UNIVERSITÉ DE NANTES

_____

FACULTÉ DE MÉDECINE

_____

Année : 2021 N° 2021-224

THÈSE

pour le

DIPLÔME D'ÉTAT DE DOCTEUR EN MÉDECINE

DES de pédiatrie

par

Géraldine APPRIOUAL

_____

Présentée et soutenue publiquement le 20 octobre 2021

_____

Impact du trimestre de naissance sur l'adaptation scolaire à cinq ans des grands prématurés

_____

Président : Madame la Professeure Élise LAUNAY

Directeur de thèse : Monsieur le Professeur Cyril FLAMANT

TABLE DES MATIERES

TABLE DES MATIERES ***2***

REMERCIEMENTS ***3***

INTRODUCTION ***5***

ARTICLE ***7***

ABSTRACT **8**

ABBREVIATIONS **9**

INTRODUCTION **10**

METHODS **12**

Patients and data sources 12

GSA score 12

ASQ 13

Psychometric tests 13

Statistical analysis 14

RESULTS **15**

DISCUSSION **20**

CONCLUSION **23**

CONCLUSION ***26***

REMERCIEMENTS

A Madame la Professeure Élise Launay, pour avoir accepté de présider mon jury de thèse ;

A Monsieur le Professeur Cyril Flamant, pour la direction de mon travail de thèse ainsi que pour ton implication, tes conseils, ta gentillesse, ta patience et ta disponibilité au long de ces années d'internat ;

A Monsieur le Professeur Xavier Durrmeyer, pour avoir accepté de participer à mon jury de thèse, pour ton accueil et celui de toute l'équipe du CHIC lors de mon interCHU. Ce fut un semestre extrêmement formateur et agréable grâce à vous tous ;

A Monsieur le Docteur Jean-Baptiste Müller, merci également d'avoir accepté de participer à mon jury, merci à toi et à tous les médecins du service pour votre bienveillance et votre passion que vous nous transmettez tous les jours ;

A Monsieur le Professeur Jean-Christophe Rozé, pour votre aide précieuse apportée à l'écriture de cet article et notamment pour les séances de statistiques ;

A mes parents, mon frère et ma sœur, pour votre soutien au cours de ces longues études, pour les valeurs que vous m'avez inculquées, et encore aujourd'hui, pour vos encouragements à chaque moment difficile ;

A mes amis landernéens, merci à vous d'être ce que vous êtes, d'avoir toujours été présents pour moi, de m'avoir soutenue pendant toutes ces années d'études et de m'avoir aidée si souvent à décompresser, avec une mention spéciale pour Anne-Gaëlle, qui m'a montré la voie, jusqu'à notre divergence finale, les petits vieux ont bien de la chance de t'avoir. Et à Geoffrey, qui a m'a harcelée avec ses espaces milliers ;

A ma promo d'internat, la meilleure dont j'aurais pu rêver : à Morgane, la première que j'ai rencontrée ici pour tous ces semestres passés ensemble et ces soirées où tu ne me laisses jamais rentrer, à Charlotte, qui est la seule à ne pas se rendre compte qu'elle est exceptionnelle, à Marie-Adé, toujours présente, que ce soit pour boire un verre ou pour soutenir les copines, Lydie et son éternel sourire (et son amour pour les intestins), Lise,

tellement sérieuse mais toujours souriante et attentionnée, grâce à vous ces années resteront parmi les plus belles de ma vie ;

A tous les internes, médecins et infirmiers rencontrés au cours de cet internat, merci d'avoir contribué à ma formation chacun à votre façon, ce sera grâce à vous si un jour j'arrive à ne pas être un trop mauvais docteur. Notamment à Morgane et Mélissa, mes deux nouvelles néonatologues préférées. Mélissa, vivement ces deux années de post-internat (« Quoiqu'il se passe on va bien s'amuser ») ;

INTRODUCTION

La population des grands prématurés est une population particulièrement à risque de troubles neurodéveloppementaux. Alors que le pronostic global de ces enfants a connu une amélioration majeure ces dernières décennies, ils restent pourtant particulièrement vulnérables(1). Les enfants nés prématurés requièrent un suivi particulier après leur sortie d'hôpital et pendant plusieurs années pour évaluer leur développement neurologique. Dans les deux premières années, une évaluation neurologique notamment motrice, est indispensable pour dépister tout déficit sévère, mais reste insuffisante au long terme(2). Un suivi régulier au-delà de deux ans est nécessaire pour identifier d'autres troubles (troubles cognitifs, des apprentissages ou comportementaux)(3) pouvant mener à des difficultés scolaires. Ces troubles du développement psychomoteur sont plus fréquents parmi la population des grands prématurés et risquent de constituer des difficultés à l'entrée à l'école primaire, entre cinq et sept ans.

Plusieurs études ont déjà montré l'impact de nombreux facteurs sur le développement cognitif et les capacités scolaires de l'enfant prématuré, notamment l'âge gestationnel, le poids de naissance, la catégorie socio-professionnelle des parents(4),(5),(6). Cependant, aucune étude française n'a jusqu'ici évalué l'impact du trimestre de naissance sur la réussite scolaire dans une population d'enfants prématurés à l'âge scolaire.

Une précédente étude de cohorte au Royaume-Uni (Odd et al.(7)), incluant 11 990 enfants nés à terme ou prématurés, a mis en évidence une augmentation des difficultés scolaires chez les enfants prématurés par rapport aux enfants nés à terme, ainsi qu'un impact de l'année de scolarisation sur les résultats à des tests standardisés. Ces résultats étaient fortement atténués en excluant de l'analyse les enfants prématurés scolarisés dans la même classe que s'ils étaient nés à terme. Les conclusions de cette étude sont en faveur d'une scolarisation en fonction de la date du terme de la grossesse, et non pas de la date de naissance de l'enfant, donc en fonction de l'âge corrigé.

Alors qu'au Royaume-Uni, tous les enfants ayant quatre ans révolus au premier septembre d'une année sont scolarisés dans la même classe, en France l'école est organisée par année civile. Tous les enfants nés au cours d'une année sont donc scolarisés dans une

même classe. Ainsi une classe regroupe des enfants nés à presque un an d'intervalle les uns des autres, les enfants prématurés nés en fin d'année sont par conséquent susceptibles d'être scolarisés un an plus tôt qu'ils ne l'auraient été s'ils étaient nés à terme. Une étude française à propos d'enfants nés à terme, a évalué l'impact du trimestre de naissance sur la réussite scolaire au début de l'enseignement primaire(8). Des enfants issus de 1 500 écoles françaises ont été inclus à l'entrée en école primaire au cours de l'année 1997. Les performances des enfants étaient évaluées dans différents domaines (parole, écriture, attention, compétences sociales…). Cette étude a établi le trimestre de naissance comme étant le facteur avec le plus d'influence en dehors du milieu social et de la nationalité de l'enfant. Nous avons émis l'hypothèse que ces différences en fonction du trimestre de naissance dans la population des enfants nés à terme seraient bien plus marquées chez les enfants nés grands prématurés, au vu de leur risque déjà plus élevé de difficultés scolaires.

Différents tests standardisés sont disponibles pour évaluer le neurodéveloppement des enfants nés prématurés. Le WPPSI (Wechsler Preschool and Primary Scale of Intelligence)(9) est l'un des outils les plus utilisés à travers le monde pour la mesure du QI (quotient intellectuel). Cette échelle globale de QI est le gold standard pour l'évaluation des fonctions cognitives de l'enfant. Cependant, les enfants prématurés peuvent présenter des difficultés dans des domaines non mesurés par les tests de QI. Il a donc été nécessaire de développer de nouveaux outils pour l'évaluation des enfants prématurés grâce à l'aide de leur entourage, afin de les évaluer dans leur environnement. A cet effet, le score GSA (Global School Adaptation), établi à partir d'un questionnaire rempli par l'instituteur, a été démontré être un outil fiable pour la détection précoce des enfants présentant des difficultés scolaires à risque de compliquer l'apprentissage de la lecture(10). Ce questionnaire, corrélé avec les échelles de QI, est un moyen rapide et fiable d'apprécier les capacités neurodéveloppementales à cinq ans(11) des enfants prématurés.

Le suivi des enfants prématurés est organisé, en France, en réseaux régionaux comprenant un suivi annuel dans l'enfance. La cohorte LIFT (Loire Infant Follow-up Team)(12), est une cohorte française régionale permettant un suivi des enfants jusqu'à leurs sept ans (entrée en école élémentaire). Cette cohorte prospective nous a permis d'évaluer l'impact du trimestre de naissance sur les performances scolaires à cinq ans chez des enfants grands prématurés.

ARTICLE

Birth trimester & school achievement at school age for very preterm infants

Authors : Géraldine Appriou[1], Cyril Flamant[1], Jean-Baptiste Müller[1], Valérie Rouger[2], Géraldine Gascoin[3], Jean-Christophe Rozé[1]

[1] Department of Neonatology, University Hospital of Nantes, Nantes, France.

[2] Réseau "Grandir Ensemble", University Hospital of Nantes, Nantes, France.

[3] Department of Neonatology, Hospital of Angers, Angers, France.

ABSTRACT

Objectives : Very preterm children's school adaptation during the first years is a key of their school achievement. We aimed to study the impact of birth trimester on school achievement at five years in a very preterm population.

Study design: Infants born before 33 weeks and followed in the LIFT cohort (Loire Infant Follow-up Team) were included. School achievement was evaluated by the GSA questionnaire (Global School Adaptation) which includes different developmental domains. This questionnaire was completed by the child's teacher at five years old. A GSA score below 48 is considered as non-optimal, predictive for special educational needs at seven years.

Results : Among the 3 704 children included in the study, 64% had a neurodevelopmental assessment at 5 years. No statistical differences on IQ or ASQ at 5 years were found according to birth trimester ($p = 0.31$ and $p = 0.66$ respectively). Children born in the last trimester had a GSA score significantly below than those born during the first three trimesters ($p < 0.001$). Among the 640 children born in the last trimester, 55.5% had a non-optimal GSA score, as compared with 22.9% among those born in the first trimester (Odds ratio = 4.52 [3.42 – 5.97]).

Conclusion : These results confirm the major impact of birth trimester on school adaptation in the preterm population, unrelated to IQ. Children born preterm during the last trimester suffer from a double disadvantage. School entry according to civil age, without considering the corrected age is associated to early school difficulties.

ABBREVIATIONS

ASQ : Ages and Stages Questionnaire

BPD : Bronchopulmonary Dysplasia

DQ : Development quotient

GSA : Global School Adaptation

IQ : Intelligence Quotient

INTRODUCTION

Very preterm infants are at major risk for adverse neurodevelopmental outcomes. Although prognosis of preterm neonates has increased for the last decades, preterm infants remain a vulnerable population(1). Those children need a specific follow-up after their hospital discharge and during several years to assess their development. At an early stage of two years, a neurological assessment is critical to diagnose any severe disabilities but is ultimately insufficient in the long run(2). A more regular follow-up is required to identify subtle problems as cognitive disorders, learning disabilities and behavioral problems(3) which can lead to scholar difficulties. These neurodevelopmental difficulties are more frequent among very preterm infants' population and may become more acute at the beginning of primary school, i.e between five and seven years of age.

Previous studies have shown that the cognitive development and school abilities in preterm children are associated with several factors, such as gestational age, birth weight and socio-economic status of the family(4),(5),(6). Nevertheless, to the best of our knowledge, no french study has identified the specific impact of birth trimester on cognitive development in the preterm population at school age.

A previous cohort study by Odd et al.(7) in England, enrolling 11 990 children born preterm or full term, has shown preterm infants have more difficulties in primary school than their term peers and that year of schooling impacts outcomes on standardized testing. These results attenuate substantially when restricting to infants who attend school in the same year as if they were born full term. It provides evidence in favor of a school year placement depending on the expected date of delivery instead of date of birth.

While in England, all children aged four on September 1st of a year are enrolled in the same class, in France, school is organized by civil year method. This means that all children born during a same civil year are enrolled in the same class. Thus, a school class brings together children who are born up to almost a year apart and children born preterm can be enrolled a year earlier than they would be if they were born full term. A French study, focused on full term children, has evaluated the impact of birth trimester on school achievement at the beginning of primary school(8). Children from 1 500 French public schools were included in

1997 at the beginning of elementary school. Children's performances were evaluated on various domains (verbal, writing skills, attention, social skills…). It found that birth trimester was the most discriminatory variable after social background and nationality. We hypothesized that these differences according to birth trimester among full term children population might be even more acute in the very preterm infant population, taking account their high risk of school difficulties.

Different formal standardized tests are available to assess the neurodevelopmental outcome of children born preterm. The Wechsler Preschool and Primary Scale of Intelligence (WPPSI)(9) is one of the most widely used psychometric assessment tools for measuring intelligence quotient (IQ). This full-scale IQ test constitutes the gold standard for evaluating children's cognitive function. Nevertheless, preterm infants can present disabilities at school age in multiple domains not assessed with IQ test. Thus, new tools have been developed to evaluate the capacities of children born preterm at school age with the support of people close to them, in order to assess the child in his/her own environment. In this regard, the Global School Adaptation (GSA) score obtained from teacher questionnaires has been established as a reliable tool for the early detection of children with school adaptation difficulties that can result in learning disabilities(10). This GSA questionnaire is an easy and reliable way of assessing neurodevelopmental skills of children born preterm at five years of age, which has been proven to be highly consistent with full-scale IQ scores and learning disabilities(11).

In preterm population, French neonate follow-up is organized in regional networks with annual follow-up. The LIFT cohort (Loire Infant Follow-up Team)(12), is a French regional cohort in which preterm children are followed until the age of seven. This prospective population-based cohort gave us the opportunity to evaluate the impact of birth trimester on school performance at five years of age on a population of very preterm children.

METHODS

Patients and data sources

This study included all surviving children born between March 2003 and December 2011, with a gestational age of less than 33 weeks, who were enrolled in LIFT Cohort.

The LIFT Cohort is a prospective, multicentric cohort(12) that enroll children born in the Pays de la Loire region since 2003. The region comprises 23 maternity units and three neonatal intensive care units. Children are followed until the age of seven with regular consultations (3, 9, 12, 18, and 24 months of corrected age and 3, 4, 5, and 7 years of civil age) to screen children for neurodevelopmental disabilities. Screening includes physical and neurological examination, ASQ at 24 and 36 months, IQ at 5 years for some children in the cohort and GSA at 5 years.

The LIFT cohort is registered with the French data protection authority in clinical research (Commission Nationale de l'Informatique et des Libertés or CNIL, No. 851117). Written consent was obtained from parents before children were included in the cohort.

Perinatal, neonatal and socioeconomic data were prospectively gathered, in particular gestational age, birth weight, antenatal corticosteroids, multiple pregnancy, mode of delivery, intubation at birth, neurological complications, parents' socioeconomic level.

GSA score

The GSA score is an evaluation tool(10), designed to assess children in class by their teacher, on their academic and behavioral skills. The evaluation takes place at the age of 5 +/- 2 months.

It is composed of 20 questions : six questions about linguistic competence, five questions about nonverbal abilities, eight questions about children's behavior in the classroom, and the 20th question is about the teacher's prognosis for future school life (adaptation to upcoming classes). Every question gives 1 to 3 points (higher mark for best result) and the total score is obtained by summing the points. A recent study demonstrated

that a 5 year GSA cut off score at 48 was optimal to detect a need for educational support at 7 years of age(13).

ASQ

The ASQ (Ages and Stages Questionnaire) is a parent-completed test composed of 21 age-specific questions covering the age range 4 to 60 months(14). In the present study, the 24-month and the 60-month questionnaires from the French translation of the second version was used. Each questionnaire includes 30 developmental items divided into five domains of child capacities : communication abilities, gross motor skills, fine motor skills, problem solving abilities and personal-social skills. For each item, three responses are possible depending on whether the child performs the task (10 points for “yes”, 5 points for “sometimes” and 3 points for “not yet”). An overall ASQ score was established with a maximum global ASQ score for 300 points. Two years ASQ score with a cut off value of 220 has been shown to be effective to detect children with DQ (Development Quotient) ≤ 85(15).

Psychometric tests

Neurodevelopmental outcome at 2 years of corrected age according to birth trimester was assessed by the revised Brunet-Lezine test(16). This test is administered by specialized psychologist to assess four domains (movements/posture, coordination, language and socialization) with establishment of a global DQ score (mean and maximum scores are 100 and 140 respectively).

Cognitive assessment of children at 5 years was also evaluated by a LIFT psychologist using the Weschler Preschool and Primary Scale of Intelligence (WPPSI). It concerns a restricted subpopulation of children born in 2003-2004 because this evaluation was possible only during this period. This psychometric test allows calculation of a full-scale IQ, performance IQ and verbal IQ. Mental retardation was defined as an IQ score below 85.

Statistical analysis

Descriptive values were reported as medians and interquartile ranges for continuous variables, and numbers of subjects, frequencies and percentages for categorical variables. First, the neonatal characteristics and neonatal morbidity of the assessed population were compared to those of the non-assessed population, to verify their comparability, with test using means comparisons. Second, Fisher's exact test and Mann-Whitney test were used to assess the eventual effect of birth trimester on IQ, ASQ and GSA scores. A logistic regression was performed to adjust for confounding variables. The level of statistical significance was set at $p < 0.05$ for all analysis performed with two-tailed tests. Analysis were performed with SPSS 17.0.

RESULTS

Of the 3 704 children enrolled in the LIFT Cohort between 2003 and 2011, 2374 (64%) completed GSA score at 5 years (figure 1) and were included in the primary analysis.

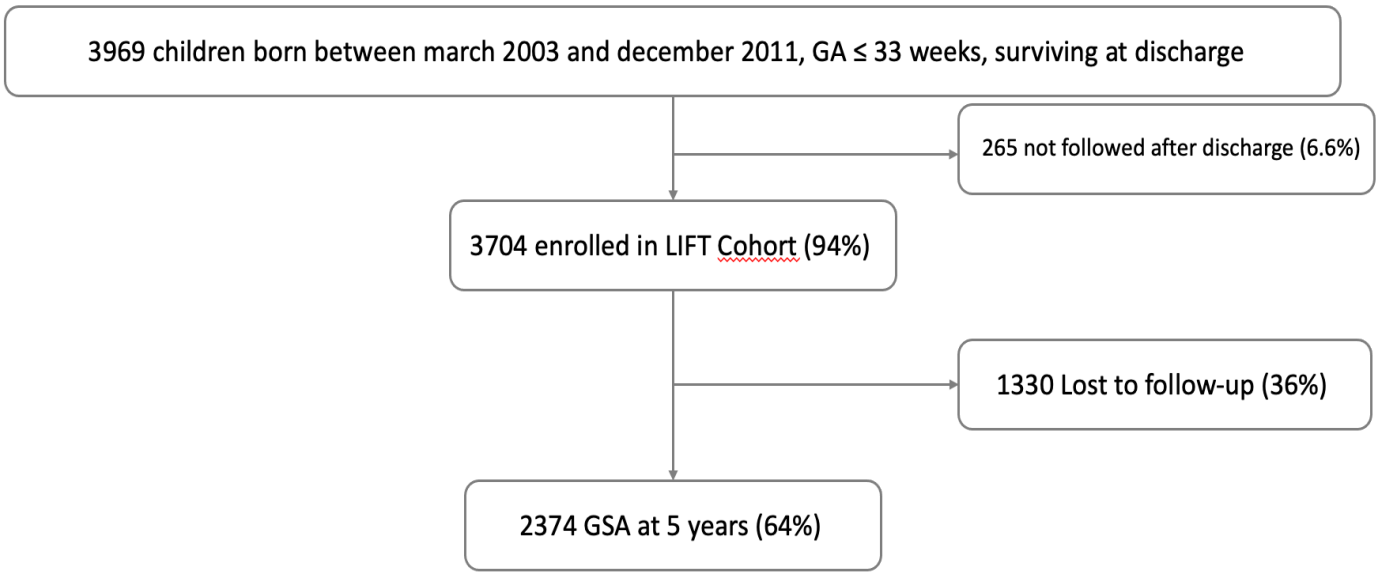

Figure 1 : Flow Chart

The infants assessed in the analysis did not differ significantly from those not assessed (Table 1) on gestational age (p = 0.86), sex (p = 0.162), Apgar score < 7 at M5 (p = 0.611) and birth weight (p = 0.68). Infants included were more likely to be born by cesarean section (70.1% vs 64.1%, p = 0.036), to have received antenatal corticosteroid therapy (63.4% vs 59.7%, p = 0.024) to be born from a multiple pregnancy (36.4% vs 32.3%, p = 0.013), and less likely to be eligible for social security benefits (13.1% vs 19.8%, p = 0.001). Regarding neonatal morbidity (Table 2), children assessed were less at risk for bronchopulmonary dysplasia (p = 0.027), for neurological abnormalities (p = 0.01). No difference was noted regarding the length of hospital stay (58.2 ± 25.9 vs 58.1 ± 25.6 p = 0.92).

	Assessed (N=2374)	Not assessed (N=1330)	p value
Gestational age, weeks	29.9 ± 2.1	29.9 ± 2.1	0.86
24-27	371 (15.6%)	200 (15.0%)	0.74
28-30	868 (36.6%)	477 (35.9%)	
31-32	1135 (47.8%)	653 (49.1%)	
Male sex	1283 (54.0%)	687 (51.7%)	0.162
Antenatal corticosteroid therapy	1506 (63.4%)	794 (59.7%)	0.024
Multiple pregnancy	864 (36.4%)	430 (32.3%)	0.013
Caesarean section	1665 (70.1%)	853 (64.1%)	0.036
Apgar < 7 at M5	173 (7.3%)	103 (7.7%)	0.611
Birth weight, mean (gr)	1358 ± 400	1360 ± 390	0.68
Birth weight Z-score	-0.23 ± 1.0	-0.20 ± 1.0	0.47
Weight Z-score at discharge	-1.08 ± 0.98	-1.06 ± 1.06	0.52
Δ Z-score weight (birth – discharge)	- 0.86 ± 0.82	- 0.84 ± 0.89	0.50
Eligibility for social security benefits*	232 (13.1%)	73 (19.8%)	0.001

* For low income (information for N= 1771 in the assessed group and N=369 in the not assessed group)

Table 1 Neonatal characteristics of the assessed children in comparison with children not assessed at 5 years of age (N=3704)

	Assessed (N=2374)	Not assessed (N=1330)	p value
Respiratory status			0.027
- No oxygenotherapy (O_2) support	1381 (58.2%)	782 (58.8%)	
- O_2 support < 28 days	793 (33.4%)	429 (32.3%)	
- O_2 support > 28 days without BPD*	157 (6.6%)	74 (5.6%)	
- O_2 support > 28 days and BPD*	43 (1.8%)	35 (3.4%)	
Neurologic status			0.01
- No cerebral lesion	2123 (89.4%)	1152 (86.6%)	
- Intraventricular hemorrhage grade 2	148 (6.2%)	72 (5.4%)	
- Intraventricular hemorrhage grade 3-4	36 (1.5%)	22 (1.7%)	
- Periventricular leukomalacia	37 (1.5%)	58 (4.4%)	
- Others	30 (1.2%)	26 (2.0%)	
Patent ductus arteriosus ≠	83 (3.5%)	48 (3.6%)	0.74
Hemodynamic support (inotrope)	144 (6.1%)	94 (7.1%)	0.40
Necrotizing enterocolitis ∅	27	21	
Length of hospital stay (days)	58.2 ± 25.9	58.1 ± 25.6	0.92

*Bronchopulmonary dysplasia assessed at 36 weeks ; ≠ requiring ligation treatment; ∅ Bell classification≥ 2

Table 2 Neonatal morbidity of the assessed children in comparison with children not assessed at 5 years of age (N=3704)

Table 3 shows characteristics of the children included in the analysis according to their birth trimester. There is no significant difference regarding gender, gestational age, birth weight, post-menstrual age at discharge and level of maternal education. Infants born at the end of the year (trimesters 3 and 4) had a significantly higher z-score birth weight ($p = 0.025$). They did not differ on respiratory or neurological comorbidities either.

Regarding ASQ evaluation, no statistical difference was found between children born on different trimesters at 2- ($p = 0.65$), 3- ($p = 0.142$), 4- ($p = 0.334$) and 5-years old ($p = 0.656$). IQ evaluation at 5 years was performed on 248 children born in 2003 and 2004, it did not differ according to birth trimester ($p = 0.310$).

GSA score was evaluated at 5 years of age on 2 374 children born preterm before 33 weeks of gestational age. Girls had significantly higher GSA means (50.4 vs 47.2 $p < 0.01$). Mean GSA score from children born during different trimesters are presented in Table 3. Figure 2 shows the decreasing of GSA score according to birth trimester. GSA score decreased significantly from the beginning to the end of the year ($p < 0.001$). Only 22.9% of children born during the first trimester had a non-optimal GSA score below the cut off value of 48, in comparison with 55.5% of those born during the last trimester ($p < 0.001$).

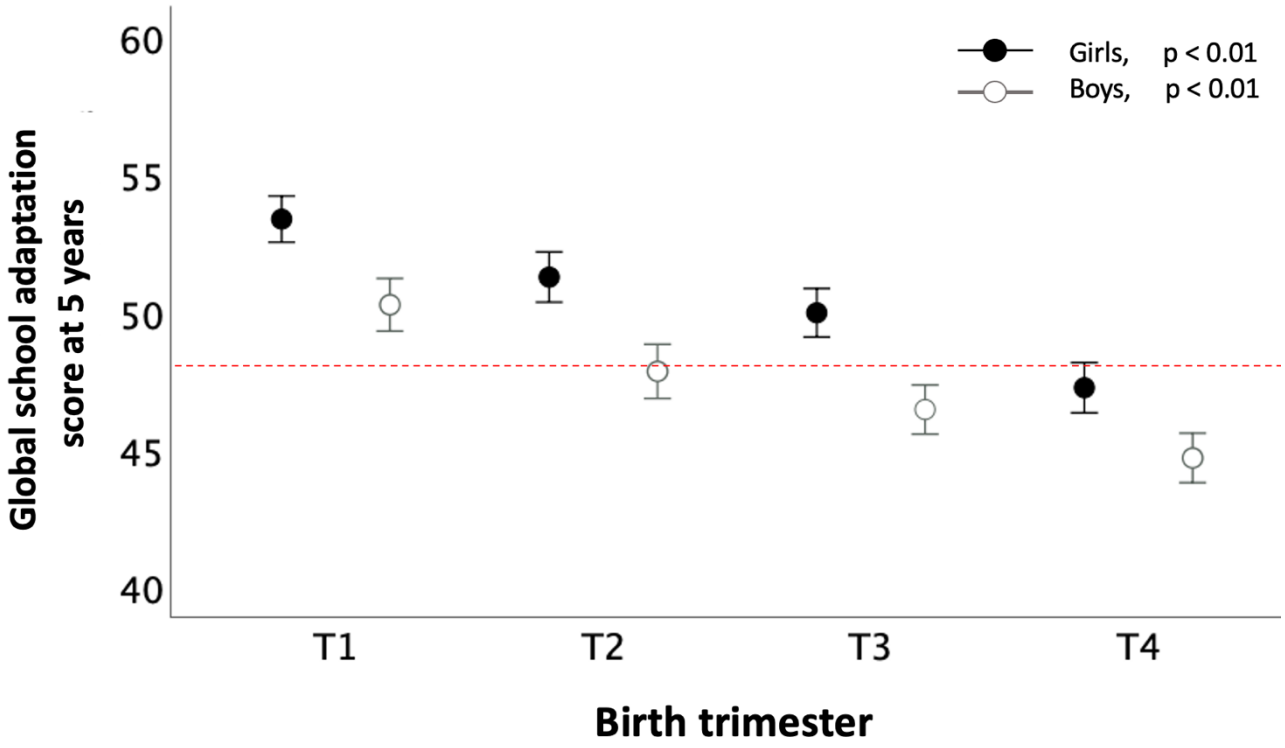

Figure 2 : GSA score according to birth trimester

Logistic regression was performed to adjust GSA scores on gender, gestational age, birth weight z-score, maternal educational level, and eligibility for social security benefits. After adjustment, children born during second trimester (OR = 1.80 [1.35 to 2.39]), third trimester (OR = 2.74 [2.07 to 3.60]) and forth trimester (OR = 4.52 [3.42 to 5.97]) have more risk to have a GSA score below 48 compared to children born on the first trimester.

	Trimester 1 N = 537	Trimester 2 N = 586	Trimester 3 N = 611	Trimester 4 N = 640	p value
Gender (male)	286 (53.3%)	310 (52.9%)	333 (54.5%)	354 (55.3%)	0.824
Gestational age, weeks	29.9 ± 2.1	29.9 ± 2.1	29.8 ± 2.0	29.9 ± 2.1	0.938
Post-menstrual age at discharge	37.7 ± 3.1 (N = 526)	37.8 ± 2.1 (N = 566)	37.9 ± 3.0 (N = 593)	37.6 ± 2.9 (N = 623)	0.437
Birth weight Z-score	-0.26 ± 1.03	-0.32 ± 1.01	-0.17 ± 1.08	-0.17 ± 1.0	0.025
Maternal education					0.540
Information missing	370 (68.9%)	402 (68.6%)	403 (66.0%)	406 (63.4%)	
Less than high school diploma	46 (8.6%)	48 (8.2%)	56 (9.2%)	70 (10.9%)	
High school diploma	71 (13.2%)	90 (15.4%)	95 (15.5%)	99 (15.5%)	
Higher than high school diploma	50 (9.3%)	46 (7.8%)	57 (9.3%)	65 (10.2%)	
Respiratory status					0.384
- No oxygenotherapy (O_2) support	295 (54.9%)	345 (58.9%)	371 (60.7%)	370 (57.8%)	
- O_2 support < 28 days	192 (35.8%)	189 (32.3%)	192 (31.4%)	220 (34.4%)	
- O_2 support > 28 days without BPD*	43 (8.0%)	36 (6.1%)	38 (6.2%)	40 (6.3%)	
- O_2 support > 28 days and BPD*	7 (1.3%)	16 (2.7%)	10 (1.6%)	10 (1.6%)	
No cerebral lesion	477 (88.8%)	522 (89.1%)	553 (90.5%)	571 (89.2%)	0.786
QD at 24 months of corrected age	94.6 ± 17.6 (N = 374)	93.9 ± 17.2 (N = 362)	94.8 ± 17.7 (N = 345)	94.6 ± 17.6 (N = 364)	0.895
ASQ at 24 months of corrected age	242 ± 37 (N = 449)	241 ± 37 (N = 488)	239 ± 40 (N = 530)	239 ± 40 (N = 548)	0.65
ASQ at 5 years	271.9 ± 39 (N = 455)	273 ± 34 (N = 486)	272 ± 30 (N = 508)	270 ± 34 (N = 540)	0.656
Intellectual Quotient at 5 years, mean (N=248)	92.9 ± 18.2 (N = 53)	88.7 ± 15.6 (N = 77)	92.6 ± 13.1 (N = 55)	93.3 ± 18.4 (N = 63)	0.310
Global school adaptation at 5 years, mean	**51.7 ± 7.7**	**49.5 ± 8.5**	**48.1 ± 8.1**	**45.8 ± 8.4**	**<0.001**
GSA < 48 at 5 years	**123 (22.9%)**	**208 (35.5%)**	**255 (41.7%)**	**355 (55.5%)**	**< 0.001**

Table 3 Association between birth trimester and neonatal morbidity, infant neurodevelopment (N = 2374)

DISCUSSION

In this large prospective cohort of French very preterm infants, we have shown that birth trimester specifically impacts school adaptation at 5 years of age. Compared to their peers born early in the year, children born in the last few months showed worse outcome concerning GSA score and a significantly higher risk to have a GSA score under 48 (which has been shown to be predictive of need for educational support at 7 years of age(13)). The influence of birth trimester on school achievement has already been shown on children born full term(8). Considering that birth trimester is the most discriminatory variable on school abilities after socioeconomic background and nationality in the term population, impact of birth trimester seems to extend to preterm infants, and to be even more critical considering they are a population at high risk of school difficulties.

Children born preterm during the last trimester in France are not placed in the same class as if they were born full term. An English cohort of 569 preterm infants(17) evaluated the effect of being schooled a year earlier due to prematurity. It showed that infants enrolled in school a year earlier are 3.5 times more at risk for not achieving a "good level of development" compared to their summer born peers, placed in the correct class. They highlighted the "double disadvantage" suffered by these children, from being born preterm, which is known to be a risk factor for poor school achievement, and from the school placement a year earlier. However, this study included a small group of preterm children, with no limitation to very preterm infants contrary to our study.

Another English cohort, by Odd et al.(7), assessed 11 990 preterm infants at 7 years of age and evaluated the effect of a school year placement according to actual date of birth compared to expected date of delivery, on school performance and need for educational support(7). The study results indicate increased need for educational support in the preterm population and an attenuation of this risk for children who attend school in the same year as if their expected due date was used.

These results are consistent with ours, showing that children born preterm at the end of the year (October, November, December), who are not placed in the school year they would have been if they were born full term, have increased school difficulties. This disadvantage

seems to last throughout all schooling. Odd et al. followed the children from their cohort until 16 years of age, an demonstrated a persistence of the impact of a school entry a year earlier because of prematurity(18).

Multiple studies(19),(20) have focused on preterm infants' school performance, and it has been demonstrated that children born preterm are more at risk for special educational needs and school difficulties. Corrected age is commonly used until 2 years and has no impact on schooling of preterm infants in France. A cohort study by Van Veen et al.(21) including 275 very preterm infants, evaluated the effect of correcting age at 5 years on IQ assessment, using the Weschler Preschool and Primary Scale of Intelligence - Third Edition – Dutch version (WPPSI-III-NL). In their cohort of preterm children, corrected age IQ was significantly higher than civil age IQ, which suggests the use of corrected age after 2 years might be helpful to evaluate very preterm infants' neurodevelopmental skills and decrease school difficulties among this particularly vulnerable population. Using a corrected age for children born preterm would impact the year of school entry and might be useful to reduce impact of birth trimester.

The decreasing of GSA score at 5 years over trimesters in preterm infants' population has no correlation with IQ evaluation in our study. Abilities evaluated by GSA score and IQ differ on multiple aspects. GSA score evaluate academic skills but also behavioral abilities(11). This difference supports the assumption of a difference in children's maturity between those born at the beginning of the year and those born later, with a possible difference concerning behavior and attention abilities.

The strength of this study is the use of a large, population-based cohort and the long-term assessment enabled by the network follow-up.

The infants included in this study were mostly similar on their characteristics throughout different trimesters. One of the few significant differences between them concerned birth weight. Infants born at the end of the year had a higher Z-score than those born during the first civil months. It is already known that low birth weight infants are prone to non-optimal neurodevelopment and school achievement(22),(23).

In our study, the assessed population presents significant differences with the not assessed population. In particular, children in the evaluated group were significantly more

prone to be breastfed at discharge, were less likely to be eligible for social benefits, to suffer from bronchopulmonary dysplasia or neurologic lesions, and were more likely to receive antenatal corticosteroid therapy. Taken together, evaluated children had overall less comorbidities than those not evaluated at 5 years old. Thus, the results of our study concerning school capacities and achievement might be even more significant in a preterm population with more comorbidities, considering children with bronchopulmonary dysplasia or neurological lesions are at higher risk of neurodevelopmental difficulties(24).

Previous studies have assessed in the past the potential benefits of delaying school entry on children born full term(25),(26). To the best of our knowledge, this has not been evaluated on preterm infants. Further studies are required to assess the effect of delaying school entry on school achievement for children born preterm particularly for preterm infants born during the last months of the civil year, an already disadvantaged population among preterm children, who could especially benefit from a school placement depending on their corrected age rather than their chronological age.

CONCLUSION

In the very preterm infants' population, birth trimester is a critical factor influencing school achievement at 5 years of age. GSA score decreases from the beginning to the end of the year and supports the idea of a school year placement based on corrected age rather than chronological age. Further studies about school placement of the children according to their chronological or corrected age are needed to assess the impact of birth trimester and prematurity on school performance and to determine whether a school placement depending on corrected age would avoid or decrease these children's difficulties.

1. Torchin H, Ancel P-Y, Jarreau P-H, Goffinet F. Épidémiologie de la prématurité : prévalence, évolution, devenir des enfants. Journal de Gynécologie Obstétrique et Biologie de la Reproduction. 1 oct 2015;44(8):723-31.

2. Potharst ES, Houtzager BA, Sonderen L van, Tamminga P, Kok JH, Last BF, et al. Prediction of cognitive abilities at the age of 5 years using developmental follow-up assessments at the age of 2 and 3 years in very preterm children. Developmental Medicine & Child Neurology. 2012;54(3):240-6.

3. Salt A, Redshaw M. Neurodevelopmental follow-up after preterm birth: follow up after two years. Early Human Development. 1 mars 2006;82(3):185-97.

4. Charkaluk ML, Truffert P, Marchand-Martin L, Mur S, Kaminski M, Ancel PY, et al. Very preterm children free of disability or delay at age 2: Predictors of schooling at age 8: A population-based longitudinal study. Early Human Development. 1 avr 2011;87(4):297-302.

5. Lin C-Y, Hsu C-H, Chang J-H. Neurodevelopmental outcomes at 2 and 5 years of age in very-low-birth-weight preterm infants born between 2002 and 2009: A prospective cohort study in Taiwan. Pediatrics & Neonatology. févr 2020;61(1):36-44.

6. Linsell L, Malouf R, Morris J, Kurinczuk JJ, Marlow N. Prognostic Factors for Poor Cognitive Development in Children Born Very Preterm or With Very Low Birth Weight: A Systematic Review. JAMA Pediatr. déc 2015;169(12):1162-72.

7. Odd D, Evans D, Emond A. Preterm Birth, Age at School Entry and Educational Performance. Carlo WA, éditeur. PLoS ONE. 16 oct 2013;8(10):e76615.

8. Florin A, Cosnefroy O, Guimard P. Trimestre de naissance et parcours scolaire. European Review of Applied Psychology. 1 déc 2004;54(4):237-46.

9. Freeman S. Wechsler Preschool and Primary Scale of Intelligence. Encyclopedia of Autism Spectrum Disorders. 2013;3351-60.

10. Florin A, Guimard P. Comportements scolaires en maternelle et parcours scolaires ultérieurs. In: Vrignaud P, éditeur. Réussir à l'école : Les effets des dimensions conatives en éducation Personnalité, motivation, estime de soi, compétences sociales [Internet]. Rennes: Presses universitaires de Rennes; 2019 [cité 11 avr 2021]. p. 47-65. (Psychologies). Disponible sur: http://books.openedition.org/pur/60127

11. Boussicault G, Tich SNT, Branger B, Guimard P, Florin A, Rozé J-C, et al. The Global School Adaptation Score: A New Neurodevelopmental Assessment Tool for Very Preterm Children at Five Years of Age. The Journal of Pediatrics. 1 août 2013;163(2):460-464.e3.

12. Hanf M, Nusinovici S, Rouger V, Olivier M, Berlie I, Flamant C, et al. Cohort Profile: Longitudinal study of preterm infants in the Pays de la Loire region of France (LIFT cohort). International Journal of Epidemiology. 1 oct 2017;46(5):1396-1397h.

13. Muller J-B, Olivier M, Guimard P, Gascoin G, Roze J-C, Flamant C, et al. Predictive Value of the Global School Adaptation Questionnaire at 5 Years of Age and Educational Support at 7 Years of Age in Very Preterm Children. The Journal of Pediatrics [Internet]. 29 juin 2020 [cité 3 sept 2020];0(0). Disponible sur: https://www.jpeds.com/article/S0022-3476(20)30768-X/abstract

14. Squires J, Bricker D, Potter L. Revision of a Parent-Completed Developmental Screening Tool: Ages and Stages Questionnaires. J Pediatr Psychol. 1997;22(3):313-28.

15. Flamant C, Branger B, Nguyen The Tich S, de La Rochebrochard E, Savagner C, Berlie I, et al. Parent-Completed Developmental Screening in Premature Children: A Valid Tool for Follow-Up Programs. PLoS One. 26 mai 2011;6(5):e20004.

16. Josse D. Brunet-Lézine révisé - Echelle de développement psychomoteur de la première enfance. Paris: ECPA; 2011.

17. Pettinger KJ, Kelly B, Sheldon TA, Mon-Williams M, Wright J, Hill LJB. Starting school: educational development as a function of age of entry and prematurity. Arch Dis Child. févr 2020;105(2):160-5.

18. Odd D, Evans D, Emond A. Preterm Birth, Age at School Entry and Long Term Educational Achievement. PLoS One [Internet]. 17 mai 2016 [cité 29 juin 2021];11(5). Disponible sur: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4871348/

19. Bhutta AT, Cleves MA, Casey PH, Cradock MM, Anand KJS. Cognitive and Behavioral Outcomes of School-Aged Children Who Were Born PretermA Meta-analysis. JAMA. 14 août 2002;288(6):728-37.

20. MacKay DF, Smith GCS, Dobbie R, Pell JP. Gestational Age at Delivery and Special Educational Need: Retrospective Cohort Study of 407,503 Schoolchildren. PLoS Med [Internet]. 8 juin 2010 [cité 11 avr 2021];7(6). Disponible sur: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2882432/

21. Veen S van, Aarnoudse-Moens CSH, Kaam AH van, Oosterlaan J, Wassenaer-Leemhuis AG van. Consequences of Correcting Intelligence Quotient for Prematurity at Age 5 Years. The Journal of Pediatrics. 1 juin 2016;173:90-5.

22. Conley D, Bennett NG. Is Biology Destiny? Birth Weight and Life Chances. American Sociological Review. 2000;65(3):458-67.

23. Royer H. Separated at Girth: US Twin Estimates of the Effects of Birth Weight. American Economic Journal: Applied Economics. janv 2009;1(1):49-85.

24. Bae SP, Shin SH, Yoon YM, Kim E-K, Kim H-S. Association of Severe Retinopathy of Prematurity and Bronchopulmonary Dysplasia with Adverse Neurodevelopmental Outcomes in Preterm Infants without Severe Brain Injury. Brain Sciences. juin 2021;11(6):699.

25. Martin A. Age Appropriateness and Motivation, Engagement, and Performance in High School: Effects of Age Within Cohort, Grade Retention, and Delayed School Entry. Journal of Educational Psychology. 1 févr 2009;101:101-14.

26. Jaekel J, Strauss VY-C, Johnson S, Gilmore C, Wolke D. Delayed school entry and academic performance: a natural experiment. Developmental Medicine & Child Neurology. 2015;57(7):652-9.

CONCLUSION

Dans cette large cohorte de grands prématurés français, nous avons montré que le trimestre de naissance impactait particulièrement l'adaptation scolaire à 5 ans. Les enfants nés au cours des derniers mois de l'année ont un résultat de score GSA significativement inférieur à ceux nés plus tôt dans l'année et sont plus à risque d'avoir un score inférieur à 48 (seuil établi comme prédictif du besoin d'un soutien scolaire particulier à 7 ans).

Cette différence entre enfants nés aux différents trimestres de l'année a déjà été mise en évidence chez les enfants nés à terme(8), elle semble s'étendre à la population des enfants prématurés, avec un risque d'autant plus important que ces enfants sont déjà particulièrement à risque de difficultés scolaires. Les enfants nés prématurés en fin d'année civile sont scolarisés en fonction de leur date de naissance, plutôt qu'en fonction de leur date de terme. La notion d'âge corrigé, habituellement utilisée pour l'évaluation psychomotrice des enfants prématurés jusqu'à 2 ans, n'est pas considérée à l'âge d'entrée à l'école.

Cette population est donc particulièrement vulnérable quant au risque d'échec scolaire et est également victime d'un phénomène de « double désavantage »(17), dû à la prématurité, en elle-même facteur de risque de troubles des apprentissages, ainsi que par la scolarisation une année plus tôt.

L'adaptation de la scolarisation à ces enfants prématurés pourrait impliquer une prise en compte de leur âge corrigé et à ce titre, une scolarisation en fonction de leur date de terme et non pas de leur date de naissance. Des études sont nécessaires afin d'évaluer l'intérêt d'une entrée dans la scolarité plus adaptée à ces enfants particulièrement fragiles afin de réduire le sur-risque de troubles des apprentissages et d'échec scolaire.

Vu, le Président du Jury,

(tampon et signature)

Professeure Élise LAUNAY

Vu, le Directeur de Thèse,

(tampon et signature)

Professeur Cyril FLAMANT

Vu, le Doyen de la Faculté,

Professeur Pascale JOLLIET

NOM : APPRIOUAL PRENOM : Géraldine

Titre de Thèse : Impact du trimestre de naissance sur l'adaptation scolaire à cinq ans des grands prématurés

---

RESUME

Objectif : La scolarisation des grands prématurés et leur adaptation scolaire durant leurs premières années est un des enjeux majeurs de leur réussite scolaire ultérieure. Nous avons étudié l'impact du trimestre de naissance sur la réussite scolaire des enfants à 5 ans dans une population de grands prématurés.

Méthode : Les enfants inclus étaient nés prématurés avant 33 semaines d'aménorrhée, suivis au sein de la cohorte LIFT. L'outil d'évaluation de la réussite scolaire était le score GSA (Global School Adaptation), un questionnaire rempli par l'instituteur de l'enfant à 5 ans, l'évaluant par rapport à l'ensemble de la classe dans différents domaines de compétences.

Résultats : 2 374 enfants prématurés ont été inclus dans l'analyse. Parmi eux, les 640 enfants nés au dernier trimestre de l'année avaient un GSA significativement plus bas que ceux nés pendant les premiers trimestres ($p < 0.001$). Ils avaient également un risque supérieur d'avoir un score GSA inférieur au seuil de 48 ($p < 0.001$), prédictif de difficultés scolaires à 7 ans.

Conclusion : Ces résultats confirment le rôle du trimestre de naissance dans la réussite scolaire des enfants prématurés. Leur scolarisation en fonction de la leur date de naissance sans prise en compte de leur particularité peut mener à des difficultés scolaires précoces.

MOTS-CLES

Prématurité ; Neurodéveloppement ; Adaptation scolaire ; Score GSA ; Trimestre de naissance ;