

Monday 11 March 2013

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Interventions and Management

1. Dev Med Child Neurol. 2013 Mar 3. doi: 10.1111/dmcn.12114. [Epub ahead of print]

Development of a generic fidelity measure for rehabilitation intervention research for children with physical disabilities.

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AIM: To increase research rigour and create a plausible way to assess clinical effectiveness, it is necessary to measure the degree to which interventions are delivered as intended (fidelity). Generic fidelity measures enable evaluation of more than one intervention through observation of unique and general characteristics relevant across interventions. This study describes the first generic fidelity measure in paediatrics. **METHOD:** Items were constructed from multiple sources to create a general attributes domain and two paediatric cerebral palsy (CP) intervention-specific domains. After a pre-testing procedure, raters were trained and videos of clinical interventions were rated to test the measure's psychometric properties. **RESULTS:** The Paediatric Rehabilitation Observational measure of Fidelity (PROF) consisted of 30 items. Six raters were trained on the PROF and rated 25 videos. Internal consistency (α) and interrater reliability (IRR) for the frequency scale showed the following results: context therapy: $\alpha=0.71$, IRR=0.75; child therapy: $\alpha=0.85$, IRR=0.87; and general attributes; $\alpha=0.78$, IRR=0.82. Quality scale scores across domains demonstrated internal consistency greater than 0.80 and interrater reliability of less than 0.40. Pearson's correlations ($r=-0.71$, $p<0.001$) and analyses of variance ($p=0.01$) validated that each intervention domain was an independent construct. **INTERPRETATION:** The PROF is reliable and valid for evaluating interventions used for children with CP. Future studies may use the measure's framework, general attributes domain, and procedures to test the psychometric properties of other interventions.

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[PMID: 23452179](https://pubmed.ncbi.nlm.nih.gov/23452179/) [PubMed - as supplied by publisher]

2. Cir Cir. 2013 Jan;81(1):14-20.**Spatial-temporal analysis and clinical findings of gait. Comparison of two modalities of treatment in children with cerebral palsy -spastic hemiplegia. Preliminary report [Article in Spanish]**

Arellano-Martínez IT, Rodríguez-Reyes G, Quiñones-Uriostegui I, Arellano-Saldaña ME.

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introduction: Cerebral palsy is the most common cause of disability among children. Parent's main concerns are the acquisition and improvement of gait. The aim of this study was to compare long term results of the effect of two modalities of gait training. Methods: Quantitative measurement of gait and clinical assessment of the gross motor function classification system and Modified Ashworth Scale were performed in 14 patients with Cerebral palsy - spastic hemiplegia and randomizedly assigned into two groups of treatment: the first one using a driven gait orthosis (Lokomat®) and the second a gait training a long a rail inside a hydrotherapy tank. Measurements and assessments, above described, were performed immediately and one year after the treatment concluded. Results: Significant change was observed in the gross motor function classification system from II to I among children ($p=0.042$) and a positive correlation between the shape functional of the march and the gross motor function classification system ($r = 0.54$, $p = 0.042$). Patients on the Lokomat® training improved on gait symmetry over patients on the conventional therapy ($p = 0.05$). A year after, this intervention showed tendency to kept the gait patterns only on patients treated with the Lokomat® Conclusion: Benefit obtained with either modality was evident for both groups. However, residual effects observed on the Lokomat group, either in clinical assessment or gait parameters, were more promising than in the conventional therapy. Due to the size of the sample used in this study the results are not conclusive and more research must be done on this subject in long term time horizon.

[PMID: 23461916](#) [PubMed - in process]

3. Clin Orthop Relat Res. 2013 Mar 6. [Epub ahead of print]**The Influence of Botulinum Toxin A Injections into the Calf Muscles on Genu Recurvatum in Children With Cerebral Palsy.**

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BACKGROUND: With cerebral palsy (CP), an equinus deformity may lead to genu recurvatum. Botulinum toxin A (BtA) injection into the calf muscles is a well-accepted treatment for dynamic equinus deformity. QUESTIONS/PURPOSES: The purpose of this study was to determine whether BtA injections into the calf muscles to decrease equinus would decrease coexisting genu recurvatum in children with diplegic CP. METHODS: In a retrospective study, 13 children (mean age, 5 years) with spastic diplegic CP showing equinus and coexisting primary genu recurvatum, who were treated with BtA injections into the calf muscles, were included. Evaluations were done before and 6 and 18 weeks after intervention using three-dimensional gait analysis and clinical examinations according to a standardized protocol. Basic statistical analyses (power analysis, ANOVA) were performed to compare genu recurvatum before treatment and at 6 and 18 weeks after injection with BtA. RESULTS: During stance phase, maximum ankle dorsiflexion was increased substantially from $-3.0^\circ \pm 14.3^\circ$ before to $6.2^\circ \pm 14.2^\circ$ 6 weeks after the injections. Despite this, with the numbers available, the amount of recurvatum in stance did not improve with treatment at either 6 or 18 weeks. There was significant improvement of knee hyperextension during stance phase of 6.2° between baseline and 18 weeks after BtA injection, but a genu recurvatum was still present in most patients. CONCLUSIONS: Despite improvement of ankle dorsiflexion after injection with BtA, genu recurvatum did not show relevant improvement at 6 or 18 weeks after injection with the numbers available. Because knee hyperextension remained in most patients, other factors leading to genu recurvatum should be taken into consideration. In addition, a botulinum toxin-induced weakness of the gastrocnemius may explain why recurvatum gait was not significantly reduced.

LEVEL OF EVIDENCE: Level IV, therapeutic study. See Guidelines for Authors for a complete description of levels of evidence.

[PMID: 23463290](#) [PubMed - as supplied by publisher]

4. Gait Posture. 2013 Feb 28. pii: S0966-6362(13)00037-4. doi: 10.1016/j.gaitpost.2013.01.014. [Epub ahead of print]

Explaining the variability improvements in gait quality as a result of single event multi-level surgery in cerebral palsy.

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PURPOSE: This is a study of all children with spastic diplegic cerebral palsy (Gross Motor Classification System levels II and III) who had single event multi-level surgery (SEMLS) at a single tertiary referral hospital between 1995 and 2008 to identify factors predicting improvement in gait quality as quantified by the gait profile score (GPS). 9 factors (5 dichotomous and 4 continuous, including preoperative GPS) that might be expected to predict outcomes were identified and univariate and multivariable analysis used to explore how these affected outcomes. **SCOPE:** Data from 121 children were included. The mean improvement in GPS of 4.3° was 2.7 times the minimal clinically important difference. Univariate analysis suggested that preoperative GPS is a very strong predictor of improvement in GPS ($p < 10^{-5}$) and when this is considered as a covariate only GMFCS level ($p = 10^{-5}$) and having had previous surgery ($p = 0.026$) were found to be statistically significant predictors of GPS improvement ($p < 0.05$). Children of GMFCS level II improved on average by 2° more than those of level III once differences in preoperative GPS had been accounted for. **CONCLUSION:** Children with the most abnormal gait patterns preoperatively, and hence those with the most potential to improve are those that improve the most and surgery has clearly been beneficial. Over a quarter of children show changes in GPS which were less than the MCID. The majority of these were those with the least abnormal gait patterns preoperatively and further research is required to establish whether and how such children benefit from SEMLS.

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[PMID: 23454043](#) [PubMed - as supplied by publisher]

5. Res Dev Disabil. 2013 Mar 2;34(5):1367-1375. doi: 10.1016/j.ridd.2013.01.034. [Epub ahead of print]

Assessment of postural control in children with cerebral palsy: A review.

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This paper aimed to review studies that assessed postural control (PC) in children with cerebral palsy (CP) and describe the methods used to investigate postural control in this population. It also intended to describe the performance of children with CP in postural control. An extensive database search was performed using the keywords: postural control, cerebral palsy, children, balance and functionality. A total of 1065 papers were identified and 25 met the inclusion criteria. The survey showed that PC is widely studied in children with CP, with reliable methods. The link between postural control and functionality was also evident. However, a lack of studies was observed assessing postural control in these children by means of scales and functional tests, as well as exploring postural control during daily functional activities. Thus research addressing these issues can be a promising field for further research on postural control.

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[PMID: 23466474](#) [PubMed - as supplied by publisher]

6. *Lancet*. 2013 Feb 16;381(9866):515-7. doi: 10.1016/S0140-6736(12)62164-3. Epub 2012 Dec 17.

Brain-machine interface: closer to therapeutic reality?

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Comment on: High-performance neuroprosthetic control by an individual with tetraplegia. [*Lancet*. 2013]

[PMID: 23253622](#) [PubMed - indexed for MEDLINE]

7. *Top Spinal Cord Inj Rehabil*. 2012 Summer;18(3):264-272.

Effects of Concurrent Respiratory Resistance Training on Health-Related Quality of Life in Wheelchair Rugby Athletes: A Pilot Study.

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PURPOSE: To compare the effects of 9 weeks of training with a concurrent flow resistance (CFR) device versus a concurrent pressure threshold resistance (CPTR) device on health-related quality of life (HRQoL) in wheelchair rugby (WR) athletes. **METHOD:** Twenty-four male WR athletes (22 with tetraplegia, 1 with a spastic cerebral palsy, and 1 with congenital upper and lower limb deformities) were matched by lesion level, completeness of injury, and rugby classification prior to being randomly assigned to 1 of 3 groups: (1) CPTR (n=8), (2) CFR (n=8), or (3) controls (CON, n=8). Pre/post testing included assessment of HRQoL as measured by the Short-Form Health Survey Version 2.0 (SF-36v2). Manufacturer protocol guidelines for the CFR and CPTR groups were followed for breathing exercises. **RESULTS:** Sixteen participants completed the study (CPTR=4, CFR=5, CON=7). The Mann-Whitney U rank order revealed significantly greater reductions in bodily pain ($P = .038$) and improvements in vitality ($P = .028$) for CFR versus CON. **CONCLUSION:** Results from this study suggest that training with a CFR device improves some aspects of HRQoL (eg, vitality and bodily pain) in WR athletes. Further research with a larger sample size is needed to examine the impact of these devices on improving HRQoL for wheelchair athletes.

[PMID: 23459144](#) [PubMed - as supplied by publisher] [PMCID: PMC3584774](#)

8. *West Afr J Med*. 2012 Sep-Oct;31(4):219-23.

A Comparative Assessment of Motor Function using the Expanded and Revised Gross Motor Function Classification System and the Manual Ability Classification System in the same Children with Cerebral Palsy in Shika, Zaria, Northwestern Nigeria.

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BACKGROUND: Assessment of motor function in children with Cerebral Palsy (CP) is vital to the identification and management of their mobility needs. **OBJECTIVE:** To compare the Expanded and Revised Gross Motor Function Classification System (GMFCS-E&R) and Manual Ability Classification System (MACS) in the assessment of motor function in children with CP. **METHODS:** A review of motor activity in children with CP documented at the Departments of Paediatrics and Physiotherapy, Ahmadu Bello University Teaching Hospital, Shika, Zaria, between January 2005 and December 2009. **RESULTS:** A total of 28 children (16M: 12 F, 1.3:1) with an age range of 4 to 12 years (mean 6.2 ± 2.4 years) were studied. Birth asphyxia (46.43%) and Spastic Hemiplegia (71.43%) were the main identified predisposing factor and clinical type of CP respectively. The GMFCS-E&R identified 13 (46.43%) children with higher levels (I & II) of gross motor function against 4 (14.29%) children identified in the MACS higher levels ($p=0.02$). Also 6 (21.43%) of the children were identified as being in the GMFCS-E&R lower levels (IV & V) against 16 (57.14%) in MACS lower levels ($p=0.00$). The difference in the number of children identified as being in

level III for GMFCS-E&R 9 (32.14%) and MACS 8 (28.57%) was not significant ($p=0.77$). Overall correlation between GMFCS-E&R and MACS levels was poor using Kappa statistics ($Kappa=0.00$). **CONCLUSION:** The GMFCS-E&R and MACS significantly identified higher and lower levels of motor functions respectively in the same children. The disparity underscores the complexity in assessing the motor function of children with CP.

[PMID: 23468021](#) [PubMed - in process]

9. Childs Nerv Syst. 2013 Mar 6. [Epub ahead of print]

Dose-dependent relapse of hiatus hernia after administration of intrathecal baclofen treatment-a rare complication.

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INTRODUCTION: Intrathecal baclofen treatment (ITB) is widely used in children with cerebral palsy. Although this treatment effectively reduces spasticity, diverse side effects are reported. **CASE REPORT:** We report about a boy with severe asphyxia-induced encephalopathy with bilateral cerebral palsy. After starting the intrathecal baclofen treatment, he episodically showed symptoms of severe gastroesophageal reflux with pale skin color, vomiting, massive drooling, acid regurgitation, and reduced well-being. An open ventral semifundoplication was done some years ago to treat a gastroesophageal reflux. These symptomatic episodes occurred strongly dose-dependent and were not observed during the short test procedure. **CONCLUSION:** For the first time, a strong dose-dependent treatment with ITB was documented as a cause for the above episodes and relapsing re-herniations.

[PMID: 23463127](#) [PubMed - as supplied by publisher]

10. J Clin Nurs. 2013 Mar 6. doi: 10.1111/jocn.12124. [Epub ahead of print]

Quality of life and mental health among parents of children with cerebral palsy: the influence of self-efficacy and coping strategies.

Guillamón N, Nieto R, Pousada M, Redolar D, Muñoz E, Hernández E, Boixadós M, Gómez-Zúñiga B.

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AIMS AND OBJECTIVES: To explore the quality of life and mental health of caregivers of children with cerebral palsy and to examine the impact of self-efficacy and coping strategies on these outcomes. **BACKGROUND:** Few studies analyse the impact of caring for a child with cerebral palsy on the caregivers' quality of life besides mental health. Also, less attention has been paid to the influence of caregiver's personal resources like self-efficacy or coping strategies on how they adjust to the child's illness and the care situation. **DESIGN:** Cross-section correlational design. **METHODS:** Sixty two parents of children with cerebral palsy completed measures to assess the quality of life (i.e. physical, environmental and social relationships), mental health (i.e. general mental health, depression and anxiety), self-efficacy and coping strategies. **RESULTS:** Parents of children with cerebral palsy had, in general terms, low levels of quality of life and mental health. Self-efficacy was related to most of the outcomes, whereas any of the coping strategies assessed was significantly related to the outcomes. **CONCLUSIONS:** Quality of life and mental health can be affected in caregivers of children with CP. Personal resources like self-efficacy also need attention as they can help in the understanding of the differences in these outcomes and the design of effective interventions. **RELEVANCE OF CLINICAL PRACTICE:** Self-efficacy should be a key element in interventions addressed to parents of children with CP to elicit a process of empowerment that can improve the well-being of the family as a whole.

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[PMID: 23461414](#) [PubMed - as supplied by publisher]

11. Acta Med Iran. 2012 Dec;50(12):819-21.**Depression in parents of children with cerebral palsy in Bosnia and Herzegovina.**

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The aim of the research is to examine depression in parents of children with cerebral palsy, with hypothesis to have more depressive symptom among mothers of children with cerebral palsy. The sample of examinees (between 23 and 62 age) was used in this research. The first subsample of examinees (N=23) was made of mothers (average 33 ± 5.83) of children with cerebral palsy. The second subsample of examinees (N=12) was made of fathers of children with cerebral palsy (average 38 ± 9.8). The third subsample of examinees (N=16) represented the control group, and it was made of mothers of children without disorders (average 38 ± 6.57). For the purpose of quantitative measurement of depression, the Zung self-evaluated method for depression was applied. All data research were processed by parametric and nonparametric statistics. The frequencies and percents were also calculated, and Kruskal-Valis single-factor analysis of variants was applied for checking the hypothesis. According to the results of this research, it was concluded that there was no statistically significant difference in the evaluation of depression between mothers and fathers of children with cerebral palsy, as well as there is no statistically significant difference in relation to mothers of children without disorders.

[PMID: 23456524](#) [PubMed - in process]

12. J Child Neurol. 2013 Mar 1. [Epub ahead of print]**Can Global Positioning Systems Quantify Participation in Cerebral Palsy?**

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This study examined whether motor-related participation could be assessed by global positioning systems in individuals with cerebral palsy. Global positioning systems monitoring devices were given to 2 adolescent girls (14-year-old with diplegic cerebral palsy and her 15-year-old healthy sister). Outcome measures were traveling distances, time spent outdoors, and Children's Assessment of Participation and Enjoyment questionnaires. Global positioning systems documented that the girl with cerebral palsy did not visit nearby friends, spent less time outdoors and traveled shorter distances than her sister ($P = .02$). Participation questionnaire corroborated that the girl with cerebral palsy performed most activities at home alone. Lower outdoor activity of the girl with cerebral palsy measured by a global positioning system was 29% to 53% of that of her sibling similar to participation questionnaires (44%). Global positioning devices objectively documented low outdoor activity in an adolescent with cerebral palsy compared to her sibling reflecting participation reported by validated questionnaires. Global positioning systems can potentially quantify certain aspects of participation.

[PMID: 23456536](#) [PubMed - as supplied by publisher]

Prevention and Cure

13. Am J Obstet Gynecol. 2013 Mar 1. pii: S0002-9378(13)00244-5. doi: 10.1016/j.ajog.2013.02.049. [Epub ahead of print]

Glial Fibrillary Acidic Protein as a Biomarker for Periventricular White Matter Injury.

Stewart A, Tekes A, Huisman TA, Jennings JM, Allen MC, Northington FJ, Everett AD, Graham EM.

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OBJECTIVE: Periventricular white matter injury (PWMI), a precursor of cerebral palsy, is traditionally not diagnosed until 6 weeks of life by head ultrasound. We sought to determine if early neonatal glial fibrillary acidic protein (GFAP) levels could identify PWMI in low birth weight (< 2500 grams) infants. **STUDY DESIGN:** Each case with PWMI on head ultrasound at 6 weeks from 4/09-4/11 was matched by gestational age and mode of delivery to 2 subsequent neonates with a normal head ultrasound. GFAP was measured in cord blood at birth, at neonatal intensive care unit (NICU) admission, and daily on days 1-4 of life. **RESULTS:** During this 2 year period, 21 cases with PWMI with gestational age 27.4±3.3 weeks were compared to 42 controls. The incidence of cesarean delivery was 61.9% in both groups. GFAP was not significantly different in cord blood or at NICU admission, but was significantly elevated on day 1 (median, 5%-95%; 0, 0-0.98 ng/mL cases; 0,0-0.06 ng/mL controls, P=0.03), day 2 (0, 0-1.21 ng/mL; 0, 0-0.05 ng/mL; P=0.02), day 3 (0.05, 0-0.33 ng/mL; 0, 0-0.04 ng/mL, P=0.004) and day 4 (0.02, 0-1.03 ng/mL; 0, 0-0.05 ng/mL, P<0.001). The odds of developing PWMI significantly increased with increasing levels of GFAP from day 1 to day 4 of life adjusting for preeclampsia, antenatal steroid administration and neonatal chronic lung disease. **CONCLUSION:** The ability to predict PWMI with a blood test for GFAP shortly after birth opens the possibility for rapid identification of infants for early intervention and provides a benchmark for qualifying new therapies to improve neurodevelopmental outcomes.

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[PMID: 23467054](#) [PubMed - as supplied by publisher]

14. Eur J Med Genet. 2013 Feb 27. pii: S1769-7212(13)00059-1. doi: 10.1016/j.ejmg.2013.02.006. [Epub ahead of print]

Familial KANK1 deletion that does not follow expected imprinting pattern.

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Deletion of the KANK1 gene (also called ANKRD15), located at chromosome position 9p24.3, has been associated with neurodevelopmental disease including congenital cerebral palsy, hypotonia, quadriplegia, and intellectual disability in a four-generation family. The inheritance pattern in this family was suggested to be maternal imprinting, as all affected individuals inherited the deletion from their fathers and monoallelic protein expression was observed. We present a family in which the proband's phenotype, including autism spectrum disorder, motor delay, and intellectual disability, is consistent with this previous report of KANK1 deletions. However, a paternally inherited deletion in the proband's unaffected sibling did not support maternal imprinting. This family raises consideration of further complexity of the KANK1 locus, including variable expressivity, incomplete penetrance, and the additive effects of additional genomic variants or the potential benign nature of inherited copy number variations (CNVs). However, when considered with the previous publication, our case also suggests that KANK1 may be subject to random monoallelic expression as a possible mode of inheritance. It is also important to consider that KANK1 has two alternately spliced transcripts, A and B. These have differential tissue expression and thus potentially differential clinical significance. Based upon cases in the literature, the present case, and information in the Database of Genomic Variants, it is possible that only aberrations of variant A contribute to neurodevelopmental disease. The familial deletion in this present case does not support maternal imprinting as an inheritance pattern.

We suggest that other inheritance patterns and caveats should be considered when evaluating KANK1 deletions, which may become increasingly recognized through whole genome microarray testing, whole genome sequencing, and whole exome sequencing techniques. Familial KANK1 deletion that does not follow expected imprinting pattern.

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[PMID: 23454270](#) [PubMed - as supplied by publisher]

15. *J Obstet Gynaecol Can.* 2013 Mar;**35(3):258-62.**

Fetal asphyxia: a case study of translational research.

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Translational research is a high priority for the Canadian Institutes of Health Research and the National Institutes of Health in the United States. The history of the significance of fetal asphyxia as a cause of brain damage and cerebral palsy reflects the challenge for translational research. An antepartum and intrapartum cause of cerebral palsy was proposed in the 19th century. Our current understanding that fetal asphyxia beyond a certain threshold will cause brain damage is built on the foundation of laboratory studies conducted over the last 50 years. However, many questions remain to be answered. Clinical studies have confirmed a similar response of the human fetus to fetal asphyxia in vivo. Translation of this knowledge into patient care during the intrapartum period has been achieved to some degree. The emphasis on translational research relates to the political, public, and professional desire to improve patient care. The challenges for translational research have been highlighted in recent publications and are evident in fetal asphyxia. The goals of translational research will only be achieved with a continuing commitment to both laboratory and clinical research.

[PMID: 23470114](#) [PubMed - in process]

16. *JAMA Pediatr.* 2013 Mar 4;**1-9.** doi: [10.1001/jamapediatrics.2013.866](#). [Epub ahead of print]

Neurodevelopmental Outcomes of Extremely Low-Gestational-Age Neonates With Low-Grade Periventricular-Intraventricular Hemorrhage.

Payne AH, Hintz SR, Hibbs AM, Walsh MC, Vohr BR, Bann CM, Wilson-Costello DE; for the Eunice Kennedy Shriver National Institute of Child Health and Human Development Neonatal Research Network.

IMPORTANCE: Low-grade periventricular-intraventricular hemorrhage is a common neurologic morbidity among extremely low-gestational-age neonates, yet the outcomes associated with this morbidity are not fully understood. In a contemporary multicenter cohort, we evaluated the impact of such hemorrhages on early (18-22 month) neurodevelopmental outcomes of extremely premature infants. **OBJECTIVE** To compare neurodevelopmental outcomes at 18 to 22 months' corrected age for extremely low-gestational-age infants with low-grade (grade 1 or 2) periventricular-intraventricular hemorrhage with those of infants with either no hemorrhage or severe (grade 3 or 4) hemorrhage demonstrated on cranial ultrasonography. **DESIGN** Longitudinal observational study. **SETTING:** Sixteen centers of the Eunice Kennedy Shriver National Institute of Child Health and Human Development Neonatal Research Network. **PARTICIPANTS:** A total of 1472 infants born at less than 27 weeks' gestational age between January 1, 2006, and December 31, 2008, with ultrasonography results within the first 28 days of life and surviving to 18 to 22 months with complete follow-up assessments were eligible. **MAIN EXPOSURE** Low-grade periventricular-intraventricular hemorrhage. **MAIN OUTCOME MEASURES** Outcomes included cerebral palsy; gross motor functional limitation; cognitive and language scores according to the Bayley Scales of Infant Development, 3rd Edition; and composite measures of neurodevelopmental impairment. Regression modeling evaluated the association of hemorrhage severity with adverse outcomes while controlling for potentially confounding variables and center differences. **RESULTS:** Low-grade hemorrhage was not associated with significant differences in unadjusted or adjusted risk of any adverse neurodevelopmental outcome compared with infants without hemorrhage. Compared with low-grade hemorrhage, severe hemorrhage was associated with decreased adjusted continuous cognitive (β , -3.91 [95% CI, -6.41 to -1.42]) and language (β , -3.19 [-6.19 to -0.19])

scores as well as increased odds of each adjusted categorical outcome except severe cognitive impairment (odds ratio [OR], 1.46 [0.74 to 2.88]) and mild language impairment (OR, 1.35 [0.88 to 2.06]). **CONCLUSIONS AND RELEVANCE:** At 18 to 22 months, the neurodevelopmental outcomes of extremely low-gestational-age infants with low-grade periventricular-intraventricular hemorrhage are not significantly different from those without hemorrhage. Additional study at school age and beyond would be informative.

[PMID: 23460139](#) [PubMed - as supplied by publisher]

17. Neurosci Bull. 2013 Feb 28. [Epub ahead of print]

Vulnerability of premyelinating oligodendrocytes to white matter damage in neonatal brain injury.

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Premature birth is a significant economic and public health burden, and its incidence is rising. Periventricular leukomalacia (PVL) is the predominant form of brain injury in premature infants and the leading cause of cerebral palsy. PVL is characterized by selective white-matter damage with prominent oligodendroglial injury. The maturation-dependent vulnerability of developing and premyelinating oligodendrocytes to excitotoxic, oxidative, and inflammatory forms of injury is a major factor in the pathogenesis of PVL. Recent studies using mouse models of PVL reveal that synapses between axons and developing oligodendrocytes are quickly and profoundly damaged in immature white matter. Axon-glia synapses are highly vulnerable to white-matter injury in the developing brain, and the loss of synapses between axons and premyelinating oligodendrocytes occurs before any cellular loss in the immature white matter. Microglial activation and astrogliosis play important roles in triggering white-matter injury. Impairment of white-matter development and function in the neonatal period contributes critically to functional and behavioral deficits. Preservation of the integrity of the white matter is likely key in the treatment of PVL and subsequent neurological consequences and disabilities.

[PMID: 23456565](#) [PubMed - as supplied by publisher]

18. PLoS One. 2013;8(2):e57552. doi: 10.1371/journal.pone.0057552. Epub 2013 Feb 27.

Risk of Cerebral Palsy and Childhood Epilepsy Related to Infections before or during Pregnancy.

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BACKGROUND AND AIM: Maternal infections pregnancy have been associated with several neurological disorders in the offspring. However, given the lack of specificity for both the exposures and the outcomes, other factors related to infection such as impaired maternal immune function may be involved in the causal pathway. If impaired maternal immune function plays a role, we would expect infection pregnancy to be associated with these neurological outcomes. **METHODS AND PRINCIPAL FINDINGS:** The study population included all first-born singletons in Denmark between January 1 1982 and December 31 2004. We identified women who had hospital-recorded infections within the 5 year period pregnancy, and women who had hospital-recorded infections pregnancy. We grouped infections into either infections of the genitourinary system, or any other infections. Cox models were used to estimate adjusted hazard ratios (aHRs) with 95% confidence interval (CI). Maternal infection of the genitourinary system pregnancy was associated with an increased risk of cerebral palsy (aHR=?1.63, 95% CI: 1.34-1.98) and epilepsy (aHR=?1.27, 95% CI: 1.13-1.42) in the children, compared to children of women without infections pregnancy. Among women without hospital-recorded infections pregnancy, maternal infection pregnancy was associated with an increased risk of epilepsy (aHR=?1.35, 95% CI: 1.21-1.50 for infections of the genitourinary system, and HR=?1.12, 95% CI: 1.03-1.22 for any other infections) and a slightly higher risk of cerebral palsy (aHR=?1.20, 95% CI: 0.96-1.49 for infections of the genitourinary system, and HR=?1.23, 95% CI: 1.06-1.43 for any other infections) in the children, compared to children of women without infections (and) pregnancy. **CONCLUSIONS:** These findings indicate that the maternal immune system, maternal infections, or factors related to maternal immune function play a role in the observed associations between maternal infections

pregnancy and cerebral diseases in the offspring.

[PMID: 23460873](#) [PubMed - in process] PMID: PMC3583873

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