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Professor Nadia Badawi

Macquarie Group Foundation Chair of Cerebral Palsy
PO Box 560, Darlinghurst, New South Wales 2010 Australia

Interventions and Management

1. J Child Neurol. 2013 Feb 21. [Epub ahead of print]

Toward the Development of the International Classification of Functioning Core Sets for Children With Cerebral Palsy: A Global Expert Survey.

Schiariti V, Mâsse LC, Cieza A, Klassen AF, Sauve K, Armstrong R, O'Donnell M.

Department of Pediatrics, University of British Columbia, Vancouver, British Columbia, Canada.

The goal of the International Classification of Functioning is to standardize the classification of health and function of children around the world. To facilitate the application of this classification, International Classification of Functioning-based tools like the "Core Sets" are being developed. We conducted an international survey of professional experts to identify the most relevant areas of functioning in children with cerebral palsy. The questionnaire covered each component of the classification. In total, 193 professionals completed the survey (response rate 78%). Overall, 9706 answers were linked to the classification (pediatric version) by 2 professionals. From the experts' perspective, movement-related areas and social participation are the most relevant areas of functioning. Experts suggest a more comprehensive profile of functioning in particular in areas of personal capacity and social participation. The results of this survey will inform the development of the International Classification of Functioning Core Sets for children with cerebral palsy.

[PMID: 23435282](#) [PubMed - as supplied by publisher]

2. Am J Occup Ther. 2013 Mar;67(2):201-8. doi: 10.5014/ajot.2013.004374.

Group constraint-induced movement therapy for children with hemiplegic cerebral palsy: a pilot study.

Wu WC, Hung JW, Tseng CY, Huang YC.

Wen-Chi Wu, MA, OTR/L, is Occupational Therapist, Department of Rehabilitation, Kaohsiung Chang Gung Memorial Hospital, Kaohsiung, Taiwan.

OBJECTIVE. We investigated the feasibility and effectiveness of group-based constraint-induced movement therapy (CIMT) for children with hemiplegic cerebral palsy in a clinical setting. **METHOD.** Seven children received CIMT together under the guidance of two occupational therapy practitioners, 2.5 hr/day, 5 days/wk for 4 wk. We used the Grasping and Visual-Motor Integration subtests of the Peabody Developmental Motor Scales to assess

the primary outcome and the Functional Skills and Caregiver Assistance Scales of the Pediatric Evaluation Disability Inventory to assess the secondary outcome. Children were examined at preintervention, postintervention, and 1- and 3-mo follow-up. **RESULTS.** Children demonstrated significant improvement on all outcome measures after intervention (all $ps < .05$, effect sizes = .39-.84), and effects were maintained at 3-mo follow-up. **CONCLUSION.** This preliminary study revealed that group-based CIMT for children with hemiplegic cerebral palsy may be a feasible and effective alternative to individual CIMT in clinical practice.

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3. *Am J Occup Ther.* 2013 Mar;67(2):218-27. doi: 10.5014/ajot.2013.005538.

Writing forces associated with four pencil grasp patterns in grade 4 children.

Schwellnus H, Carnahan H, Kushki A, Polatajko H, Missiuna C, Chau T.

Heidi Schwellnus, PhD, is Postdoctoral Fellow in Cerebral Palsy, Bloorview Research Institute, Toronto, Ontario, and Centre for Interdisciplinary Research in Rehabilitation and Social Integration, Quebec, Quebec, Canada.

OBJECTIVE. We investigated differences in handwriting kinetics, speed, and legibility among four pencil grasps after a 10-min copy task. **METHOD.** Seventy-four Grade 4 students completed a handwriting assessment before and after a copy task. Grip and axial forces were measured with an instrumented stylus and force-sensitive tablet. We used multiple linear regression to analyze the relationship between grasp pattern and grip and axial forces. **RESULTS.** We found no kinetic differences among grasps, whether considered individually or grouped by the number of fingers on the barrel. However, when grasps were grouped according to the thumb position, the adducted grasps exhibited higher mean grip and axial forces. **CONCLUSION.** Grip forces were generally similar across the different grasps. Kinetic differences resulting from thumb position seemed to have no bearing on speed and legibility. Interventions for handwriting difficulties should focus more on speed and letter formation than on grasp pattern.

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4. *Dev Med Child Neurol.* 2013 Mar 1. doi: 10.1111/dmcn.12120. [Epub ahead of print]

Criterion validity of the GMFM-66 item set and the GMFM-66 basal and ceiling approaches for estimating GMFM-66 scores.

Avery LM, Russell DJ, Rosenbaum PL.

CanChild Centre for Childhood Disability Research, McMaster University, Canada.

AIM: The aim of this study was to compare the accuracy of two abbreviated approaches for estimating Gross Motor Function Measure 66 (GMFM-66) scores against the full GMFM-66 and to explore their strengths and limitations. **METHOD:** An existing dataset ($n=224$) comprising children aged 1 to 13 years (mean age 6y 11mo, SD 4y 6mo; 132 males, 92 females) with cerebral palsy (CP) of all Gross Motor Function Classification System (GMFCS) levels was used to compare the validity of the item set version (GMFM-66-IS) and the basal and ceiling version (GMFM-66-B&C) with the full GMFM-66 scores. Follow-up assessment at 1 year ($n=109$) allowed evaluation of change scores and accuracy at a single point in time. **RESULTS:** The cross-sectional agreement was excellent for both abbreviated measures (all intraclass correlation coefficients [ICCs] >0.98). When measuring change over time, both the GMFM-66-IS and the GMFM-66-B&C showed good agreement for children with bilateral CP (ICCs >0.9). However, the GMFM-66-IS assessed change over 1 year more accurately than the GMFM-66-B&C in children with unilateral CP (ICC=0.89 vs ICC=0.58; 95% confidence intervals do not overlap). **INTERPRETATION:** Both approaches for estimating GMFM-66 scores are accurate at a single point in time. If the primary goal of assessment is to measure change, the full GMFM-66 should still be regarded as the criterion standard. The GMFM-66-IS should be the preferred shortened measure for children with unilateral CP.

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5. J Musculoskelet Neuronal Interact. 2013 Mar;13(1):19-26.

The acute effects of whole-body vibration on gait parameters in adults with cerebral palsy.

Dickin DC, Faust KA, Wang H, Frame J.

Biomechanics Laboratory, Ball State University, Muncie, IN 47306, USA.

Objectives: As adults with cerebral palsy (CP) are surviving longer, interventions are needed to reduce spasticity and increase strength to improve mobility and life quality. Adults with CP are lacking a form of independent exercise that allows them to maintain or improve their ambulation skills. A new approach to increase muscle strength and flexibility called whole-body vibration (WBV) was assessed. **Methods:** Using an individualized frequency (I-Freq) approach to WBV therapy the acute effects on gait in adults with CP was measured. In this study, eight adults with CP (age 20-51 years, two female) participated in two testing sessions: session one determined each individual's I-Freq; and session two included a 3D gait analysis before and after a WBV treatment. The WBV was administered in five, one minute bouts of vibration followed by one minute of rest. **Results:** Following WBV exposure subjects experienced a significant increase in walking speed ($P=0.047$), stride length ($P=0.017$) and dynamic ankle range of motion ($P=0.042$). **Conclusions:** These data show that acute WBV treatments at I-Freq can improve measures of gait and mobility in adults with CP, however, future should assess potential long-term improvements.

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6. J Rehabil Med. 2013 Feb 28. doi: 10.2340/16501977-1114. [Epub ahead of print]

Functional effects of robotic-assisted locomotor treadmill therapy in children with cerebral palsy.

Druzbicki M, Rusek W, Snela S, Dudek J, Szczepanik M, Zak E, Durmala J, Czernuszenko A, Bonikowski M, Sobota G.

Institute of Physiotherapy, University of Rzeszów, 35-205 Rzeszow, Poland. mdruzb@univ.rzeszow.pl.

Objective: The aim of this study was to assess gait in children with spastic diplegic cerebral palsy rehabilitated with the use of Lokomat active orthosis. **Design:** A randomized controlled trial. **Subjects:** Fifty-two children with spastic diplegic cerebral palsy. **Methods:** Temporospatial parameters of gait and selected kinematic parameters were assessed. Children from the study group used active orthosis in addition to following a programme of individual exercises. Children in the control group participated only in individual exercises. **Results:** The difference between the initial and control examinations was statistically insignificant. After the programme was finished, there was a slight improvement in walking speed in both groups. Improvement in the mean walking speed was not significantly different between the groups ($p = 0.5905$). Range of motion decreased slightly in both groups, and the difference between mean amounts of change was not significant ($p = 0.8676$). There was significant improvement in maximal range of flexion in the hip joint ($p = 0.0065$) in the study. It was shown that with a decrease in the mean value of adduction in hip joint, the mean walking speed increased ($r = -0.53$, $p = 0.0011$). **Conclusion:** There are several limitations to this study, therefore these results should be regarded as preliminary. Further research consistent with the above indications is needed to investigate the impact of this new treatment option in patients with cerebral palsy.

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7. Prosthet Orthot Int. 2013 Feb 22. [Epub ahead of print]**Treadmill training with partial body weight support compared with conventional gait training for low-functioning children and adolescents with nonspastic cerebral palsy: A two-period crossover study.**

Su IY, Chung KK, Chow DH.

SAHK, Hong Kong, China.

Background: Partial body weight-supported treadmill training has been shown to be effective in gait training for patients with neurological disorders such as spinal cord injuries and stroke. Recent applications on children with cerebral palsy were reported, mostly on spastic cerebral palsy with single subject design. There is lack of evidence on the effectiveness of such training for nonspastic cerebral palsy, particularly those who are low functioning with limited intellectual capacity. **Objectives:** This study evaluated the effectiveness of partial body weight-supported treadmill training for improving gross motor skills among these clients. **Study design:** A two-period randomized crossover design with repeated measures. **Methods:** A crossover design following an A-B versus a B-A pattern was adopted. The two training periods consisted of 12-week partial body weight-supported treadmill training (Training A) and 12-week conventional gait training (Training B) with a 10-week washout in between. Ten school-age participants with nonspastic cerebral palsy and severe mental retardation were recruited. The Gross Motor Function Measure-66 was administered immediately before and after each training period. **Results:** Significant improvements in dimensions D and E of the Gross Motor Function Measure-66 and the Gross Motor Ability Estimator were obtained. **Conclusions:** Our findings revealed that the partial body weight-supported treadmill training was effective in improving gross motor skills for low-functioning children and adolescents with nonspastic cerebral palsy. **Clinical relevance:** Our preliminary findings demonstrated that partial body weight-supported treadmill training was a treatment of choice for improving gross motor functioning related to standing and ambulation for low-functioning children and adolescents with nonspastic cerebral palsy and limited intellectual capacity.

[PMID: 23436693](#) [PubMed - as supplied by publisher]**8. Dev Med Child Neurol. 2013 Feb 22. doi: 10.1111/dmcn.12094. [Epub ahead of print]****The impact of complementary and alternative medicine on hip development in children with cerebral palsy.**

Willoughby K, Jachno K, Ang SG, Thomason P, Graham HK.

Orthopaedic Department, The Royal Children's Hospital, Parkville, Victoria, Victoria, Australia.

AIM: This study aimed to evaluate the effect of complementary and alternative medicine (CAM) approaches on long-term surgical requirements, and clinical and radiographic outcomes for children with cerebral palsy and hip displacement. **METHOD:** Twenty-three children with cerebral palsy and early hip displacement who were offered preventive hip surgery and whose parents declined in favour of CAM approaches were followed (13 males, 10 females; mean age 13y 9mo [SD 3y 1mo]; mean length of follow-up 10y 2mo [SD 2y 11mo]; 17 with spastic quadriplegia, two with spastic triplegia, and four with spastic diplegia; three with gross motor function classified at Gross Motor Function Classification System [GMFCS] level II, four at level III, six at level IV, and 10 at level V). Principal outcome measures were progression of hip displacement (measured by migration percentage: the percentage of the femoral head sitting outside of the acetabulum), eventual need for reconstructive or salvage surgery, and long-term hip morphology (classified by the Melbourne Cerebral Palsy Hip Classification Scale). The results were compared with a previously reported cohort of 46 children who had surgery when recommended (31 males, 15 females; mean age 13y 11mo [SD 1y 6mo]; mean length of follow-up 10y 10mo; 10 with diplegia and 36 with quadriplegia; three at GMFCS level II, 11 at level III, 20 at level IV, and 12 at level V). **RESULTS:** Outcomes for 23 children who had pursued CAM were analysed (mean length of follow-up 10y 2mo). Hip displacement progressed in one or both hips in all non-ambulant children (GMFCS level IV or V). Of the 20 children with documented progressive hip displacement, eight developed pain and deformity requiring salvage surgery. An additional 11 children with progressive hip displacement had late reconstructive surgery when symptoms first started. There was strong evidence of a relationship between GMFCS and both progressive hip displacement ($\chi^2 = 17.78$; $p = 0.001$) and final Melbourne Cerebral Palsy Hip Classification Scale grade (odds ratio 12.5; $p = 0.012$; 95% confidence interval 1.7-90.4). There was also evidence of those children who pursued CAM requiring more complex surgery than the group who had surgery when recommended (odds ratio 2.5; $p = 0.002$; 95% confidence interval 1.4-4.5). **INTERPRETATION:** CAM therapy did not appear to influence the progression of hip displacement in children

with cerebral palsy. Most children required major reconstructive surgery or salvage surgery despite pursuing CAM.

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9. *Dev Med Child Neurol.* 2013 Feb 26. doi: 10.1111/dmcn.12098. [Epub ahead of print]

Intensive dysarthria therapy for younger children with cerebral palsy.

Pennington L, Roelant E, Thompson V, Robson S, Steen N, Miller N.

Institute of Health and Society, Newcastle University, Newcastle upon Tyne, UK.

AIM: The aim of this study was to investigate if intervention targeting breath support, phonation, and speech rate increases speech intelligibility and participation in the conversational interactions of younger children with dysarthria and cerebral palsy (CP). **METHOD:** Fifteen children with dysarthria and CP (nine males, six females; age range 5-11y, mean age 8y, SD 2y; CP type: eight spastic, four dyskinetic, one ataxia, two Worster Drought syndrome; Gross Motor Function Classification System levels II-IV, median level II) participated in this study. Children received three sessions of individual therapy per week for 6 weeks. Intelligibility of single words and connected speech was compared across five points: 1 and 6 weeks before therapy and 1, 6, and 12 weeks after therapy. Three familiar listeners and three unfamiliar listeners scored each recording. Participation in communicative interactions was measured using the Focus on the Outcomes of Communication Under Six (FOCUS) tool. Analyses of variance and paired t-tests were used to investigate change. **RESULTS:** Mean speech intelligibility increased after therapy to familiar listeners (single words 10.8%, 95% confidence interval [CI] 7.2-14.4; connected speech 9.4%, 95% CI 4.8-14.1) and unfamiliar listeners (single words 9.3%, 95% CI 6.8-11.8; connected speech 10.5%, 95% CI 7.3-13.8). FOCUS scores increased following therapy for parents (mean increase 30.3, 95% CI 10.2-50.4) and for teachers (28.25, 95% CI 14.4-42.1), but changes did not correlate with intelligibility. A wide variation was seen in individual responses to therapy. **INTERPRETATION:** Brief intensive therapy is associated with gains in intelligibility and communicative interactions for some younger children with dysarthria.

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10. *J Oral Rehabil.* 2013 Feb 28. doi: 10.1111/joor.12040. [Epub ahead of print]

Assessment of mastication in healthy children and children with cerebral palsy: a validity and consistency study.

Remijn L, Speyer R, Groen BE, Holtus PC, van Limbeek J, Nijhuis-van der Sanden MW.

Department of Child Rehabilitation, Rehabilitation Centre, Sint Maartenskliniek, Nijmegen, the Netherlands; Institute of Health Studies, HAN University of Applied Sciences, Nijmegen, the Netherlands.

The aim of this study was to develop the Mastication Observation and Evaluation instrument for observing and assessing the chewing ability of children eating solid and lumpy foods. This study describes the process of item definition and item selection and reports the content validity, reproducibility and consistency of the instrument. In the developmental phase, 15 experienced speech therapists assessed item relevance and descriptions over three Delphi rounds. Potential items were selected based on the results from a literature review. At the initial Delphi round, 17 potential items were included. After three Delphi rounds, 14 items that regarded as providing distinctive value in assessment of mastication (consensus >75%) were included in the Mastication Observation and Evaluation instrument. To test item reproducibility and consistency, two experts and five students evaluated video recordings of 20 children (10 children with cerebral palsy aged 29-65 months and 10 healthy children aged 11-42 months) eating bread and a biscuit. Reproducibility was estimated by means of the intraclass correlation coefficient (ICC). With the exception of one item concerning chewing duration, all items showed good to excellent intra-observer agreement (ICC students: 0.73-1.0). With the exception of chewing duration and number of swallows, inter-observer agreement was fair to excellent for all items (ICC experts: 0.68-1.0 and ICC students: 0.42-1.0). Results

indicate that this tool is a feasible instrument and could be used in clinical practice after further research is completed on the reliability of the tool.

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11. BMJ Open. 2013 Feb 14;3(2). pii: e002512. doi: 10.1136/bmjopen-2012-002512. Print 2013.

UP-BEAT (Upper Limb Baby Early Action-observation Training): protocol of two parallel randomised controlled trials of action-observation training for typically developing infants and infants with asymmetric brain lesions.

Guzzetta A, Boyd RN, Perez M, Ziviani J, Burzi V, Slaughter V, Rose S, Provan K, Findlay L, Fisher I, Colombini F, Tealdi G, Marchi V, Whittingham K.

Department of Developmental Neuroscience, Stella Maris Scientific Institute, Pisa, Tuscany, Italy.

INTRODUCTION: Infants with asymmetric brain lesions are at high risk of developing congenital hemiplegia. Action-observation training (AOT) has been shown to effectively improve upper limb motor function in adults with chronic stroke. AOT is based on action observation, whereby new motor skills can be learnt by observing motor actions. This process is facilitated by the Mirror Neuron System, which matches observed and performed motor actions. This study aims to determine the efficacy of AOT in: (1) influencing the early development of reaching and grasping of typically developing infants and (2) improving the upper limb activity of infants with asymmetric brain lesions. **METHODS AND ANALYSIS:** This study design comprises two parallel randomised sham-controlled trials (RCTs) in: (1) typically developing infants (cohort I) and (2) infants with asymmetric brain lesions (eg, arterial stroke, venous infarction, intraventricular haemorrhage or periventricular leukomalacia; cohort II). Cohort II will be identified through a neonatal ultrasound or neonatal MRI. A sham control will be used for both RCTs, taking into consideration that it would be unethical to give no intervention to an at-risk population. Based on a two-tailed t test of two independent means, with a significance (α) level of 0.05, 80% power, predicted effect size of 0.8 and a 90% retention rate, we require 20 participants in each group (total sample of 40) for cohort I. The sample size for cohort II was based on the assumption that the effect size of the proposed training would be similar to that found by Heathcock et al in preterm born infants (n=26) with a mean effect size of 2.4. Given the high effect size, the calculation returned a sample of only four participants per group, on a two-tailed t test, with a significance (α) level of 0.05 and 80% power. As cohort II will consist of two subgroups of lesion type (ie, arterial stroke and venous infarction), we have quadrupled the sample to include 16 participants in each group (total sample of 32). Infants will be randomised to receive either AOT or standard Toy Observation Training (TOT). Both interventions will be of 4 weeks' duration, from the infant's 9th-13th post-term week of age. Three sessions of 5 min each will be performed each day for 6 days/week (total of 6 h over 28 days). Parents of the AOT group will repeatedly show the infant a grasping action on a set of three toys, presented in random order. Parents of the TOT group will show the infant the same set of three toys, in random order, without demonstrating the grasping action. At 14, 16 and 18 weeks, the quantity and quality of reaching and grasping will be measured using the Grasping and Reaching Assessment of Brisbane; symmetry of reaching and grasping will be measured using the Hand Assessment of Infants (HAI) and pressure of grasping for each hand with a customised pressure sensor. At 6 months' corrected age, the primary outcome measures will be the HAI and Bayley Scales of Infant and Toddler Development (third edition; BSID III), to measure cognitive and motor development. At 8 months, HAI and EEG will be used to measure brain activity and cortical coherence. At 12 months, the primary outcome measures will again be HAI and BSID III. **DISSEMINATION:** This paper outlines the theoretical basis, study hypotheses and outcome measures for two parallel RCTs comparing the novel intervention Action-observation training with standard TOT in: (1) influencing the early development of reaching and grasping of typically developing infants and (2) improving the upper limb motor activity of infants with asymmetric brain lesions.

TRIAL REGISTRATION: ACTRN1261100991910. [Web address of UP-BEAT trial](#)

[PMID: 23418301](#) [PubMed] [Free full text](#)

12. World J Urol. 2013 Feb 27. [Epub ahead of print]**The effect of delayed percutaneous nephrolithotomy on the risk of bacteremia and sepsis in patients with neuromuscular disorders.**

Eswara JR, Lee H, Dretler SP, Sacco D.

Department of Urology, Massachusetts General Hospital, 55 Fruit Street, Boston, MA, 02114, USA, jeswara@partners.org.

PURPOSE: To determine whether a delayed percutaneous nephrolithotomy (PCNL) reduces the rate of bacteremia/sepsis in patients with neuromuscular disorders. Patients with neuromuscular disorders are at higher risk of developing complications after PCNL. One strategy to reduce the risk of infectious complications is to place a percutaneous nephrostomy tube at least 24 h prior to performing PCNL. We analyzed the rates of bacteremia/sepsis in patients with neuromuscular disorders who had access on the day of PCNL (same-day) versus more than 24 h prior to the treatment for the stone (delayed). **MATERIALS AND METHODS:** We identified 246 consecutive patients who underwent PCNL at our institution between 8/2003 and 8/2008, 35 of whom (14 %) had neuromuscular disorders. The primary end point was postoperative bacteremia (fever and positive blood culture) or sepsis (SIRS and documented infection), which was compared between those who had percutaneous access on the day of surgery versus those who had access at least 24 h prior to the operative event. All patients had negative urine cultures preoperatively or were treated with antibiotics for 4-7 days prior to the surgery for a positive preoperative urine culture. **RESULTS:** The neuromuscular disorders in the 35 patients were multiple sclerosis (16), spina bifida (10), quadriplegia (4) paraplegia/Guillain-Barre (3), and cerebral palsy (2). The rate of bacteremia/sepsis among patients with neuromuscular disorders was 14 %. The rate of sepsis/bacteremia was 26 % for same-day PCNL versus 0 % for delayed PCNL (OR 8.4, $p = 0.05$). **CONCLUSIONS:** Delayed PCNL results in lower rates of bacteremia and/or sepsis in patients with neuromuscular disorders.

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Prevention and Cure

13. Cochrane Database Syst Rev. 2013 Feb 28;2:CD009395. doi: 10.1002/14651858.CD009395.pub2.**Magnesium sulphate for women at term for neuroprotection of the fetus.**

Nguyen TM, Crowther CA, Wilkinson D, Bain E.

ARCH: Australian Research Centre for Health of Women and Babies, Discipline of Obstetrics and Gynaecology, The University of Adelaide, Women's and Children's Hospital, 72 King William Road, Adelaide, South Australia, Australia, 5006.

BACKGROUND: Magnesium sulphate is extensively used in obstetrics for the treatment and prevention of eclampsia. A recent meta-analysis has shown that magnesium sulphate is an effective fetal neuroprotective agent when given antenatally to women at risk of very preterm birth. Term infants account for more than half of all cases of cerebral palsy, and the incidence has remained fairly constant. It is important to assess if antenatal administration of magnesium sulphate to women at term protects the fetus from brain injury, and associated neurosensory disabilities including cerebral palsy. **OBJECTIVES:** To assess the effectiveness of magnesium sulphate given to women at term as a neuroprotective agent for the fetus. **SEARCH METHODS:** We searched the Cochrane Pregnancy and Childbirth Group's Trial Register (31 July 2012) and the reference lists of other Cochrane reviews assessing magnesium sulphate in pregnancy. **SELECTION CRITERIA:** Randomised controlled trials comparing antenatally administered magnesium sulphate to women at term with placebo, no treatment or a different fetal neuroprotective agent. We also planned to include cluster-randomised trials, and exclude cross-over trials and quasi-randomised trials. We planned to exclude studies reported as abstracts only. **DATA COLLECTION AND ANALYSIS:** Two review authors independently assessed trials for eligibility and for risk of bias. Two authors independently extracted data. Data were checked for accuracy. **MAIN RESULTS:** We included one trial (involving

135 women with mild pre-eclampsia at term). An additional six studies are awaiting further assessment. The included trial compared magnesium sulphate with a placebo and was at a low risk of bias. The trial did not report any of this review's prespecified primary outcomes. There was no significant difference between magnesium sulphate and placebo in Apgar score less than seven at five minutes (risk ratio (RR) 0.51; 95% confidence interval (CI) 0.05 to 5.46; 135 infants), nor gestational age at birth (mean difference (MD) -0.20 weeks; 95% CI -0.62 to 0.22; 135 infants). There were significantly more maternal side effects (feeling warm and flushed) in the magnesium sulphate group than in the placebo group (RR 3.81; 95% CI 2.22 to 6.53; 135 women). However, no significant difference in adverse effects severe enough to cease treatment was observed (RR 3.04; 95% CI 0.13 to 73.42; 135 women). There were no significant differences seen between groups in the rates of postpartum haemorrhage (RR 4.06; 95% CI 0.47 to 35.38; 135 women) and caesarean section (RR 0.80; 95% CI 0.39 to 1.63; 135 women). **AUTHORS' CONCLUSIONS:** There is currently insufficient evidence to assess the efficacy and safety of magnesium sulphate when administered to women for neuroprotection of the term fetus. As there has been recent evidence for the use of magnesium sulphate for neuroprotection of the preterm fetus, high-quality randomised controlled trials are needed to determine the safety profile and neurological outcomes for the term fetus. Strategies to reduce maternal side effects during treatment also require evaluation.

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14. Am J Obstet Gynecol. 2013 Mar;208(3):213.e1-6. doi: 10.1016/j.ajog.2013.01.023.

Prophylactic maternal N-acetylcysteine in rats prevents maternal inflammation-induced offspring cerebral injury shown on magnetic resonance imaging.

Beloosesky R, Ginsberg Y, Khatib N, Maravi N, Ross MG, Itskovitz-Eldor J, Weiner Z.

Department of Obstetrics and Gynecology, Rambam Medical Center, Haifa, Israel. Electronic address: tomor2304@yahoo.com.

OBJECTIVE: Maternal infection or inflammation may induce fetal inflammatory responses associated with fetal injury and cerebral palsy. We sought to assess the inflammation-associated neuroprotective potential of prophylactic N-acetyl-cysteine (NAC). We examined the effect of NAC on prevention of maternal lipopolysaccharide (LPS)-induced neonatal brain injury using magnetic resonance imaging. **STUDY DESIGN:** Pregnant Sprague Dawley dams (n = 5-8) at embryonic day 18 received intraperitoneal injection of LPS or saline at time 0. Animals were randomized to receive 2 intravenous injections of NAC or saline (time -30 and 120 minutes). Pups were delivered spontaneously and allowed to mature until postnatal day 25. Female offspring were examined by magnetic resonance brain imaging and analyzed using voxel-based analysis after spatial normalization. T2 relaxation time was used to assess white matter injury and diffusion tensor imaging for apparent diffusion coefficient (ADC) to assess white and gray matter injury. **RESULTS:** Offspring of LPS-treated dams exhibited significantly increased T2 levels and increased ADC levels in white and gray matter (eg, hypothalamus, motor cortex, corpus callosum, thalamus, hippocampus), consistent with diffuse cerebral injury. In contrast, offspring of NAC-treated LPS dams demonstrated similar T2 and ADC levels as control in both white and gray matter. **CONCLUSION:** Maternal NAC treatment significantly reduced evidence of neonatal brain injury associated with maternal LPS. These studies suggest that maternal NAC therapy may be effective in human deliveries associated with maternal/fetal inflammation.

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15. Dev Med Child Neurol. 2013 Feb 26. doi: 10.1111/dmcn.12099. [Epub ahead of print]

Tractography of white-matter tracts in very preterm infants: a 2-year follow-up study.

De Bruïne FT, Van Wezel-Meijler G, Leijser LM, Steggerda SJ, Van Den Berg-Huysmans AA, Rijken M, Van Buchem MA, Van Der Grond J.

Department of Radiology, Leiden University Medical Center, Leiden, the Netherlands.

AIM: The aim of this study was to determine whether tractography of white-matter tracts can independently predict neurodevelopmental outcome in very preterm infants. **METHOD:** Out of 84 very preterm infants admitted to a neonatal intensive care unit, 64 (41 males, 23 females; median gestational age 29.1 weeks [range 25.6-31.9]; birthweight 1163g [range 585-1960]) underwent follow-up at 2 years. Diffusion tensor imaging (DTI) values obtained around term were associated with a neurological examination and mental and psychomotor developmental index scores at 2 years based on the Bayley Scales of Infant Development (version 3). Univariate and logistic regression analyses tested for associations between DTI values and follow-up parameters. Cut-off values predicting motor delay and cerebral palsy (CP) were determined for fractional anisotropy, apparent diffusion coefficient (ADC), and fibre lengths. **RESULTS:** Infants with psychomotor delay and CP had significantly lower fractional anisotropy values ($p=0.002$, $p=0.04$ respectively) and shorter fibre lengths ($p=0.02$, $p=0.02$ respectively) of the posterior limb of the internal capsule. Infants with psychomotor delay also had significantly higher ADC values ($p=0.03$) and shorter fibre lengths ($p=0.002$) of the callosal splenium. Fractional anisotropy values of the posterior limb of the internal capsule independently predicted motor delay and CP, with sensitivity between 80 and 100% and specificity between 66 and 69%. ADC values of the splenium independently predicted motor delay with sensitivity of 100% and specificity of 65%. **INTERPRETATION:** Diffusion tensor imaging tractography at term-equivalent age independently predicts psychomotor delay at 2 years of age in preterm infants.

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16. Dev Neurosci. 2013 Feb 27. [Epub ahead of print]

Ischemia-Induced Neuroinflammation Is Associated with Disrupted Development of Oligodendrocyte Progenitors in a Model of Periventricular Leukomalacia.

Falahati S, Breu M, Waickman AT, Phillips AW, Arauz EJ, Snyder S, Porambo M, Goeral K, Comi AM, Wilson MA, Johnston MV, Fatemi A.

The Hugo W. Moser Research Institute at Kennedy Krieger Institute, Baltimore, Md., USA.

Microglial activation in crossing white matter tracts is a hallmark of noncystic periventricular leukomalacia (PVL), the leading pathology underlying cerebral palsy in prematurely born infants. Recent studies indicate that neuroinflammation within an early time window can produce long-lasting defects in oligodendroglial maturation, myelination deficit, as well as disruption of transcription factors important in oligodendroglial maturation. We recently reported an ischemic mouse model of PVL, induced by unilateral neonatal carotid artery ligation, leading to selective long-lasting bilateral myelination deficits, ipsilateral thinning of the corpus callosum, ventriculomegaly, as well as evidence of axonopathy. Here, we report that permanent unilateral carotid ligation on postnatal day 5 in CD-1 mice induces an inflammatory response, as defined by microglial activation and recruitment, as well as significant changes in cytokine expression (increased IL-1 β , IL-6, TGF- β 1, and TNF- α) following ischemia. Transient reduction in counts of oligodendrocyte progenitor cells (OPCs) at 24 and 48 h after ischemia, a shift in OPC cell size and morphology towards the more immature form, as well as likely migration of OPCs were found. These OPC changes were topographically associated with areas showing microglial activation, and OPC counts negatively correlated with increased microglial staining. The presented data show a striking neuroinflammatory response in an ischemia-induced model of PVL, associated with oligodendroglial injury. Future studies modulating the neuroinflammatory response in this model may contribute to a better understanding of the interaction between microglia and OPCs in PVL and open opportunities for future therapies.

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17. Dev Neurosci. 2013 Feb 27. [Epub ahead of print]**Maternal Exposure to Lipopolysaccharide Leads to Transient Motor Dysfunction in Neonatal Rats.**

Rousset CI, Kassem J, Aubert A, Planchenault D, Gressens P, Chalon S, Belzung C, Saliba E.

INSERM U930, CHRU Tours, Tours, France.

Epidemiological and experimental data implicate maternal infection and inflammation in the etiology of brain white matter injury, which may lead to cerebral palsy in preterm newborns. Our aim was to investigate motor development of the offspring after maternal administration of lipopolysaccharide (LPS). Wistar rats were intraperitoneally injected with *Escherichia coli* LPS or saline on gestational days 19 and 20. From birth to 3 weeks, pups were tested for neurobehavioral development, neurological signs and reflexes. From 3 to 6 weeks, motor coordination was investigated. At 4 months, animals were tested for locomotion. Brain myelination was assessed by myelin basic protein immunohistochemistry. Days of appearance of several neurological reflexes were significantly delayed, and neonate LPS pups displayed retarded performance in righting, gait and negative geotaxis. At the juvenile stage, LPS animals showed important impairment in coordination. However, although the LPS group performed worse in most tests, they reached vehicle levels by 5 weeks. At 4 months, LPS animals did not show variations in locomotion performances compared to vehicle. No myelination differences have been observed in the brains at adulthood. Maternal LPS administration results in delayed motor development even though these alterations fade to reach control level by 5 weeks. Motor impairments observed at the early stage in this study could be linked to previously reported hypomyelination of the white matter induced by maternal LPS challenge in the neonates. Finally, the normal myelination shown here at adulthood may explain the functional recovery of the animals and suggest either a potential remyelination of the brain or a delayed myelination in LPS pups.

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18. Hum Reprod Update. 2013 Feb 28. [Epub ahead of print]**The longer-term health outcomes for children born as a result of IVF treatment. Part II: mental health and development outcomes.**

Hart R, Norman RJ.

School of Women's and Infant's Health, University of Western Australia, King Edward Memorial Hospital, Subiaco, Perth, WA 6008, Australia.

BACKGROUND: Limited data exist with regard to longer-term mental health and psychological functioning of children born from IVF treatment. With the known adverse perinatal outcome for children born from IVF treatment, it would be expected that there is a negative impact upon their mental development. **METHODS:** A search strategy restricted to studies relating to the medical condition of children of at least 1 year of age, born from IVF treatment was performed to include case series, data linkage and prospective studies published from 1 January 2000 to 1 April 2012. **RESULTS:** Limited long-term follow-up data suggest that there is an increase in the incidence of cerebral palsy and neurodevelopmental delay related to the confounders of prematurity and low birthweight. Previous reports of associations with autism and attention-deficit disorder are believed to be related to maternal and obstetric factors. There exists a potential increase in the prevalence of early adulthood clinical depression and binge drinking in the offspring of IVF, with the reassuring data of no changes with respect to cognitive development, school performance, social functioning and behaviour. Whether these potential associations are related to the IVF treatment, the adverse obstetric outcomes associated with IVF treatment, the genetic or subsequent environmental influences on the children is yet to be determined. **CONCLUSIONS:** In general, the longer-term mental and emotional health outcome for children born from IVF treatment is reassuring, and is very similar to that of naturally conceived children; however, further studies are required to explore any association with depression, and its causality in more detail.

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