



Monday 7 February 2011

This free weekly bulletin lists the latest research on cerebral palsy (CP), as indexed in the NCBI, PubMed (Medline) and Entrez (GenBank) databases. These articles were identified by a search using the key term "cerebral palsy".

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Interventions

1. *Dev Med Child Neurol.* 2011 Mar;**53(3):280**. doi: [10.1111/j.1469-8749.2010.03916.x](https://doi.org/10.1111/j.1469-8749.2010.03916.x).

Does physiotherapeutic intervention affect motor outcome in high-risk infants? An approach combining a randomized controlled trial and process evaluation

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Aim. The aim of this study was to examine the effects of intervention in infants at risk of developmental disorders on motor outcome, as measured by the Infant Motor Profile (IMP) and using the combined approach of a randomized controlled trial and process evaluation. **Method.** At a corrected age of 3 months, 46 infants (20 males, 26 females) recruited from the neonatal intensive care unit at the University Medical Centre Groningen (median birth-weight 1210g, range 585-4750g; median gestational age 30wks, range 25-40wks) were included on the basis of definitely abnormal general movements. Exclusion criteria were severe congenital disorders and insufficient understanding of the Dutch language. The infants were assigned to either the family-centred COPing with and CARing for Infants with Special Needs (COPCA) intervention group (n=21; 9 males, 12 females) or the traditional infant physiotherapy (TIP) intervention group (n=25; 11 males, 14 females) for a period of 3 months. Three infants assigned to the TIP group (one male, two females) did not receive physiotherapy. IMP scores were measured by blinded assessors at 3, 4, 5, 6, and 18 months. At each age, the infants were neurologically examined. Physiotherapeutic sessions at 4 and 6 months were videotaped. Quantified physiotherapeutic actions were correlated with IMP scores at 6 and 18 months. **Results.** The IMP scores of both the COPCA and TIP groups before, during, and after the intervention did not differ. Some physiotherapeutic actions were associated with IMP outcomes; the associations differed for infants who developed cerebral palsy (n=10) and those who did not (n=33). **Interpretation.** At randomized controlled trial level, the scores of both the TIP and COPCA groups did not differ in effect on motor outcome, as measured with the IMP. The analysis of physiotherapeutic actions revealed associations between these actions and IMP outcomes. However, the small sample size of this study precludes pertinent conclusions.

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PMID: 21291467 [PubMed - in process]

2. Curr Opin Psychiatry. 2011 Mar;24(2):168-72.**Internet-delivered treatment to promote health.**

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PURPOSE OF REVIEW: The aim of this paper is to provide an updated review of recent controlled trials of Internet interventions for health conditions and how the Internet is used to promote health. **RECENT FINDINGS:** We identified 18 published trials including studies on diabetes, cancer, pain conditions, obesity, irritable bowel syndrome, stress management, hypertension, metabolic syndrome, cerebral palsy, infertility, HIV infection, and fruit/vegetable consumption. Of the 18 trials, one-third targeted children and adolescents. Two cancer studies investigated the role of peer support in an online environment that failed to result in any major improvements. Overall, several trials did not result in any substantial significant improvements, but there are exceptions, such as treatment of irritable bowel syndrome, headache, and chronic pain. Although a few of the reviewed studies had sufficient sample sizes, the majority were small and underpowered. In particular, this was the case for the studies on children and adolescents. **SUMMARY:** This review suggests that Internet interventions hold some promise as a complement to other treatments such as cognitive behavior therapy. The benefits from participating in online peer support groups are not clear. Although studies on children and adolescents have emerged, there is a lack of studies on older adults with health problems.

PMID: 21285706 [PubMed - in process]

3. Dev Med Child Neurol. 2011 Mar;53(3):210-6. doi: 10.1111/j.1469-8749.2010.03890.x.**Effects of leg muscle botulinum toxin A injections on walking in children with spasticity-related cerebral palsy: a systematic review.**

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Department of Epidemiology, Caphri Research Institute, Maastricht University, Maastricht, The Netherlands Scientific Institute for the Quality of Healthcare, Radboud University Medical Centre, Nijmegen, The Netherlands.

Aim. To assess treatment effects of botulinum toxin type A (BoNT-A) on walking of children with leg spasticity due to cerebral palsy (CP) compared with usual care. **Method.** We systematically searched the databases CINAHL, Cochrane, PEDro, EMBASE, and PubMed from July 1993 until July 2009 and additionally screened reference lists. Randomized controlled trials assessing functional outcomes on walking of children with CP were included. The intervention had to contain BoNT-A into the lower limb and be compared with usual care. The methodological quality and clinical relevance were independently assessed by two of the authors (UCR, CHGB). If statistical pooling was not feasible, we performed a best-evidence synthesis. **Results.** Eight trials were included. Trials comparing BoNT-A plus usual care or physiotherapy versus usual care or physiotherapy alone showed moderate evidence for functional outcomes at 2 to 6, 12, and 24 weeks follow-up in favour of BoNT-A. Studies comparing BoNT-A versus casting showed strong evidence for no difference in effects between these interventions. A limitation of our review was the exclusion of studies not published in English, Dutch, or German. The heterogeneity of the included studies, especially for outcome measures and follow-up assessments, prompted us to refrain from statistical pooling, which might also be considered a limitation. **Interpretation.** The use of BoNT-A with usual care or physiotherapy seems to improve walking of children with CP, but results should be appraised carefully owing to the limited quality of included trials.

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PMID: 21291464 [PubMed - in process]

4. IEEE Trans Neural Syst Rehabil Eng. 2011 Jan 28. [Epub ahead of print]**Point-and-Click Cursor Control With an Intracortical Neural Interface System in Humans With Tetraplegia.**

Simeral J, Hochberg L, Donoghue J, Friehs G, Black M.

We present a point-and-click intracortical neural interface system (NIS) that enables humans with tetraplegia to volitionally move a 2D computer cursor in any desired direction on a computer screen, hold it still, and click on the area of interest. This direct brain-computer interface extracts both discrete (click) and continuous (cursor velocity) signals from a single small population of neurons in human motor cortex. A key component of this system is a multi-state probabilistic decoding algorithm that simultaneously decodes neural spiking activity of a small population of neurons and outputs either a click signal or the velocity of the cursor. The algorithm combines a linear classifier, which determines whether the user is intending to click or move the cursor, with a Kalman filter that translates the neural population activity into cursor velocity. We present a paradigm for training the multi-state decoding algorithm using neural activity observed during imagined actions. Two human participants with tetraplegia (paralysis of the four limbs) performed a closed-loop radial target acquisition task using the point-and-click NIS over multiple sessions. We quantified point-and-click performance using various human-computer interaction measurements for pointing devices. We found that participants could control the cursor motion and click on specified targets with a small error rate (< 3% in one participant). This study suggests that signals from a small ensemble of motor cortical neurons (~40) can be used for natural point-and-click 2D cursor control of a personal computer.

PMID: 21278024 [PubMed - as supplied by publisher]

5. J Biomech. 2011 Jan 31. [Epub ahead of print]**Design and validation of surface-marker clusters for the quantification of joint rotations in general movements in early infancy.**

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Lack of complexity in general movements in early infancy is an important marker of potential motor disorders of neurological origin, such as cerebral palsy. Quantitative approaches to characterising this complexity are hampered by experimental difficulties in recording from infants in their first few months of life. The aim of this study was to design and validate bespoke surface-marker clusters to facilitate data acquisition and enable full quantification of joint rotations. The clusters were validated by recording the controlled movements of a soft-body dummy doll simultaneously with an optical (Qualisys) and inertial (XSens) motion capture system. The angles estimated from the optical system were compared with those measured by the inertial system. We demonstrate that the surface-marker based approach compares well with the use of an inertial system to obtain "direct" readings of the rotations whilst alleviating the issues associated with the use of an optical motion capture system. We briefly report use of this technique in 1-5 month old infants. By enabling full quantification of joint rotation, use of the custom made markers could pave the way for early diagnosis of movement disorders.

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PMID: 21288525 [PubMed - as supplied by publisher]

6. Arch Pediatr. 2010 Sep;17(9):1368-72. Epub 2010 Aug 14.**Toe walker [Article in French]**

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Toe walking is a frequent situation for a clinic in pediatric orthopedic. It is, in most cases, an idiopathic trouble. Neurologic examination is very important to recognize spastic diplegia or neuromuscular disease. A contracture of the triceps can occur and will require a specific treatment from physiotherapy to surgery. A psychological approach is sometimes necessary.

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PMID: 20709510 [PubMed - indexed for MEDLINE]

7. Acta Med Iran. 2010 Jul-Aug;48(4):250-4.

Depression in mothers of children with cerebral palsy and its relation to severity and type of cerebral palsy.

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Children with cerebral palsy (CP) suffer from several problems, so the family especially the mothers undertake a lot of social and emotional difficulties. The purpose of this study was to determine the severity of depression in mothers of children with CP in comparison with mothers who have normal children and its relation to the type of CP and severity of the disability. During this descriptive-analytic study, 43 mothers who had younger than 8 year-old children with CP under rehabilitation services in SABA clinic, related to the University of Social Welfare and Rehabilitation Sciences (USWR), Tehran, Iran, were selected as the case group by simple sampling. A data registration form and the Beck Depression Inventory II were completed by them. The type of CP and the severity of disability were determined by a pediatrician and an occupational therapist respectively, using the Gross Motor Function Classification System (GMFCS). Seventy-seven mothers of normal children, serving as the control group for comparing with case group, filled in the same questionnaires. There were significant differences in the mean depression scores ($P=0.003$) between the two groups. Having a child with CP also increases the risk of developing depression in mothers as much as 2.26 times ($OR=2.26$). There were no statistically significant differences in depression scores and the severity of disability and also among the five types of CP. It seems that having a child with CP is probably associated with higher prevalence and severity of depression in mothers. So treatment or prevention of depression in mothers of children with CP is highly recommended for improving the rehabilitation process and achieve better results in these children.

PMID: 21279939 [PubMed - in process]

Epidemiology / Aetiology / Diagnosis & Early Treatment

8. Acta Obstet Gynecol Scand. 2011 Jan;90(1):83-91. doi: 10.1111/j.1600-0412.2010.01022.x. Epub 2010 Nov 26.

Induction of labor and cerebral palsy: a population-based study in Norway.

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Objective. To investigate the association between labor induction and later development of cerebral palsy (CP). Design. Registry-based cohort study. Setting. Perinatal data on all children born in Norway 1996-1998 were ob-

tained from the Medical Birth Registry of Norway (MBRN). Neurodevelopmental data were collected from the Norwegian Cerebral Palsy Registry (CPRN). Population. A total of 176,591 children surviving the neonatal period. Of 373 children with CP, detailed data were available on 241. Methods. Unadjusted and adjusted odds ratios (OR) with 95% confidence intervals (CI) were calculated as estimates of the relative risk that a child with CP was born after labor induction. Main outcome measures. Total CP and spastic CP subtypes. Results. Bilateral cerebral palsy was more frequently observed after induced labor (OR: 3.1; 95% CI 2.1-4.5). For children born at term the association between bilateral CP and labor induction was stronger (OR: 4.4; 95% CI 2.3-8.6). The association persisted after adjustment for maternal disease, gestational age, standard deviation score for birthweight (z-score) and prelabor rupture of membranes (PROM) (adjusted OR: 3.7; 95%CI 1.8-7.5). Among children with CP born at term, four-limb involvement (quadriplegia) was significantly more frequent after induced (45.5%) compared with non-induced labor (8.0%). There was no significant association between labor induction and unilateral CP subtype or CP in preterm born children. Conclusions. In this study population, we found that labor induction at term was associated with excess risk of bilateral spastic CP and in particular CP with four-limb involvement.

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PMID: 21275920 [PubMed - as supplied by publisher]

9. Acta Obstet Gynecol Scand. 2011 Jan;90(1):4-5. doi: 10.1111/j.1600-0412.2010.01052.x.

Cerebral palsy and induction of labor.

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PMID: 21275909 [PubMed - in process]

10. Clin Obstet Gynecol. 2011 Mar;54(1):74-82.

Labor and fetal heart rate decelerations: relation to fetal metabolic acidosis.

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Although intrauterine fetal compromise during labor accounts for a small proportion of cerebral palsy cases, fetal hypoxic-ischemic encephalopathy remains an important and sometimes preventable etiology. This paper reviews the mechanisms regulating fetal heart rate responses, pathogenesis of fetal metabolic acidosis, and thresholds for metabolic acidosis associated with hypoxic-ischemic encephalopathy. The knowledge of normal changes in fetal metabolic acidosis during labor together with changes in association with fetal heart rate decelerations, can aid in the interpretation and management of fetal heart rate tracings.

PMID: 21278504 [PubMed - in process]

11. Dev Med Child Neurol. 2011 Mar;53(3):226-232. doi: 10.1111/j.1469-8749.2010.03810.x.

Should children with cerebral palsy and normal imaging undergo testing for inherited metabolic disorders?

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bourne, Victoria, Australia. Department of Developmental Medicine, Royal Children's Hospital, Melbourne, Victoria, Australia.

Aim. For the 9% to 16% of children with cerebral palsy (CP) who have normal brain imaging, further testing for metabolic and/or genetic conditions has been recommended. This study aimed to identify a cohort of children with CP with normal magnetic resonance imaging (MRI), clinically review and describe the cases, and assess the value of testing for inherited metabolic disorders in these children. **Method.** Children with congenital CP born from 1999 to 2005 were selected from a population register. Normal MRI reports were identified and the scans reassessed. Children whose scans were performed before 18 months were excluded, as were children with spastic CP (Gross Motor Function Classification System [GMFCS] level I). The remainder were reviewed clinically and offered investigations. **Results.** Of 730 children identified, 515 had available imaging and 54 were confirmed as normal. Cases with non-spastic CP and those with milder clinical severity were more likely to have normal imaging. Twenty-three children (17 males, six females; mean age 6y 11mo, SD 1y 10mo, range 3y 0mo to 10y 0mo) were reviewed clinically and offered investigations. Twelve children had spasticity (11 with diplegia, one quadriplegia), three had dyskinesia, five ataxia, and three hypotonia. Two children functioned in GMFCS level I, 11 in level II, seven in level III and three in level IV. Four children with spasticity had unusual features. No alternative diagnoses were made. **Interpretation.** Although important to consider in individual cases, comprehensive metabolic testing failed to clarify the aetiology of CP further in this large cohort of children with normal MRIs, even those with atypical features.

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12. Dev Med Child Neurol. 2011 Mar;53(3):217-225. doi: 10.1111/j.1469-8749.2010.03884.x.

The association of genetic polymorphisms with cerebral palsy: a meta-analysis.

Wu D, Zou YF, Xu XY, Feng XL, Yang L, Zhang GC, Bu XS, Tang JL.

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Aim: The aim of our meta-analysis was to summarize quantitatively the association of genetic polymorphisms with cerebral palsy (CP). **Method.** We identified 16 studies on the association of genetic polymorphisms with CP in PubMed, Elsevier Science Direct, Chinese Biomedical Literature Database, Chinese National Knowledge Infrastructure, and Wanfang. Eleven of these studies (involving a total of 2533 cases and 4432 controls) were used in the current meta-analysis. A study was included if (1) it was published up to September 2010 and (2) it was a case-control study. We excluded one study of family members because the analysis was based on linkage considerations. Meta odds ratios and 95% confidence intervals based on fixed-effects models or random-effects models were dependent on Cochran's Q statistic. We examined the relationship between alleles, as well as genotypes and susceptibility to CP. **Results.** Meta-analysis was performed for 17 genetic polymorphisms: apolipoprotein E (e2,e3,e4), methylenetetrahydrofolate reductase (MTHFR) (rs1801133), coagulation factor II (rs1799963), coagulation factor V (rs6025), coagulation factor VII (rs5742910/rs6046), interleukin-6 (IL-6) (rs1800795), endothelial nitric oxide (rs1800779/rs1799983/rs3918226), fibrinogen β -polypeptide (rs1800790), plasminogen activator inhibitor 1 (rs1799768/rs7242), TNF- β lymphotoxin a precursor (rs1041981), adducin 1 (a) (rs4961), ADRB2 (rs1042714), and tumour necrosis factor a (rs1800629). We found a significant association between CP and IL-6 (rs1800795) [C vs G: odds ratio (OR) 1.79, 95% confidence interval (CI) 1.44-2.22, $p < 0.001$; CC+GC vs GG: OR 1.72, 95% CI 1.29-2.29, $p = 0.002$; CC vs GG+GC: OR 2.17, 95% CI 1.52-3.09, $p < 0.001$], but no other genetic polymorphisms. **Interpretation.** This meta-analysis demonstrated that CP is associated with the genetic polymorphism IL-6 (rs1800795).

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13. Dev Med Child Neurol. 2011 Mar;53(3):199-200. doi: 10.1111/j.1469-8749.2010.03855.x. Epub 2010 Dec 17.

Distribution of motor types in cerebral palsy: how do registry data compare?

Yeargin-Allsopp M.

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PMID: 21291462 [PubMed - in process]

14. Dev Med Child Neurol. 2011 Mar;53(3):198-9. doi: 10.1111/j.1469-8749.2010.03885.x.

Metabolic testing in children with cerebral palsy: less doing and more thinking?

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PMID: 21291460 [PubMed - in process]

15. Eur J Paediatr Neurol. 2011 Jan 31. [Epub ahead of print]

Is there an increased risk for drug treated attention deficit/hyperactivity disorder in children born after in vitro fertilization?

Källén AJ, Finnström OO, Lindam AP, Nilsson EM, Nygren KG, Otterblad Olausson PM.

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BACKGROUND: There is mounting evidence that children born after in vitro fertilization (IVF) run an increased risk of neurological complications and notably cerebral palsy. Whether developmental disturbances occur more often than expected is debated. **AIM:** To investigate the risk for ADHD in children conceived after IVF. **METHODS:** Children conceived after IVF and born between 1982 and 2005 were identified from all IVF clinics in Sweden. Children who developed attention deficit/hyperactivity disorder (ADHD) were identified with the use of a register over all prescribed drugs in Sweden, using prescriptions for methylphenidate or atomoxetine as indicators of ADHD. Maternal and neonatal characteristics were obtained by linkage with the Medical Birth Register and relevant confounders were adjusted for using Mantel-Haenszel procedures. We studied 28 158 children born after IVF and compared them with 2 417 886 children in the population. **RESULTS:** After adjustment for year of birth, maternal age, parity, smoking, BMI, and maternal education and after exclusion of women who did not cohabit, a weak but statistically significant association was found with an odds ratio=1.18, 95% confidence interval 1.03-1.36. The effect was stronger in girls (OR=1.40) than boys (OR=1.11) but this difference could be random. After adjustment for length of involuntary childlessness, the OR decreased slightly and lost statistical significance. **CONCLUSIONS:** The study suggests a weak association between IVF and drug treated ADHD.

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16. J Pediatr. 2011 Feb;158(2 Suppl):e51-4.

Hypoxic-ischemic encephalopathy: challenges in outcome and prediction.

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The outcomes of hypoxic-ischemic encephalopathy vary between death and intact survival. The spectrum of long-

term morbidity in survivors ranges from mild motor and cognitive deficits to cerebral palsy and severe cognitive deficits. Our literature review reinforces the notion that the spectrum of hypoxic-ischemic encephalopathy outcomes represents a continuum, which has important implications for the prediction of outcome and the indications for intervention. We summarize predictive criteria at 3 time points: the first 6 hours of life, 6-72 hours of life, and at hospital discharge. In this era of neuroprotection, predictive models that aid therapeutic decision making, including the withdrawal of support, need to be revised.

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PMID: 21238707 [PubMed - in process]

17. J Physiol. 2011 Feb 1;589(Pt 3):559-73. Epub 2010 Nov 22.

Morphological and electrical properties of oligodendrocytes in the white matter of the corpus callosum and cerebellum.

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Non-technical summary In the central nervous system, electrical signals passing along nerve cells are speeded by cells called oligodendrocytes, which wrap the nerve cells with a fatty layer called myelin. This layer is important for rapid information processing, and is often lost in disease, causing mental or physical impairment in multiple sclerosis, stroke, cerebral palsy and spinal cord injury. The myelin speeds the information flow in two ways, by decreasing the capacitance of the nerve cell and by increasing its membrane resistance, but little is known about the latter aspect of myelin function. By recording electrically from oligodendrocytes and imaging their morphology we characterised the geometry and, for the first time, the resistance of myelin in the brain. This revealed differences between the properties of oligodendrocytes in two brain areas and established that the resistance of myelin is sufficiently high to prevent significant slowing of the nerve electrical signal by current leakage through the myelin.

PMID: 21098009 [PubMed - in process]

18. Med Sci Monit. 2011 Feb 1;17(2):CR110-116.

A descriptive analysis of abnormal postural patterns in children with hemiplegic cerebral palsy.

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Background: Functional classification systems generally divide children with cerebral palsy (CP) into mild, moderate, and severe types. Although depending on functional limitations, they do not seem to evaluate abnormal postural patterns in standing. Since the most asymmetrical patterns can be observed in hemiplegia, the goal of this case series study was to provide their objective analysis and to establish any potential clinical value for evaluation and management of CP. Material/Methods: A group of 36 children (aged 5-10 years) with spastic hemiplegic CP, who could stand and ambulate independently, were selected. The photogrammetric and pedobarographic studies were obtained for the postural analysis in standing. Results: Two different anti- and pro-gravitational postural patterns were identified. They seem not only to affect functional status and rehabilitation potential, but also clinical value for evaluation and management of CP hemiplegia. Conclusions: The importance of strong study design cannot be overemphasized. The 2 different postural patterns indicate dissimilar compensatory tendencies, which may help in prognosis of deformity and functional outcomes of rehabilitation. The use of objective photogrammetric and the pedobarographic studies may also help to develop a more specific therapeutic intervention in order to facilitate the pattern leading towards better outcome (orthosis in the anti-gravitational postural pattern vs focal spasticity management in the pro-gravitational postural pattern).

PMID: 21278687 [PubMed - in process]

19. *Paediatr Perinat Epidemiol.* 2011 Mar;25(2):111-5. doi: 10.1111/j.1365-3016.2010.01175.x. Epub 2010 Dec 9.

Is there a direct effect of pre-eclampsia on cerebral palsy not through preterm birth?

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20. *Paediatr Perinat Epidemiol.* 2011 Mar;25(2):100-10. doi: 10.1111/j.1365-3016.2010.01157.x. Epub 2010 Aug 16.

Uncovering the complex relationship between pre-eclampsia, preterm birth and cerebral palsy.

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Uncovering the complex relationship between pre-eclampsia, preterm birth and cerebral palsy. *Paediatric and Perinatal Epidemiology* 2010. Pre-eclampsia is a leading cause of preterm birth, which is strongly associated with cerebral palsy (CP). However, there is controversy about whether pre-eclampsia is associated with increased risk of CP. We evaluated the association between pre-eclampsia and CP in 122,476 mother-child pairs insured by the South Carolina Medicaid programme, with births between 1996 and 2002. Prenatal billing records were linked to the children's Medicaid billing records after birth until December 2008. The odds of CP were modelled using logistic regression with generalised estimating equations. There were 337 children (0.28%) diagnosed with CP by at least two different health care providers, and 4226 (3.5%) women were diagnosed with pre-eclampsia at least twice during pregnancy. Children whose mothers had pre-eclampsia were almost twice as likely to have CP compared with children of mothers without pre-eclampsia [odds ratio (OR) = 1.94, 95% confidence interval (CI) 1.25, 2.97]. The association was only significant for pre-eclampsia diagnosed prior to 37 weeks' gestation. Full term (gestational age \geq 37 weeks) infants whose mothers were diagnosed with pre-eclampsia prior to 37 weeks had increased odds of CP compared with full term children whose mothers did not have pre-eclampsia (OR = 3.41, 95% CI 1.40, 8.31). Pre-term infants whose mothers had pre-eclampsia were at significantly increased risk of CP compared with full term infants whose mothers did not have pre-eclampsia (OR = 5.88, 95% CI 3.40, 10.17). The greatest risk for CP was in preterm infants whose mothers did not have pre-eclampsia (OR = 8.12, 95% CI 6.49, 10.17 compared with full term infants without exposure to pre-eclampsia). We conclude that pre-eclampsia with onset before 37 weeks' gestation is a significant risk factor for CP. Some of the association is probably attributable to high risk of preterm birth because of early pre-eclampsia, while a 'direct' effect of pre-eclampsia on fetal brain development also seems likely.

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