design and management, reviewed and critically revised the manuscript and approved it for submission.

Conflict of interest statement: The authors have no conflicts of interest to disclose

References

[1] MacKay DF, Smith GC, Dobbie R, Pell JP. Gestational age at delivery and special educational need: retrospective cohort study of 407,503 schoolchildren. PLoS Med. 2010;7:e1000289.

[2] Chan E, Quigley MA. School performance at age 7 years in late preterm and early term birth: a cohort study. Archives of disease in childhood Fetal and neonatal edition. 2014;99:F451-7.

[3] Mathiasen R, Hansen BM, Andersen AM, Forman JL, Greisen G. Gestational age and basic school achievements: a national follow-up study in Denmark. Pediatrics. 2010;126:e1553-61.

[4] Saigal S, den Ouden L, Wolke D, Hoult L, Paneth N, Streiner DL, et al. School-age outcomes in children who were extremely low birth weight from four international population-based cohorts. Pediatrics. 2003;112:943-50.

[5] Johnson S, Hennessy E, Smith R, Trikic R, Wolke D, Marlow N. Academic attainment and special educational needs in extremely preterm children at 11 years. The EPICure Study. Archives of Disease in Childhood Fetal and Neonatal Edition. 2009;94:F283-F9.

[6] Anderson P, Doyle LW. Neurobehavioral outcomes of school-age children born extremely low birth weight or very preterm in the 1990s. JAMA-Journal Of The American Medical Association. 2003;289:3264-72.

[7] Grunau RE, Whitfield MF, Davis C. Pattern of learning disabilities in children with extremely low birth weight and broadly average intelligence. Archives of Pediatric and Adolescent Medicine. 2002;156:615-20.

[8] Pritchard VE, Clark CA, Liberty K, Champion PR, Wilson K, Woodward LJ. Early school-based learning difficulties in children born very preterm. Early Hum Dev. 2009;85:215-24.

[9] Taylor HG, Klein N, Anselmo MG, Minich N, Espy KA, Hack M. Learning problems in kindergarten students with extremely preterm birth. Archives of pediatrics & adolescent medicine. 2011;165:819-25.

[10] Litt JS, Gerry Taylor H, Margevicius S, Schluchter M, Andreias L, Hack M. Academic achievement of adolescents born with extremely low birth weight. Acta Paediatr. 2012;101:1240-5.

[11] Litt J, Taylor HG, Klein N, Hack M. Learning disabilities in children with very low birthweight: Prevalence, neuropsychological correlates, and educational interventions. Journal Of Learning Disabilities. 2005;38:130-41.

[12] Hutchinson EA, De Luca CR, Doyle LW, Roberts G, Anderson PJ, Victorian Infant Collaborative Study G. School-age outcomes of extremely preterm or extremely low birth weight children. Pediatrics. 2013;131:e1053-61.

[13] Taylor HG, Hack M, Klein N, Schatschneider C. Achievement In Children With Birth Weights Less-Than-750 Grams With Normal Cognitive-Abilities - Evidence For Specific Learning-Disabilities. Journal of pediatric psychology. 1995;20:703-19.

[14] Simms V, Cragg L, Gilmore C, Marlow N, Johnson S. Mathematics difficulties in children born very preterm: current research and future directions. Archives of disease in childhood Fetal and neonatal edition. 2013;98:F457-63.

[15] Simms V, Gilmore C, Cragg L, Marlow N, Wolke D, Johnson S. Mathematics difficulties in extremely preterm children: evidence of a specific deficit in basic mathematics processing. Pediatr Res. 2013;73:236-44.

[16] Simms V, Gilmore C, Cragg L, Clayton S, Marlow N, Johnson S. Nature and origins of mathematics difficulties in very preterm children: a different etiology than developmental dyscalculia. Pediatr Res. 2015;77:389-95.

[17] Son S, Meisels S. The Relationship of Young Children's Motor Skills to Later Reading and Math Achievement. Merrill Palmer Quarterly. 2006;52.

[18] Cragg L, Gilmore C. Skills underlying mathematics: The role of executive function in the development of mathematics proficiency. Trends in Neuroscience and Education. 2013;3:63-8.

[19] Marlow N, Hennessy E, Bracewell M, Wolke D. Motor and executive function at 6 years of age following extremely preterm birth. Pediatrics 2007;120:793-804.

[20] Anderson PJ. Neuropsychological outcomes of children born very preterm. Seminars in fetal & neonatal medicine. 2014;19:90-6.

[21] Aarnoudse-Moens CS, Duivenvoorden HJ, Weisglas-Kuperus N, Van Goudoever JB, Oosterlaan J. The profile of executive function in very preterm children at 4 to 12 years. Dev Med Child Neurol. 2012;54:247-53.

[22] Woodward LJ, Moor S, Hood KM, Champion PR, Foster-Cohen S, Inder TE, et al. Very preterm children show impairments across multiple neurodevelopmental domains by age 4 years. Archives of disease in childhood Fetal and neonatal edition. 2009;94:F339-44.

[23] Wolke D, Meyer R. Cognitive status, language attainment, and prereading skills of 6-year-old very preterm children and their peers: the Bavarian Longitudinal Study. Developmental Medicine and Child Neurology. 1999;41:94-109.

[24] Roberts G, Lim J, Doyle LW, Anderson PJ. High rates of school readiness difficulties at 5 years of age in very preterm infants compared with term controls. Journal of developmental and behavioral pediatrics : JDBP. 2011;32:117-24.

[25] Wood NS, Marlow N, Costeloe K, Gibson AT, Wilkinson AR. Neurologic and developmental disability after extremely preterm birth. EPICure Study Group. N Engl J Med. 2000;343:378-84.

[26] Marlow N, Wolke D, Bracewell MA, Samara M, Group EPS. Neurologic and developmental disability at six years of age after extremely preterm birth. N Engl J Med. 2005;352:9-19.

[27] Johnson S, Fawke J, Hennessy E, Rowell V, Thomas S, Wolke D, et al. Neurodevelopmental disability through 11 years in children born before 26 weeks of gestation: The EPICure Study. Pediatrics 2009:e249-e57.

[28] Kaufman AS, Kaufman NL. Kaufman Assessment Battery for Children. Circle Pines, MN: American Guidance Service, Inc; 1983.

[29] Wolke D, Ratschinski G, Ohrt B, Riegel K. The cognitive outcome of very preterm infants may be poorer than often reported: an empirical investigation of how methodological issues make a big difference. European Journal of Pediatrics. 1994;153:906-15.

[30] Flynn J. Searching for justice: the discovery of IQ gains over time. American Psychologist. 1999;54:5-20.

[31] Wechsler D. Wechsler Individual Achievement Test, 2nd Edition UK: Harcourt Assessment Inc; 2004.

[32] Johnson S, Wolke D, Hennessy E, Marlow N. Educational outcomes in extremely preterm children: neuropsychological correlates and predictors of attainment. Dev Neuropsychol. 2011;36:74-95.

[33] Korkman M, Kirk U, Kemp S. NEPSY. A Developmental Neuropsychological Assessment. San Antonio, TX: The Psychological Corporation; 1998.

[34] Johnson S, Marlow N, Wolke D. Assessing educational outcomes in middle childhood: validation of the Teacher Academic Attainment Scale. Dev Med Child Neurol. 2012;54:544-51.

[35] Department for Education, Health Do. Special educational needs and disability code of practice: 0 to 25 years. London, UK2015.

[36] Office for National Statistics. The National Statistics Socio-Economic Classification User Manual.: Palgrave Macmillan; 2005.

[37] Volpe JJ. Brain injury in premature infants: a complex amalgam of destructive and developmental disturbances. Lancet neurology. 2009;8:110-24.

[38] Burnett AC, Scratch SE, Lee KJ, Cheong J, Searle K, Hutchinson E, et al. Executive function in adolescents born <1000 g or <28 weeks: a prospective cohort study. Pediatrics. 2015;135:e826-34.

[39] Taylor HG, Espy KA, Anderson PJ. Mathematics deficiencies in children with very low birth weight or very preterm. Developmental Disabilities Research Reviews. 2009;15:52-9.

[40] Aarnoudse-Moens CS, Weisglas-Kuperus N, Duivenvoorden HJ, van Goudoever JB, Oosterlaan J. Executive function and IQ predict mathematical and attention problems in very preterm children. PLoS One. 2013;8:e55994.

[41] Rose SA, Feldman JF, Jankowski JJ. Modeling a cascade of effects: the role of speed and executive functioning in preterm/full-term differences in academic achievement. Developmental science. 2011;14:1161-75.

[42] Clark CA, Sheffield TD, Wiebe SA, Espy KA. Longitudinal associations between executive control and developing mathematical competence in preschool boys and girls. Child Dev. 2013;84:662-77.

[43] Clark CA, Pritchard VE, Woodward LJ. Preschool executive functioning abilities predict early mathematics achievement. Dev Psychol. 2010;46:1176-91.

[44] Roberts G, Howard K, Spittle AJ, Brown NC, Anderson PJ, Doyle LW. Rates of early intervention services in very preterm children with developmental disabilities at age 2 years. J Paediatr Child Health. 2008;44:276-80.

[45] van Baar AL, Wassenaer AGv, Briet JM, Dekker FW, Kok JH. Very preterm birth is associated with disabilities in multiple developmental domains. Journal of pediatric psychology. 2005;30:247-55.

[46] Johnson S, Gilmore C, Gallimore I, Jaekel J, Wolke D. The long-term consequences of preterm birth: what do teachers know? Dev Med Child Neurol. 2015.

[47] Petrou S, Abangma G, Johnson S, Wolke D, Marlow N. Costs and health utilities associated with extremely preterm birth: evidence from the EPICure study. Value in health : the journal of the International Society for Pharmacoeconomics and Outcomes Research. 2009;12:1124-34.

Table 1. Characteristics of extremely preterm (<26^{+0} weeks' gestation) children and term-born controls (≥37 weeks gestation) without neurosensory impairment assessed at 11 years of age.

Characteristic	Term-born controls (n=152)	Extremely preterm (n=161)	p
Male, n (%)	64 (42.11)	69 (42.86)	0.89
Age at assessment, mean (SD)	131.16 (6.56)	130.87 (4.53)	0.64
SES Low, n (%)	37 (27.41)	40 (28.37)	0.15
Middle, n (%)	21 (15.56)	34 (24.11)	
High, n (%)	77 (57.04)	67 (47.52)	
MPC (IQ), mean (SD) [a]	103.96 (11.00)	88.60 (12.66)	<0.001
Reading, mean (SD) [b]	98.45 (11.67)	85.10 (16.24)	<0.001
Mathematics, mean (SD) [b]	98.42 (15.01)	75.99 (18.75)	<0.001
Attention/Executive function, mean (SD) [c]	104.20 (11.28)	87.66 (17.41)	<0.001
Sensorimotor skills, mean (SD) [c]	99.62 (11.44)	85.96 (13.12)	<0.001
Visuospatial processing, mean (SD) [c]	107.43 (13.50)	88.44 (17.74)	<0.001
Special school placement, n (%)	0 (0)	5 (3.11)	0.03
Special educational needs, n (%)	17 (11.18)	87 (55.41)	<0.001

[a]Mental Processing Composite of the Kaufman Assessment Battery for Children, age-standardised test scores with normative mean 100, SD 15, range 40-160. [b]Wechsler Individual Achievement Test-II, age-standardised test scores with normative mean 100, SD 15, range 40-160. [c]NEPSY test scores, age-standardised test scores with normative mean 100, SD 15, range 50-150. [d]Maths Estimation T, total scores range 0-12. SES Socio-economic status classified as high, middle or low using UK National statistics.

Table 2. Prevalence and co-morbidity of cognitive and learning disabilities in 161 extremely preterm (<26^{+0} weeks' gestation) children and 152 term-born controls (≥ 37 weeks gestation) assessed at 11 years of age.

Learning disabilities (LD)[a]	Term-born controls (n=152) N (%)	Extremely preterm (n=161) N (%)
No disability	145 (95%)	86 (53%)
ID only	2 (1%)	15 (9%)
Specific RLD	3 (2%)	3 (2%)
Specific MLD	2 (1%)	11 (7%)
Specific RLD & MLD	-	8 (5%)
ID & RLD	-	1 (1%)
ID & MLD	-	14 (9%)
ID, RLD & MLD	-	23 (14%)

ID Intellectual disability; RLD Reading learning disability; MLD Mathematics learning disability; all defined as standardised scores < -2SD of term reference group.

Table 3. Mental Processing Composite (MPC) scores in 161 extremely preterm (<26^{+0} weeks' gestation) and 152 term-born children (≥ 37 weeks gestation) at 11 years of age.

Learning disabilities (LD)[a]	Term-born controls without intellectual disability (n=150)[b]		Extremely preterm without intellectual disability (n=108)		Extremely preterm with intellectual disability (n=53)	
	N (%)	Mean (SD) MPC score	N (%)	Mean (SD) MPC score	N (%)	Mean (SD) MPC score
No LD	146 (97)	104.8 (10.4)	86 (80)	97.4 (9.2)	15 (28)	78.4 (2.4)
Reading LD	3 (2)	93.0 (4.6)	3 (3)	91.0 (8.2)	1 (2)	78.0 (n/a)
Mathematics LD	2 (1)	91.0 (11.3)	11 (10)	86.7 (3.7)	14 (26)	74.9 (4.9)
Reading & mathematics LD	0	-	8 (7)	87.3 (3.0)	23 (43)	72.2 (5.3)

[a] Learning disability is defined as low attainment scores < -2SD of the term reference group (WIAT-II^{UK} reading score <74; WIAT-II^{UK} mathematics score <69). [b] As two controls who had intellectual disability did not have learning disabilities data are shown only for term-born controls without intellectual disability; MPC scores for the two children with intellectual disability are Mean 75.5 SD 4.9.

Table 4. Risk for being identified with special educational needs (SEN) in 156 extremely preterm (<26^{+0} weeks' gestation) children in mainstream schools according to presence of intellectual disability (ID) and/or learning disabilities (LD).

	Special educational needs (SEN)	
	Unadjusted RR (95% CI)	Adjusted RR (95% CI)
No disability	Baseline	Baseline
ID only	1.55 (0.82, 2.92)	1.81 (0.97, 3.38)
Specific LD	3.00 (2.10, 4.29)	3.43 (2.36, 5.00)
Comorbid ID+LD	3.15 (2.24, 4.41)	3.31 (2.28, 4.79)

[a] Below average attainment classified as TAAS score < 2.5. [b] Adjusted for sex, age in months and SES. RR Relative Risk

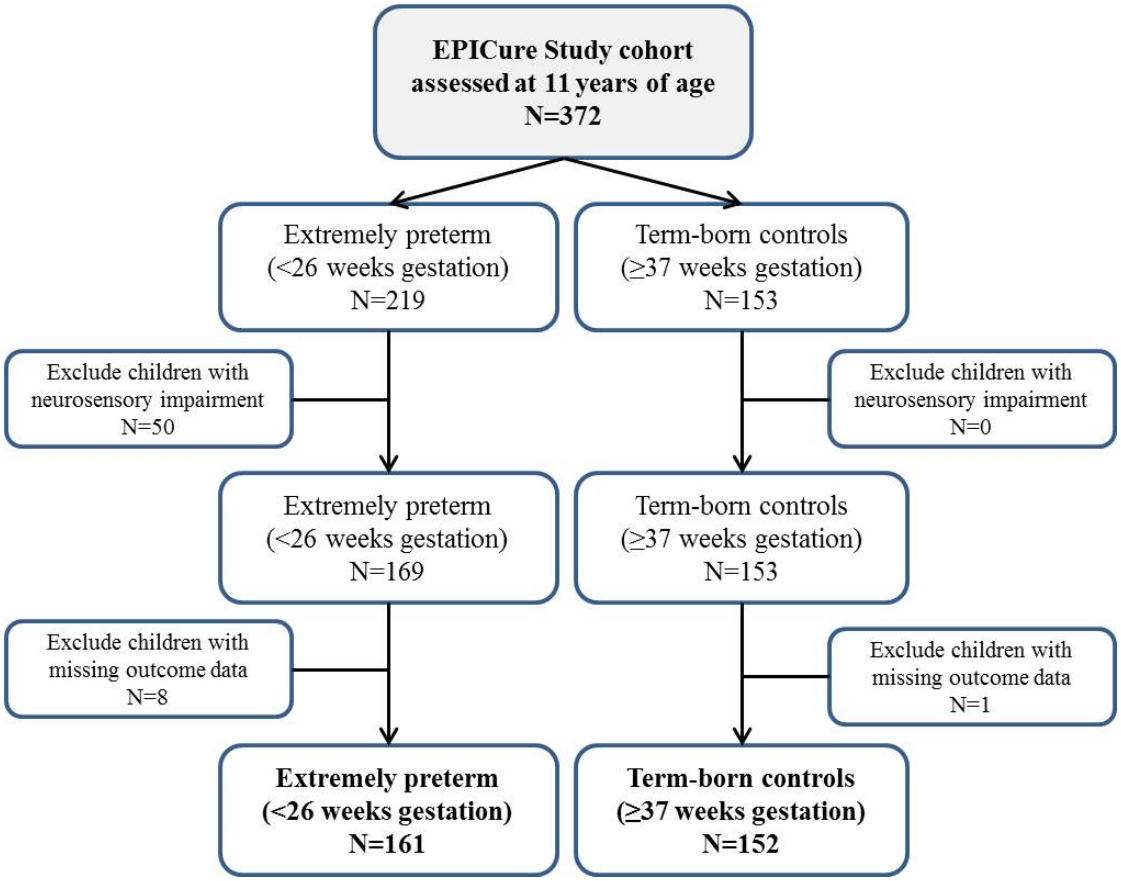

Figure 1. EPICure study cohort assessed at 11 years of age and composition of the sample for the present report.

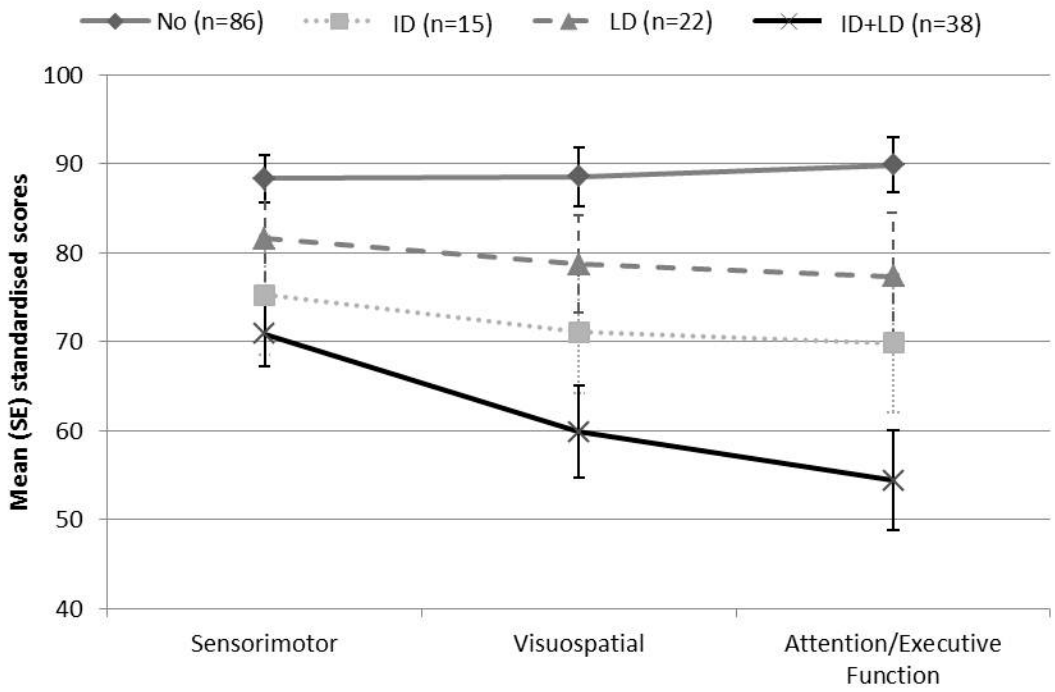

Figure 2. Neuropsychological profiles of 161 extremely preterm (<26^{+0} weeks' gestation) children grouped by patterns of intellectual disability (ID) and/or learning disabilities (LD). The Y axis shows mean (SE) standardised core domain scores on the NEPSY Sensorimotor skills, Visuospatial Processing and Attention and Executive Function tests respectively (Normative Mean 100; SD 15).

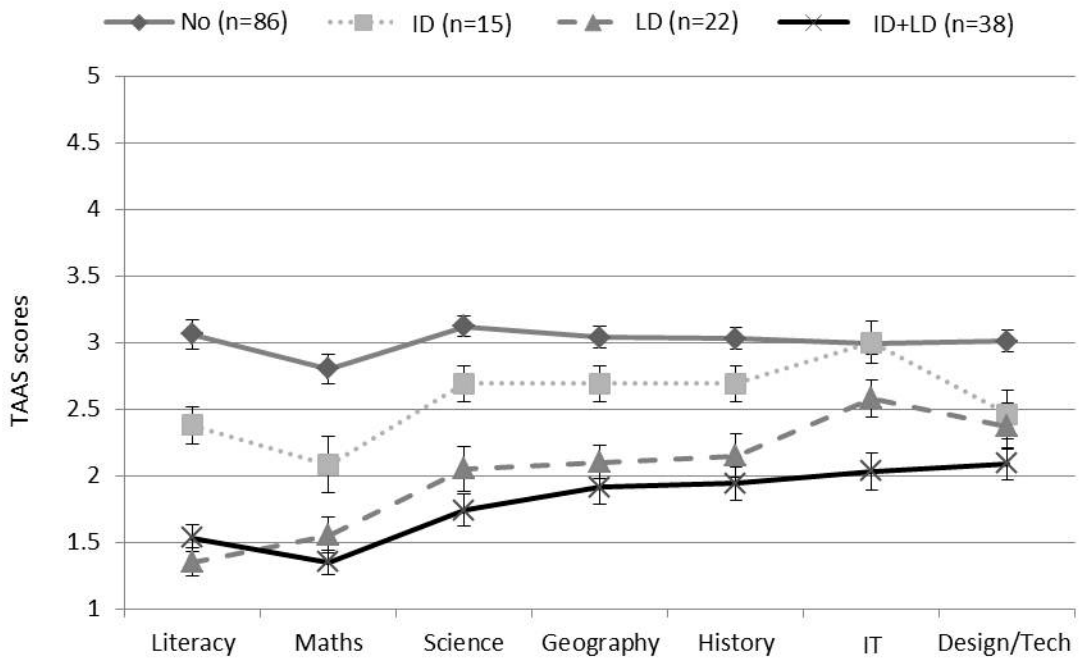

Figure 3. Teacher rated attainment in 156 extremely preterm (<26^{+0} weeks' gestation) children grouped by patterns of intellectual disability (ID) and/or learning disabilities (LD). Y axis shows mean (SE) Teacher Academic Attainment Scale (TAAS) scores for seven school subjects shown on the x axis. Higher scores indicate better attainment; scores < 2.5 represent below average attainment.

APPENDIX A

Mean difference (SE) in neuropsychological test scores between 161 extremely preterm (<26^{+0} weeks' gestation) according to presence of intellectual disability (ID) and/or learning disabilities (LD).

	NEPSY Visuospatial processing	NEPSY Sensorimotor skills	NEPSY Attention /executive function
ID vs. no disability	-17.48 (4.43)**	-13.14(4.32)**	-20.02 (5.09)**
LD vs. no disability	-9.83 (3.78)**	-6.76 (3.69)	-12.52 (4.35)**
ID+LD vs. no disability	-28.69 (3.08)**	-17.52 (3.01)**	-35.46 (3.54)**
LD vs. ID	7.65 (5.30)	6.38 (5.17)	-7.50 (6.09)
ID+LD vs. ID	-11.20 (4.82)*	-4.38 (4.70)	-15.43 (5.54)**
ID+LD vs. LD	-18.56 (4.24)**	-10.76 (4.13)**	-22.94 (4.87)**

* p<0.05; ** p<0.01.

APPENDIX B

Mean difference (SE) in Teacher Academic Attainment Scale (TAAS) ratings for 156 extremely preterm (<26^{+0} weeks' gestation) according to presence of intellectual disability (ID) and/or learning disabilities (LD).

	Literacy	Mathematics	Science	Geography	History	IT	Design & Technology
ID vs. no disability	-0.72 (-1.16, -0.28)**	-0.77 (-1.25, -0.29)**	-0.46 (-0.87, -0.05)*	-0.35 (-0.73, 0.03)	-0.35 (-0.75, 0.05)	0.02 (-0.41, 0.44)	-0.52 (-0.94, -0.11)*
LD vs. no disability	-1.73 (-2.12, -1.36)**	-1.27 (-1.68, -0.86)**	-1.05 (-1.40, -0.69) **	-0.94 (-1.27, -0.61)**	-0.89 (-1.23, -0.55)**	-0.41 (-0.77, -0.04)*	-0.62 (-0.97, -0.26)**
ID+LD vs. no disability	-1.54 (-1.86, -1.23)**	-1.47 (-1.81, -1.13)**	-1.37 (-1.66, -1.08)**	-1.11 (-1.38, -0.84)**	-1.08 (-1.36, -0.80)**	-0.95 (-1.26, -0.65)**	-0.89 (-1.19, -0.60)**
LD vs. ID	-1.02 (-1.54, -0.49)**	-0.50 (-1.07, 0.07)	-0.59 (-1.08, -0.10) *	-0.59 (-1.04, -0.14)*	-0.53 (-1.00, -0.07)*	-0.42 (-0.93, 0.08)	-0.09 (-0.59, 0.40)
ID+LD vs. ID	-0.82 (-1.30, -0.34)**	-0.70 (-1.22, -0.18)**	-0.91 (-1.36, -0.46)**	-0.75 (-1.17, -0.34)**	-0.72 (-1.15, -0.30)**	-0.97 (-1.43, -0.51)**	-0.37 (-0.82, 0.08)
ID+LD vs. LD	0.19 (-0.23, 0.62)	-0.20 (-0.66, 0.25)	-0.32 (-0.72, 0.07)	-0.17 (-0.53, 0.19)	-0.19 (-0.56, 0.19)	-0.55 (-0.95, -0.14)**	-0.27 (-0.67, 0.12)

* p<0.05; ** p<0.01.

.