



CLINICAL RESEARCH ARTICLE

Specific cognitive correlates of the quality of life of extremely preterm school-aged children without major neurodevelopmental disability

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BACKGROUND: We examined how specific cognitive behavioral impairments impacted quality of life (QoL) within a large multicenter cohort of 7–10 year olds surviving extremely preterm (EPT) without major neurodevelopmental disability.

METHODS: Between 7 and 10 years of age, two generic, self-proxy, and parental evaluations were obtained. QoL measurement questionnaires (Kidscreen-10/VSPA (Vécu et Santé Perçue de l'Enfant et de l'Adolescent)) were used and compared to a reference population. The general and specific cognitive functions, such as executive functions, behavior and anxiety, and clinical neurologic examination, were also assessed.

RESULTS: We analyzed 211 school-aged EPT children. The mean gestational age was 26.2 (± 0.8) weeks, birth weight was 879 g (± 181) and the mean age was 8.4 years (± 0.87). Children with a Full-Scale Index Quotient ≥ 89 , who were considered as normal, had a lower QoL. Specific cognitive impairments: comprehensive language delay, visuo-spatial integration defect, and dysexecutive disorders) were the QoL correlates in the domains of school performance and body image.

CONCLUSIONS: School and health care professionals need to increase their focus on EPT children's lower so as to recognize the preterm behavioral/cognitive phenotype and their potential need for supportive measures. Research on preventive interventions is warranted to investigate if these long-term effects of an EPT birth can be attenuated in neonatal period and after.

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INTRODUCTION

Extremely preterm (EPT) children's survival rates have improved over the past decades. Regarding the outcome of EPT, if major neurodevelopmental disabilities (intellectual disability, autism, neurosensory disorders, and cerebral palsy) remain stable, the low severity dysfunctions are increased: borderline intellectual disabilities, learning disabilities, attention deficit hyperactivity disorder, specific neuropsychological deficits, and behavioral disorders.^{1–3} This achievement, self-competency and the quality of life (QoL) for EPTs during both childhood and adulthood.⁴

The QoL reported by the preterm school-aged children seemed to have little relationship to their cognitive and/or motor performances.⁵ The parents' perception of their children's QoL, however, was different concerning the gravity of the children's neurologic problems. Thus, parents reported a lower QoL than those described in the same-age reference group reported by their children.⁵

Studies of EPTs, regardless of their age, have shown that the main correlates of a child's QoL lowering were: gestational age,

sex, severity of disabilities (Full-Scale Intelligence Quotient (FSIQ)), behavioral disorders, cerebral palsy, and low socio-economic status.^{5,6} While many studies described EPT children with specific neuropsychological and behavioral disorders, there are few studies discussing whether or not these disorders have an impact on QoL.^{5–7}

Currently, Hack⁸ has the only published study concerning the correlates self-assessed QoL by EPT school-aged children. Actually there is no robust international study regarding the impact of a low severity disabilities and/or specific behavioral/cognitive impairments on the QoL, for school-age EPT children without major neurodevelopmental disabilities who were born in the modern era of neonatal intensive care. We recently published a study showing lower QoLs of school-aged EPT children having no major neurodevelopmental disabilities as compared to a national history French reference population from both the parents' and the child's points of view.^{9,10} A new, separate study on the same population sample should add to our current understanding and be of special interest to clinicians and policymakers.

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Our main objective was to study, within the population of those with low QoL, the relationships between QoL, specific cognitive impairments, and behavioral problems independent of other known QoL correlates in a population of school-aged children EPT without major neurodevelopmental disabilities.

MATERIALS AND METHODS

Participants

Our eligible population ($n = 302$) was the sample included in GPQOL study (PHRC 2010).⁹ All the patients included had a day-long evaluation encompassing a clinical examination as well as an assessment of cognitive function and QoL. Those patients with incomplete data were excluded.

General framework

This is a cross-sectional,⁹ multicenter study of EPT school-aged children born between 1 December 2004 and 31 December 2007, who were discharged alive and free from severe neurodevelopmental disabilities (cerebral palsy, autism, and/or major cognitive disabilities). These children received a clinical examination when they were between 7 and 10 years of age and an assessment of their motor and cognitive functions as well as QoL assessment. Their parents or legal representatives accepted the study's participation principles and signed an informed consent. Additionally, we obtained the children's assent to participate in the study. Motor skills were assessed by the Touwen Infant neurological examination.¹¹ A psychometric assessment was performed, using the Wechsler Intelligence Scale for Children – Fourth Edition (WISC IV),¹² the Rey's figure: a short perceptual organization and memory test and the NEPSY (NEuroPSYchological assessment) with subtests evaluating attention and executive functions.^{13,14} Behavior evaluation was obtained by the Goodman Strengths and Difficulties Questionnaire for the parents.^{15,16} Anxiety evaluation was achieved by the Spielberger questionnaire (STAI-C), directed towards children.¹⁷ Two generic, self- and by parental QoL measurement questionnaires (Kidscreen-10/VSPA (Vécu et Santé Perçue de l'Enfant et de l'Adolescent)), with scores ranging from 0 to 100, were used, with the higher score reflected as a higher QoL level.¹⁸ The VSPA is a self-administered questionnaire with an index total score measuring a nine dimensions (vitality, psychological well-being, relationships with friends, hobbies, relationships with family, physical well-being, relationships with teacher, school work, and self-esteem).¹⁸ The questionnaires used were the VSPA child-version (VSP-Ae: 35 items) and the parent-version (VSP-Ap: 34 items).

The full version of the Kidscreen questionnaire explored physical well-being, psychological well-being (positive and negative), emotions, relations with parents and autonomy, relations with friends, and social and school support.¹⁹

Our study used the 10-item child and parent versions (short Kidscreen-10) to obtain a total index score.

QoL scores were compared to the French population reference data derived from a 2003 established European database. This included a French sample ($N = 989$) obtained by randomly dialing telephone numbers (CATI method: Computer Assisted Telephone Interview – RDD: Random Digital Dialing).

Psychometric assessment

Disability was defined according to the mean of the FSIQ and the results of the Touwen Infant neurological examination:

no disability: an FSIQ ≥ 89 and a Touwen normal,
mild disability: an FSIQ < 89 and ≥ 79 or a Touwen abnormal,
moderate disability: an FSIQ < 79 and ≥ 65 .²⁰ A "specific cognitive impairment" was considered if at least one of the following five specific neuropsychological mental illness disorders (Diagnostic

and Statistical Manual of Mental Disorders, fourth edition (DSM IV) classification of mental diseases) were observed.²¹

language delay if verbal comprehension index (VCI) (WISC IV) were < 85 ,
subtypes of developmental coordination disorder:

ideomotor dyspraxia: a complex coordination disorder with anomaly of movement planning with complex minor neuromotor disorder in the Touwen assessment test and a perceptual reasoning index (PRI) was < 85 (WISC IV);
visuo-spatial integration delay if there was PRI ≤ 85 (WISC IV) and poor copy of Rey's figure (< 10 th percentile);

dysexecutive disorders if the working memory index (WMI) was < 85 (WISC IV) and/or motor inhibition < 10 th percentile (statue) (NEPSY 2) and/or mental flexibility (fluidity of patterns) and/or planification (Tower) were < 8 (subtests NEPSY 2),
attention deficit if selective auditory and/or visual attention < 8 (NEPSY 2) and a processing speed index (PSI) < 85 (WISC IV).

Data collection

Perinatal and pregnancy data were collected using medical records. Socio-demographic and family data, collected at the time of the school-aged assessment, included age, gender, parental education, parents' employment, family's material wealth, as reported by the child, using the Family Affluence Scale,²² and the child's school life.

Ethics statement

This study was approved by the CPP (Committee for the Protection of Persons) (18/12/2012 ref. 12.018) and is registered on ClinicalTrials.gov, number NCT01675726.

Statistical analysis

As the sample size of this study was sufficiently large, the central limit theorem would have led us to apply "classical" procedures even if the distributions were somewhat far from normal.

A descriptive analysis was conducted with categorical variables described as numbers, percentages, and quantitative variables as means and standard deviations. Both the median and the mean were proximate in all quantitative variables. All quantitative variables were normally distributed and assessed using histograms and QQ plots.

Perinatal, socio-demographic, and QoL data were compared to those children not present at the day-long evaluation visit but who had completed the QoL questionnaires. The χ^2 test (or the Fisher's test) was used for categorical variables, and the Student's t test (or the Mann-Whitney U test) was used for quantitative variables.

QoL scores were compared to the "normal" (without disability) study population and the age- and gender-matched French reference population using paired Student's t test.

Multiple linear regression analyses were performed to determine if disability levels and specific cognitive impairments might independently be associated with QoL levels. Factors associated with QoL levels were determined by using what is currently known in the literature (associated with low QoL). Thus, the multivariable analysis consisted of modeling the QoL scores in cases of disability or specific impairments or behavior according to the previously selected parameters: gender, gestational age, weight birth, multiple pregnancies, overweight and obese children, family material wealth (score FAS (family affluence score)), the parents' educational level, and professional activities. Statistical analyses were carried out using the R software.

RESULTS

Population

Three hundred and two EPTs were eligible for the analysis of QoL correlates. There were 240 (79%) who had a day-long evaluation, but only the data of 211 patients (70%) with a complete motor, psychometric, and QoL assessment were included in the analysis. The non-study group of 91 was formed using a non-included sample (without clinical data) and excluded any samples with incomplete data (Fig. 1).

Study population characteristic

The mean gestational age was 26.25 (±0.89) weeks, birth weight was 879.57(±175.75) g, and the mean age at evaluation was 8.4 (±0.87) years.

In Table 1, the study group (n = 211) versus the non-study group (n = 91) was similar in gestational age, gender, level of education, socio-economic status, and QoL. There were 48% (101) of the participants with mild or moderate cognitive disabilities. Only 37% (78) did not have any neuropsychological disorders, and 55.4% (117) had a dysexecutive syndrome. The children’s anxiety levels were in the low range.

QoL population considered as “normal” (no disability) versus the reference population

In Table 2, the EPT children QoL deemed as “normal” (no disability) was significantly lower as compared to the French reference population data (gender- and age-matched children). The most significant lowering in the QoL evaluation domain, from the children’s point of view were: (1) relationships with friends, (2) body image, and (3) leisure; and from the parents’ perception it was: (1) psychological well-being, (2) vitality, and (3) body image. The EPT children’s QoL assessment by Kidscreen was significantly lower from (the) children’s report.

Relationships between QoL and FSIQ scores

Table 3 showed an association between the EPT children’s lowered QoL and the presence of mild or moderate disabilities. From the child’s perception, the areas of QoL significantly lowered

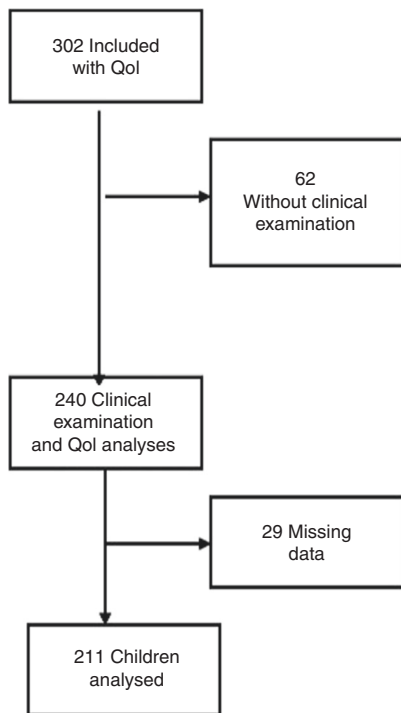


Fig. 1 Flow chart.

Table 1. Study population characteristics.

	Study population (n = 211)	Non-study population (n = 91)	P value
Perinatal data			
GA at birth in WA (mean ± SD)	26.2 (±0.89)	26.2 (±0.83)	0.85
Weight (g) (mean ± SD)	879.5 (±175.5)	877.7 (±195.9)	0.93
Males, n (%)	104 (49.29)	39 (46.43)	0.65
SGA, n (%)	15 (7.11)	6 (6.59)	1.00
Multiple pregnancy, n (%)	69 (32.70)	34 (37.78)	0.39
Neonatal morbidities			
Severe CLD, n (%)	108 (51.92)	53 (59.55)	0.22
Parents’ academic level			
No university, n (%)	88 (41.71)	31 (42.47)	0.90
Parents’ professional activity, n (%)			
Mother’s professional activity	147 (69.67)	47 (58.02)	0.05
Father’s professional activity	188 (89.10)	66 (91.67)	0.53
Socio-economic data			
High family affluence score (FAS)	127 (60.19)	41 (50.00)	0.11
Average age (mean ± SD)	8.47 (±0.75)		
Quality of life^a (mean ± SD)			
VSP-Ae global index (children’s assessment)	68.69 (±13.42)	68.72 (±13.56)	0.98
VSP-Ap global index (parent’s assessment)	70.07 (±10.62)	70.26 (±12.22)	0.90
Kidscreen global index (children’s assessment)	69.93 (±14.01)	68.66 (±15.08)	0.48
Kidscreen global index (parent assessment)	70.84 (±17.60)	70.8916 (±21)	0.98
Neurocognitive evaluation^b			
WISC- IV ^c (mean ± SD)			
FSIQ	91.78 (±15.10)		
VCI (verbal comprehension index)	98.30 (±15.95)		
PRI (perceptual reasoning index)	91.30 (±15.31)		
WMI (working memory index)	91.27 (±14.36)		
PSI (processing speed index)	92.56 (±14.72)		
FSIQ disability categories^d, n (%)			
None (FSIQ >89)	110 (52.80)		
Mild (FSIQ 77–89)	63 (29.86)		
Moderate (FSIQ 65–77)	38 (18.01)		
NEPSY (mean ± SD)			
Score planning (Touwen)	10.70 (±2.66)		
Score design fluency	8.46 (±2.98)		
Score auditory attention	8.88 (±1.72)		
Score visual attention	10.39 (±3.38)		
Neuropsychological disorders^e, n (%)			
Language delay ^f	43 (20.38)		
Visuo-spatial integration delay ^g	29 (14.15)		
Attention delay ^h	30 (14.85)		

Table 1 continued

	Study population (n = 211)	Non-study population (n = 91)	P value
Dysexecutive disorders ⁱ	117 (56.25)		
Ideomotor dyspraxia ^j	17 (8.21)		
Number neuropsychological disorders, n (%)			
0	78 (36.97)		
1	60 (28.44)		
2	51 (24.17)		
>2	22 (10.48)		
Goodman-SDQ-parent ^k			
Emotional symptoms	3.53		
Behavioral problems	1.90		
Hyperactivity/inattention	4.58		
Peer relationship problems	2.03		
Prosocial behaviors	8.75		
Total difficulties score ^l	12.03		
Spielberg index (STAI) ^m (mean ± SD)	32.92 (±7.70)		

Data are expressed as n (%) or mean (±SD); SD: standard deviation; P value: value for difference between groups with available data was obtained with χ^2 test. $P > 0.05$.

GA gestational age, WA weeks of amenorrhea, BW birth weight, SGA small for gestational age, CLD chronic lung disease, WISC IV Wechsler Intelligence Scale for Children – Fourth Edition, FSIQ full-scale intellectual quotient, NEPSY NEuroPSYchological assessment, PSI processing speed index, SDQ Strengths and Difficulties Questionnaire, STAI State-Trait Anxiety Inventory for Adults.

^aQuality of life: VSP-Ae and VSP-Ap: Vécu et Santé Perçue de l'Enfant et de l'Adolescent: QoL questionnaires (children and parent assessments, respectively) whose scores vary between 0 and 100, higher scores indicating better QoL; Kidscreen-children and Kidscreen-parents: QoL questionnaires (children and parent assessments) whose scores vary between 0 and 100.

^bNeurocognitive evaluation.

^cFSIQ: cognition was tested in 240 EPT children but data from 211 children were used in the study.

^dFSIQ categories were defined according to the mean ± SD of the WISC IV: no disability as FSIQ ≥ -1 SD and Touwen as normal mild disabilities as FSIQ < -1 SD and ≥ -2 SDs and/or Touwen as abnormal; moderate disability as FSIQ < -2 SDs and ≥ -3 SDs.

^eNeuropsychological Disorders: Classification of cognitive disorders according to the DSM IV classification: we consider a delay (1) of language if VCI < 85 (-1 SD)^f; (2) of visually spatial integration if PRI < 85 and Rey figure is less than or equal at the 10th in copy^g; (3) attention deficit if auditory attention < 8 and/or visual attention < 8 and PSI < 85 ^h; (4) dysexecutive disorders if WMI < 85 and/or score planning < 8 and/or design fluency < 8 and/or statue < 10 ^h; (5) ideomotor dyspraxia if Touwen = complex coordination disorder and (PRI < 85 and/or IVT < 85)ⁱ.

^kGoodman-SDQ: Score correlated with Achenbach's Child Behavior Checklist, including 25 items answered by parents. The questionnaire gives a total assessment of the difficulties and defines five subscales composed of five items each: emotional disorders, behavioral disorders, hyperactivity, relational disorders added together to generate a total score of "prosocial" difficulties, and behaviors. A total difficulties score without prosocial behaviors (excluded from total difficulties score) is calculated using the SDQ, which ranges from 0 to 40^l. Each one point increase in the total difficulties score corresponds with an increase in the risk of developing a mental health disorder. Categories have been proposed in order to assess whether a child's score is close to average 0–13, slightly above average 14–16, high 17–19, or very high 20–40.

^mSTAI: A self-assessment questionnaire containing 40 items, which obtains two scores (state and trait) ranging from 20 (absence of anxiety) to 80 (high anxiety).

in cases of disablements were: school performance, body image, general well-being, and leisure activities. The overall Kidscreen index and the school performance were reported from the parents' perception.

Relationships between QoL and specific cognitive impairment
From the child's perception, QoL in the school work domain was negatively associated with the presence of verbal comprehension and/or visuo-perception disturbances. From the parents' perception, it was the same relationships and with a negative correlation to dysexecutive disorders (Table 4).

Relationships between QoL and specific dysexecutive disorders, anxiety, and behavioral disorders
From the child's perspective, there was a positive correlation between QoL in school performance, body image domains, and the WMI. From the parents' perspective, there was a positive correlation between QoL in the school work domain, the WMI and between QoL in the body image domain and planning index. From both the children's and parents' perspectives there was a negative association between QoL and anxiety and behavior scores. See Table 5 for further information.

DISCUSSION

This study showed that the FSIQ index value, comprehensive language, visuo-spatial integration delay, and dysexecutive disorders, particularly in working memory and in planning ability, were independent of QoL lowering correlates in EPT children having no major neurodevelopmental disabilities. Among the domains of EPT children's QoL, the most impacted were school work and body image, whether by a self- or proxy questionnaire.

As stated in literature regarding EPT children,^{5–7} our study found that anxiety and/or behavioral disorders were strongly associated with a lowered QoL. In EPT adolescents, a lowered QoL was correlated to a language delay on comprehension from both self and parent perspectives.^{7,23,24} In the general school-aged populations' lower QoL levels are found in cases of learning disorders, especially in the domains of body image, general well-being, and relationships with family and friends.²⁴

We had three group classifications: normal, moderate, and mild disability, as traditionally seen in the literature, based on data from our FSIQ scores. A threshold ≥ 89 was considered normal, which is a low average.²⁵ Furthermore, for EPT infants, the FSIQ is most often calculated on a dissociated subtest value, which is not necessarily reflective of the child's cognitive function, and thus constitutes a false methodology.^{25,26} Indeed, a child considered "normal" in our study was likely to have impairments such as a dysexecutive syndrome that could disrupt brain function. Since these disorders can alter the QoL, we compared our "normal" study population to the reference population, which resulted in a significantly lowered QoL. A recent study by Korzeniewski et al.²⁷ confirmed that 70% of EPT children with a FSIQ ≥ 85 had social adjustment disorders. The prevalence of this social impairment was four times greater than expected in the general population norms among school-age children, and higher with neuropsychological defects such as language, communication, emotional, and behavioral regulation deficits irrespective of the FSIQ.

The extent of social adaptation is indirectly measured by the QoL evaluation. In fact, QoL measures the individual's health status by means of his basic needs: human warmth, organic, work, and leisure.²⁸

In our study, specific cognitive impairment correlates of the children's lowered QoL in school performance and body image domains reflected the child's academic well-being and was also able to provide useful information about their social competency. It could be argued that their academic difficulties and feelings about their school life became distressing and functioning was

Table 2. QoL data of population considered “normal” (no disability) versus reference population.

	“Normal” population ^a (N = 110) (mean ± SD)	Reference population ^b (expected mean)	Difference between “normal” population and reference population		P value	Effect size ^c
			Mean ± SD	[95% CI]		
VSPA-infant^d						
Vitality	76.50 ± 19.99	82.47	-5.97 ± 19.94	[-9.74 to -2.20]	0.0022	0.29
General well-being ^e	74.02 ± 16.70	78.51	-4.49 ± 16.43	[-7.60 to -1.39]	0.0050	0.27
Relationships with friends	44.00 ± 28.16	59.03	-15.04 ± 28.36	[-20.39 to -9.68]	<0.001	0.53 (1)
Leisure	62.27 ± 19.40	69.69	-7.42 ± 19.03	[-11.02 to -3.82]	<0.001	0.38 (3)
Relationships with family	71.53 ± 20.69	73.19	-1.66 ± 20.73	[-5.58 to 2.26]	0.4029	0.08
School performance	80.34 ± 20.00	82.51	-2.17 ± 19.64	[-5.88 to 1.54]	0.2496	0.11
Body image	76.59 ± 19.18	84.76	-8.17 ± 19.27	[-11.81 to -4.52]	<0.001	0.42 (2)
Global index	69.32 ± 13.08	75.71	-6.39 ± 13.06	[-8.86 to -3.92]	<0.001	0.48
VSPA-parent^d						
Vitality	71.17 ± 15.79	77.61	-6.45 ± 15.48	[-9.39 to -3.51]	<0.001	0.41 (2)
Psychological well-being	70.23 ± 19.17	81.46	-11.24 ± 19.06	[-14.85 to -7.62]	<0.001	0.58 (1)
Relationships with friends	60.65 ± 19.05	64.49	-3.84 ± 19.08	[-7.63 to -0.06]	0.0467	0.2
Leisure	52.16 ± 20.10	57.06	-4.90 ± 19.97	[-8.67 to -1.12]	0.0115	0.24
Relationships with family	76.84 ± 13.59	78.67	-1.83 ± 13.56	[-4.39 to 0.73]	0.1598	0.13
Physical well-being	77.05 ± 15.05	78.73	-1.68 ± 15.07	[-4.53 to 1.16]	0.2437	0.11
Relationships with teacher	74.49 ± 17.58	75.36	-0.87 ± 17.31	[-4.34 to 2.60]	0.6203	0.05
School performance	75.23 ± 17.59	80.19	-4.96 ± 17.25	[-8.25 to -1.67]	0.0035	0.28
Body image	80.80 ± 25.21	88.87	-8.07 ± 25.77	[-12.94 to -3.20]	0.0014	0.31 (3)
General well-being	73.30 ± 14.86	80.26	-6.96 ± 14.78	[-9.75 to -4.17]	<0.001	
Global index	71.13 ± 10.63	76.14	-5.01 ± 10.40	[-7.19 to -2.83]	<0.001	
Kidscreen-infant						
Index	70.13 ± 17.43	76.87	-6.75 ± 17.60	[-10.07 to -3.42]	<0.001	
Kidscreen-parent						
Index	71.82 ± 13.54	71.84	-0.02 ± 13.54	[-2.58 to 2.54]	0.9876	

Numbers 1, 2, and 3 within parentheses are top three of the most decreased QoL domains.

^a“Normal” population (n = 110): no disability, FSQ ≥89.

^bReference data: Samples included children aged 8 to 10 years who responded to the VSP-Ae and Kidscreen QoL questionnaires, as well as their parents who responded to the VSP-Ap and Kidscreen QoL questionnaires. This national, general population, data sampling of ~1000 children provided a baseline comparable to the preterm group studied for the confounding factors of age and gender.

^cEffect size: Rank of decrease in QoL in each domain for the VSP-Ae and VSP-Ap QoL questionnaires (standardized effect size obtained by dividing the mean difference by the standard deviation).

^dVSP-Ae and VSP-Ap: Vécu et Santé Perçue de l’Enfant et de l’Adolescent. QoL questionnaires (children and parent assessments, respectively) whose scores vary between 0 and 100, with higher scores indicating better QoL; Kidscreen-children and Kidscreen-parents: QoL questionnaires (children and parent assessments) whose scores vary between 0 and 100.

^ePsychological and physical well-being dimensions of the VSP-Ap are gathered together under the general well-being dimensions of the VSP-Ae.

negative with lower self-competencies. This finding in EPT children is in keeping with the concept of a “preterm behavioral phenotype,” as reported by Korzeniewski et al. with deficits of multiple developmental systems, including those that influence the development of social abilities.²⁷ A systematic review of 23 studies using an array of instruments (Health related QoL, and so on) showed that children born very preterm have poorer social competencies, emerging early and persisting throughout childhood with correlates that included gestational age, neonatal brain abnormalities, and family socio-economic status.²⁹ Being born preterm affects brain development, which causes reductions in total brain volume, disruptions in specific regional structures,

structural connectome, and functional connectivity, with a neuroinflammation possibly contributing to the disruption of neural development.³⁰ Some are similar to the structural abnormalities associated with visuo-spatial integration delay executive dysfunction and/or language and communication impairment in EPT children, all of which are associated in our study by a lowered QoL in school performances.³¹

Our participating centers annually care for 20% of those EPT children born in France. Our study’s neuropsychological assessment was exhaustive and comprehensive, and the neuropsychological characteristics of our study’s population were similar to the “EXPRESS” study.² We used generic measuring instruments of QoL

Table 3. Association between QoL and FSIQ scores (multiple linear regression models).

FSIQ categories ^a	Subscale of VSPA-e (mean ± SD, R; β standard adjust (β), P value adjust (p))							Kidscreen-children index (mean ± SD or R, P adjust)				
	Vit	GenWB	RFR	LA	RFa	SP	BI		Global index			
Normal	76.5 ± 19.9	74.0 ± 16.7	44.0 ± 28.1	62.2 ± 19.4	71.5 ± 20.6	80.3 ± 20	76.5 ± 19.1	69.3 ± 13.0	70.1 ± 17.4			
Mild disability	78.3 ± 19.9	74.9 ± 18.0	48.3 ± 26.9	68.4 ± 19.9	75.8 ± 18.8	78.7 ± 20.1	76.5 ± 21.5	71.6 ± 12.9	75.2 ± 15.5			
β	0.05	0.05	0.13	0.13	0.13	-0.02	0.05	0.09	0.13			
Moderate disability	72.50 ± 21.7	65.0 ± 21.2	42.4 ± 26.39	55.3 ± 18.5	71.7 ± 17.7	60.5 ± 27.5	66.3 ± 23.0	62.0 ± 13.3	65.5 ± 19.2			
β	-0.16	-0.16	-0.13	-0.13	-0.13	-0.32	-0.15	-0.21	-0.21			
p	0.28	0.03	0.45	0.01	0.37	<0.001	0.050	0.0019	0.0182			
FSIQ (β)	0.08	0.12	-0.01	0.03	0.01	0.3	0.19	0.16	0.1			
p	0.29	0.094	0.89	0.67	0.90	<0.001	0.01	0.03	0.18			
FSIQ categories ^a Subscale of VSPA-p (mean ± SD, R; β standard adjust (β), P value adjust (p))												
FSIQ categories ^a	Subscale of VSPA-p (mean ± SD, R; β standard adjust (β), P value adjust (p))							Kidscreen-parents index (mean ± SD or R, P adjust)				
	Vit	GenWB	RFR	LA	RFa	SP	BI		Global index			
Normal	71.8 ± 16	75.8 ± 17.8	60.3 ± 19.0	52.5 ± 20.9	76.8 ± 13.5	73.6 ± 14.9	80.4 ± 26.0	71.3 ± 19.0	76.6 ± 15.1	74.3 ± 17.5	70.2 ± 10.2	72.24 ± 13.6
Mild disability	69.8 ± 14.4	67.07 ± 15.2	61.4 ± 19.5	55.1 ± 16.5	76.8 ± 12.9	71.8 ± 16.0	83.1 ± 23.7	69.4 ± 18.7	74.8 ± 18.7	74.0 ± 16.2	66.3 ± 10.7	68.9 ± 15.6
β	-0.20	-0.26	-0.11	-0.11	-0.26	-0.11	-0.26	-0.11	-0.11	-0.11	-0.11	-0.20
Moderate disability	65.8 ± 17.0	61.2 ± 22.1	53.06 ± 20.4	50.6 ± 17.2	79.9 ± 15.7	71.0 ± 18.6	69.5 ± 28.9	66.2 ± 25.9	76.6 ± 15.5	73.6 ± 19.4	71.1 ± 10.6	66.5 ± 12.5
β	0.51	0.82	0.38	0.6	0.49	0.16	0.72	0.75	0.68	0.52	0.33	0.33
p	0.18	0.04	0.05	-0.06	-0.07	0.37	0.06	0.01	-0.05	0.13	0.15	0.15
FSIQ (β)	0.03	0.61	0.51	0.5	0.4	<0.001	0.5	0.9	0.52	0.099	0.05	0.05

VSPA-e children's QoL self-evaluation, VSPA-p children's QoL as reported by parents; score ranges from 0 to 100. Subscale index: Vit vitality index, GenWB general well-being global, RFR relationships with friends, LA leisure, RFa relationships with family, SP school performance, BI body image, Psywb psychological well-being, Phywb physical well-being, RT relationships with teacher.

^aFSIQ categories: were defined according to the mean ± SD of the WISC IV: no disability as FSIQ \geq -1 SD, Mild disabilities as FSIQ $<$ -1 SD and \geq -2 SDs. Moderate disability as FSIQ $<$ -2 SDs and \geq -3 SDs. FSIQ categories are categorical variables. The FSIQ score is a quantitative variable. Each QoL sub-score is presented (evaluated either by the children at the top of the table or by the parents at the bottom of the table) according to the FSIQ category variable and according to the FSIQ score in multiple regression. The categorical and quantitative variables influencing the QoL and/or correlated in univariable analysis ($P < 0.2$) entering the model are: gender, multiple pregnancies, the child's trophicity at the time of the assessment, FAS score, mother's and/or father's professional activity, mother's and/or father's educational level, term, and birth weight. The adjusted standardized β (β adjust.) is calculated based on the adjustment variables. The β expresses the increase in quality of life by an increase of one unit of the determinant considered (quantitative variable) or the average difference of QoL between the modalities of the determinant considered (categorical variable). The adjusted standardized β is noted only if: P adjusted $<$ 0.2 (threshold).

Table 4. Correlation between QoL scores and specific cognitive/behavioral impairment: language delay, visual spatial integration defect, executive dysfunction, attention difficulties, or motor dyspraxia (multiple linear regression models).

Neuropsychological disorders ^a		Children: Subscale of VSPA-e (mean ± SD) or R: β standard adjusted (β), P value (p)										Kidscreen-children index (mean ± SD or R)		
		Vit	GenWB	RFr	LA	RFa	SP	BI	Global index					
Language defects														
No		77.1 ± 20.5	73.3 ± 18.4	45.5 ± 28.2	63.7 ± 19.4	72.5 ± 20.3	78.2 ± 22.1	75.8 ± 20.7	69.4 ± 13.3	71.2 ± 17.7				
Yes		73.1 ± 9.1	70.3 ± 7.7	43.1 ± 24.4	59.2 ± 20.9	74.0 ± 17.0	68.9 ± 23.8	70.2 ± 21.2	65.5 ± 13.5	69.3 ± 17.0				
<i>p</i>		0.29	0.45	0.61	0.23	0.85	0.0361	0.12	0.11	0.72				
<i>β</i>							-0.15	-0.10						
Visuo-spatial integration defect														
No		76.5 ± 20.8	73.6 ± 17.4	45.6 ± 27.2	63.1 ± 20.1	72.2 ± 19.9	78.6 ± 20.7	75.520.4	69.3 ± 13.3	71.8 ± 17.3				
Yes		76.5 ± 15.3	68.7 ± 19.0	46.2 ± 29.3	60.3 ± 16.13	77.4 ± 14.9	64.6 ± 26.7	68.8 ± 24.4	66.1 ± 11.6	67.8 ± 16.4				
<i>p</i>		0.78	0.33	0.87	0.44	0.22	0.0018	0.29	0.27	0.11				
<i>β</i>							-0.22							
Executive dysfunction														
No		76.2 ± 18.8	71.7 ± 17.2	45.3 ± 27.1	64.3 ± 19.1	70.7 ± 20.9	79.9 ± 20.3	76.619.8	69.3 ± 12.3	69.9 ± 17.2				
Yes		76.6 ± 21.4	73.9 ± 17.9	45.1 ± 27.7	61.4 ± 20.0	74.4 ± 18.4	73.9 ± 23.3	73.2 ± 21.7	68.4 ± 13.7	72.1 ± 17.2				
<i>p</i>		0.87	0.09	0.89	0.39	0.27	0.13	0.84	0.98	0.48				
<i>β</i>							-0.11							
Attention defect														
No		77.6 ± 18.9	72.6 ± 17.9	47.0 ± 27.2	63.3 ± 19.3	73.1 ± 18.8	76.8 ± 22.6	74.8 ± 21.2	69.3 ± 12.9	71.3 ± 17.1				
Yes		72.0 ± 25.2	72.4 ± 16.1	40.9 ± 27.6	60.0 ± 22.1	76.5 ± 18.5	74.5 ± 20.6	73.3 ± 18.7	67.1 ± 13.9	72.2 ± 17.9				
<i>p</i>		0.17	0.81	0.33	0.37	0.36	0.78	0.85	0.57	0.63				
<i>β</i>														
Motor dyspraxia														
No		76.4 ± 20.5	72.9 ± 17.9	44.3 ± 27.8	63.6 ± 19.7	72.9 ± 19.7	76.6 ± 22.4	75.0 ± 21.3	68.8 ± 13.3	71.2 ± 17.3				
Yes		78.2 ± 14.8	74.1 ± 15.3	53.8 ± 20.3	59.9 ± 17.2	77.1 ± 13.4	77.2 ± 19.3	69.0 ± 16.3	69.9 ± 9.6	69.7 ± 15.2				
<i>p</i>		0.86	0.82	0.15	0.67	0.33	0.81	0.32	0.64	0.63				
Neuropsychological disorders ^a		Parents: Subscale of VSPA-p (mean ± SD) or R: β standard adjusted (β), P value (p)										Kidscreen-parents index (mean ± SD or R)		
		Vit	GenWB	RFr	LA	RFa	SP	BI	Phywb	RT	Global index			
Language defect														
No		71.1 ± 15.4	72.8 ± 15.6	60.6 ± 18.9	53.4 ± 19.2	77.7 ± 13.3	72.5 ± 17.5	81.0 ± 25.6	70.4 ± 19.3	75.8 ± 16.5	74.9 ± 17.4	70.8 ± 0.38	70.9 ± 14.2	
Yes		65.8 ± 16.8	71.8 ± 17.2	53.9 ± 21.5	50.7 ± 18.3	75.5 ± 15.7	62.1 ± 22.0	71.7 ± 27.3	67.3 ± 24.4	77.0 ± 15.2	70.4 ± 17.0	66.0 ± 0.9	60.4 ± 7.10	
<i>p</i>		0.23	0.95	0.25	0.77	0.39	0.0089	0.076	0.55	0.51	0.6	0.078	0.47	
<i>β</i>							-0.2	-0.14						
Visuo-spatial integration defect														
No		70.1 ± 16.0	72.5 ± 15.6	59.5 ± 20.2	52.2 ± 19.3	76.7 ± 13.6	72.1 ± 17.7	79.7 ± 26.3	70.1 ± 19.9	75.6 ± 16.1	73.6 ± 17.4	69.9 ± 10.6	70.52 ± 14.3	
Yes		70.7 ± 15.1	74.3 ± 16.3	58.6 ± 15.7	58.0 ± 12.8	80.0 ± 13.2	58.9 ± 22.0	80.9 ± 24.8	69.7 ± 21.6	80.0 ± 15.0	75.7 ± 17.8	70.3 ± 10.7	67.8 ± 13.1	

Table 4 continued

Neuropsychological disorders ^a		Parents: Subscale of VSPA-p (mean ± SD) or R: β standard adjusted (β), P value (p)										Kidscreen-parents index (mean ± SD or R)
		Vit	GenWB	RFr	LA	RFa	SP	BI	Psywb	Phywb	RT	
<i>p</i>	0.77	0.46	0.86	0.12	0.25	0.011	0.54	0.78	0.16	0.44	0.49	0.55
<i>β</i>				0.12		-0.19			0.11			
Dysexecutive disorders												
No	72.5 ± 15.6	74.7 ± 15.1	62.7 ± 18.5	55.0 ± 20.5	77.2 ± 13.6	76.5 ± 16.9	81.7 ± 23.6	71.9 ± 18.8	78.3 ± 15.3	76.7 ± 16.4	72.5 ± 9.9	72.8 ± 14.3
Yes	68.3 ± 15.7	71.3 ± 15.8	56.8 ± 20.0	51.5 ± 17.7	77.0 ± 13.7	66.0 ± 19.0	77.8 ± 27.7	68.4 ± 21.1	74.7 ± 16.3	71.6 ± 17.7	68.0 ± 10.6	68.2 ± 13.8
<i>p</i>	0.20	0.34	0.26	0.50	0.93	0.059	0.79	0.61	0.18	0.17	0.069	0.14
<i>β</i>	-0.10					-0.22			-0.11		-0.14	-0.11
Attention defect												
No	70.2 ± 16.0	73.4 ± 15.8	60.5 ± 19.1	53.3 ± 18.1	77.0 ± 13.8	71.2 ± 19.6	80.0 ± 26.6	70.7 ± 20.1	76.7 ± 16.4	73.3 ± 17.4	70.3 ± 10.4	70.7 ± 14.1
Yes	69.6 ± 16.0	69.5 ± 15.1	53.0 ± 21.7	50.7 ± 21.6	77.7 ± 13.8	65.2 ± 13.1	75.4 ± 24.3	66.8 ± 20.7	72.9 ± 14.1	77.1 ± 18.4	67.6 ± 11.0	67.6 ± 15.3
<i>p</i>	0.94	0.29	0.10	0.68	0.6	0.20	0.51	0.38	0.31	0.24	0.38	0.33
<i>β</i>			-0.12									
Motor dyspraxia												
No	70.0 ± 16.0	72.8 ± 15.6	59.7 ± 19.5	53.6 ± 19.1	77.2 ± 13.9	70.4 ± 19.3	80.1 ± 26.2	69.4 ± 20.1	77.0 ± 15.86	74.3 ± 17.3	70.2 ± 10.7	70.6 ± 14.4
Yes	73.6 ± 15.0	75.4 ± 15.2	53.9 ± 22.2	48.1 ± 19.3	79.9 ± 9.06	73.8 ± 10.3	73.8 ± 25.2	80.0 ± 18.4	69.7 ± 15.7	68.9 ± 20.1	69.1 ± 9.4	65.9 ± 12.9
<i>p</i>	0.36	0.61	0.48	0.67	0.47	0.55	0.77	0.11	0.16	0.62	0.96	0.35
<i>β</i>									-0.11			

VSPA-e children's QoL self-evaluation, VSPA-p children's QoL as reported by parents: score ranges from 0 to 100. Subscale: *Vit* vitality index, *GenWB* general well-being global, *RFr* relationships with friends, *LA* leisure, *RFa* relationships with family, *SP* school performance, *BI* body image, *Psywb* psychological well-being, *Phywb* physical well-being, *RT* relationships with teacher. Neuropsychological disorders^a: Classification of cognitive disorders according to the DSM IV classification: (1) delay of language if VCI <85 ± 1 SD; (2) Visual spatial integration delay if PRI <85 and Rey figure is ≤10th percentile in copy; (3) Ideomotor dyspraxia if Touwen = complex coordination disorder and ±PRI <85 and/or IVT <85; (4) Dysexecutive disorders if WMI <85 and/or planning <8 and/or fluidity of drawings <8 and/or statue <10th; (5) Attention defect if ±auditory attention <8 and/or visual attention <8) and PSI <85. Results are shown as mean ± standard deviations (SD) of QoL. Each quality of life sub-score ± assessed either by the children at the top of the table or by the parents at the bottom of the table is expressed according to the qualitative variables. These variables are language delay, visual spatial integration delay, dysexecutive disorders, attention defect, and ideomotor dyspraxia. For each variable and for each quality of life sub-score, the same indicators are always presented: average of the QoL/SD/P value of the adjusted β, β expressing the average difference of QoL between the modalities of the considered determinant ± is noted only if: P adjusted <0.2 ± threshold. The adjustment variables chosen for the model are categorical and quantitative variables relevant to the QoL and/or correlated in univariate with P <0.2: gender, multiple pregnancies, FAS score, mother's and/or father's professional activities/educational levels, term and birth weight, and trophicity at the assessment.

Table 5. Correlation of QoL with WMI, mental flexibility, planification, anxiety, and behavior scores in multiple regressions.

Neuropsychological disorders	Children: subscale VSPA-e, R: β standard adjusted (β) and P value adjusted (p)										Kidscreen-children index									
	Vit		GenWB		RFR		LA		RFA		SP		BI		Phywb		RT		Global index	
	β	p	β	p	β	p	β	p	β	p	β	p	β	p	β	p	β	p	β	p
Working memory index	0.02	0.03	-0.13	0.06	0.14	0.27	0.28	0.10	0.08	0.08	0.17	0.08	0.10	0.08	0.08	0.17	0.08	0.17	0.08	0.40
	0.8	0.75	0.37	0.58	0.17	0.020	0.009	0.020	0.40	0.020	0.009	0.020	0.40	0.020	0.009	0.020	0.40	0.020	0.009	0.020
Planification index	-0.08	0.00	-0.09	0.01	0.00	0.01	0.08	0.01	0.10	0.01	0.01	0.08	-0.02	0.01	0.01	0.01	-0.02	0.01	0.01	0.17
	0.24	0.97	0.19	0.86	0.95	0.83	0.24	0.83	0.95	0.83	0.24	0.83	0.95	0.83	0.24	0.83	0.95	0.83	0.24	0.17
Flexibility index	0.03	0.03	0.01	0.06	-0.13	0.11	-0.05	0.01	0.01	0.11	0.11	-0.05	0.01	0.01	0.11	0.11	-0.05	0.01	0.01	-0.05
	0.71	0.70	0.90	0.43	0.076	0.12	0.48	0.12	0.076	0.12	0.48	0.12	0.076	0.12	0.48	0.12	0.076	0.12	0.48	0.51
Anxiety score	-0.20	-0.58	-0.18	-0.19	-0.16	-0.24	-0.61	-0.19	-0.16	-0.24	-0.61	-0.19	-0.16	-0.24	-0.61	-0.19	-0.16	-0.24	-0.61	-0.42
	<0.001	<0.001	0.009	0.007	0.029	<0.001	<0.001	<0.001	0.029	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
Behavior score	-0.30	-0.40	-0.15	-0.35	-0.23	-0.32	-0.29	-0.35	-0.23	-0.32	-0.29	-0.35	-0.23	-0.32	-0.29	-0.35	-0.23	-0.32	-0.29	-0.42
	<0.001	<0.001	0.04	<0.001	0.002	<0.001	<0.001	<0.001	0.002	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001

Neuropsychological disorders	Parents: Subscale of VSPA-p, R: β standard adjusted (β) and P value adjusted (p)										Kidscreen-parents index (β standard and P value adjusted)									
	Vit		GenWB		RFR		LA		RFA		SP		BI		Phywb		RT		Global index	
	β	p	β	p	β	p	β	p	β	p	β	p	β	p	β	p	β	p	β	p
Working memory index	0.00	-0.07	-0.04	-0.04	-0.03	0.23	0.05	0.05	0.05	0.05	-0.05	-0.08	0.00	0.06	0.41	0.06	0.41	0.06	0.41	0.06
	0.95	0.38	0.59	0.64	0.69	0.0031	0.53	0.53	0.0031	0.53	0.53	0.0031	0.53	0.53	0.0031	0.53	0.53	0.0031	0.53	0.41
Planification index	-0.05	-0.07	-0.07	0.02	-0.02	-0.02	0.16	-0.02	0.16	-0.02	-0.09	-0.01	-0.01	-0.01	-0.01	-0.01	-0.01	-0.01	-0.01	0.02
	0.50	0.36	0.38	0.83	0.80	0.77	0.034	0.77	0.034	0.77	0.034	0.77	0.034	0.77	0.034	0.77	0.034	0.77	0.034	0.81
Flexibility index	-0.05	0.09	0.13	0.06	-0.01	0.14	-0.02	0.14	-0.02	0.14	0.09	0.06	0.13	0.05	0.05	0.05	0.05	0.05	0.05	0.05
	0.50	0.27	0.10	0.44	0.91	0.0718	0.77	0.0718	0.77	0.0718	0.27	0.46	0.09	0.09	0.09	0.09	0.09	0.09	0.09	0.54
Anxiety score	-0.28	-0.25	-0.17	-0.06	0.02	-0.30	-0.18	-0.30	-0.18	-0.30	-0.30	-0.09	-0.07	-0.24	0.0021	-0.24	0.0021	-0.24	0.0021	0.0021
	<0.001	0.0014	0.025	0.4542	0.78	<0.001	0.023	<0.001	0.023	<0.001	<0.001	0.28	0.40	<0.001	0.0021	<0.001	0.0021	<0.001	0.0021	0.0021
Behavior score	-0.58	-0.67	-0.67	-0.26	-0.17	-0.43	-0.20	-0.43	-0.20	-0.43	-0.67	-0.44	-0.31	-1.07	<0.001	-1.07	<0.001	-1.07	<0.001	<0.001
	<0.001	<0.001	<0.001	0.0019	0.040	<0.001	0.0159	<0.001	0.0159	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001

VSPA-e children's QoL self-evaluation, VSPA-p children's QoL as reported by parents: score ranges from 0 to 100, NEPSY NeuroPsychological assessment, SDQ Strengths and Difficulties Questionnaire. Subscale index: Vit vitality index, GenWB general well-being global, RFR relationships with friends, LA leisure, RFA relationships with family, SP school performance, BI body image, Phywb psychological well-being, Phywb physical well-being, RT relationships with teacher.

Dysexecutive disorders: WMI by WISC IV, planning index, flexibility index by NEPSY.

SDQ: Score well correlated with Achenbach's Child Behavior Checklist, including 25 items answered by parents. The questionnaire gives a total assessment of the difficulties and defines five subscales composed of five items each: emotional disorders, behavioral disorders, hyperactivity, relational disorders added together to generate a total score of "prosocial" difficulties and behaviors. Categories have been proposed in order to assess whether a child's score is close to average 0-13, slightly above average 14-16, high 17-19, or very high 20-40.

Spielberg index (STA): self-assessment questionnaire containing 40 items to obtain 2 scores (state and trait) ranging from 20 (absence of anxiety) to 80 (high anxiety).

Each quality of life sub-score assessed either by the children at the top of the table or by the parents at the bottom of the table is expressed according to the quantitative variables: WMI, planning index, flexibility index, and anxiety and behavior total score. For each variable and for each quality of life sub-score, the same indicators are always presented, adjusted β , P value of the adjusted β , β expressing the increase in quality of life for an increase of one unit of the considered determinant for quantitative variable. The adjusted β is noted if P value adjusted <0.2 (threshold).

The adjustment variables chosen for the model are relevant categorical and quantitative variables affecting QoL and/or correlated in univariate analysis with P <0.2: gender, multiple pregnancies, FAS score, mother's and/or father's professional activities, mother's and/or father's educational levels, term and birth weight, and tropicity at the adjustment.

with a high validity and reliability: Kidscreen and VSPA, with age-appropriate and intercultural relevant content, and measuring the school-aged children's most meaningful QoL dimensions as recommended by the World Health Organization. Given self-evaluation is not possible in cases of serious sequelae, we did not include any severe disorders since QoL assessments for cerebral palsy already exist.

With a 30% attrition rate, a high number of participants were lost to follow-up for the QoL analysis. Moreover, the cognitive correlates could only be calculated on the population with psychometric assessment, that is, 70% of the included population. To ensure that our population was representative of the target population and to discuss the extrapolation power of the highlighted results, we compared perinatal characteristics, socio-economic status, and QoL results and found no differences. This was a cross-sectional study and temporal relationships between variables could not be established. Our study chose not to establish a specific control group, but rather a reference group representative of French children of the same age in a European sample. Indeed, data collected from a control group of children born at term in each participating center would be a solid complement for our results.

Subclinical developmental health problems such as comprehensive language and visuo-spatial integration delay, and dysexecutive syndrome in EPT children without global deficiency are associated with a lower QoL in their school performance and body image. The spectrum of these sequelae does not differ dramatically from the array of problems found in the general population, with the difference being the disproportionately greater incidence and complexity of dysexecutive disorders, mediating behavioral, learning, and social problems.³² In addition, although studies on parenting sensitivity with preterm children are varied,³³ prematurity may cause long-term challenges for the development of the parent-child relationship that fosters the emotional and behavioral development of the child.³⁴ Finally a recent self-meta-analysis data report in adults born preterm (<1500 g) reveals a characteristic preterm behavioral phenotype that includes a heightened risk for internalizing problems and avoidant personality problems in combination with a lowered risk for externalizing problems.³⁵

Thus, preterm birth constitutes an early vulnerability factor with long-term consequences following the individual into adulthood.³⁶ This calls for increasing attention to be paid from school and health care professionals so as to recognize the preterm behavioral phenotype and the potential need for supportive measures.³⁷ Research on preventive interventions is warranted to investigate if these long-term EPT birth effects can be attenuated. The Development Care Assessment Program continues to make a strong argument for potential social and developmental benefits in neonatal period.³⁸ Early intervention to minimize language impairment and social limitation of children considered at risk such as the "Reach Out and Read" program seems to hold some promise in preschool age.³⁹ Furthermore, EPT children experience executive function problems that impede their scholastic prospects, especially if they are from low socio-economic families. The school-based intervention's effectiveness of programs designed specifically to enhance children's executive functions, and social skills may also serve as an important option going forward at school age.

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AUTHOR CONTRIBUTIONS

C.G. performed the literature search. C.G., P.A. and N.R. conceptualized the study and drafted the study protocol. C.G., B.T., V.B.-M., P.A. and N.R. acquired, analyzed, and

interpreted the data and planned the statistical analyses. C.G., B.T., V.B.-M. and N.R. drafted and revised the manuscript. All authors had full access to the data in the study and take full responsibility for the integrity of the data and the accuracy of the data analysis. All authors have approved the final submitted manuscript and have agreed to be accountable for all aspects of the manuscript.

ADDITIONAL INFORMATION

Competing interests: The authors declare no competing interests.

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The GPQoL Study Group

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