

Monday 24 January 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" and cover the period 20 December 2010 to 9 January 2011.

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## Interventions

### 1. *Acta Bioeng Biomech.* 2010;12(3):53-8.

#### **Assessment of the impact of orthotic gait training on balance in children with cerebral palsy.**

Drużbicki M, Rusek W, Szczepanik M, Dudek J, Snela S.

Institute of Physiotherapy, Rzeszów University; Voivodship Hospital No. 2 in Rzeszów.

The cerebral palsy symptoms are, among others, balance and gait disorders. The goal of this study was to assess balance capabilities in children with spastic diplegic cerebral palsy rehabilitated using Lokomat active orthosis. The experimental group included children with cerebral palsy, aged 6-14 years, independent standing, level II-III according to GMFCS classification. The cohort was randomly divided into two groups. The balance was assessed on a stabilometric platform. The experimental group was administered a rehabilitation program with the use of Lokomat active orthosis. Statistically significant improvement of balance was found in the experimental group; however, in the control group the improvement was also visible, but not on the statistically significant level. While comparing the results of both groups, significantly bigger improvement was achieved by the children from the experimental group. Lokomat active orthosis is one of the newest devices applied in the rehabilitation. The study shows that training with active orthosis can have positive influence on the balance improvement in children with CP and that further analysis of the impact of such training on locomotive functions is needed.

PMID: 21243970 [PubMed - in process]

### 2. *Dev Med Child Neurol.* 2011 Feb;53(2):125-30. doi: 10.1111/j.1469-8749.2010.03814.x.

#### **Adverse events and health status following botulinum toxin type A injections in children with cerebral palsy.**

O'Flaherty SJ, Janakan V, Morrow AM, Scheinberg AM, Waugh MC.

Kids Rehab, The Children's Hospital at Westmead, Westmead, NSW, Australia. Victorian Paediatric Rehabilitation Service, Royal Children's Hospital, Parkville, VIC, Australia.

**Aim:** The aim of this study was to assess changes in health status before and after, as well as adverse events after, botulinum toxin type A (BoNT-A) injections in children with cerebral palsy (CP). **Method:** A total of 334 children (190 male; 144 female) aged 1y 6mo to 19y 4mo (mean 9y 2mo, SD 4y) with CP who were undergoing BoNT-A injections (596 injection courses in total) were clinically audited over a 16-month period. Of the 334 children, 62 were classified at Gross Motor Function Classification System (GMFCS) level I, 52 of whom had unilateral CP and 10 of whom had bilateral CP. Eighty-six children were classified at GMFCS level II, 39 of whom had unilateral CP and 47 of whom had bilateral CP. Forty-four children were classified at GMFCS level III, two of whom had unilateral CP and 42 of whom had bilateral CP. Sixty-six of the 334 children were classified at GMFCS level IV and 76

as level V. All the children classified as level IV or V had bilateral involvement. The health status of the children in the month before and a prospective audit of health status and adverse events in the month after BoNT-A injections were examined in order to assess the effects of the toxin. Results: The data gathered for the month before administration of BoNT-A indicated that children with CP had significant background morbidities. After injection of BoNT-A, adverse events occurred in 23.2% of children. All adverse events were temporary and there were no deaths. Interpretation: The results of this audit indicate that there is insufficient evidence to warrant restriction of the administration of BoNT-A in children with CP at any GMFCS level in our service.

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PMID: 21244412 [PubMed - in process]

**3. Dev Med Child Neurol. 2011 Feb;53(2):191. doi: 10.1111/j.1469-8749.2010.03872.x.**

**'Physical activity measurement instruments for children with cerebral palsy: a systematic review'.**

Maltais DB, van den Berg-Emons RJ.

Laval University, Quebec City, QC, Canada. Erasmus Medical Center, Department Rehabilitation Medicine and Physical Therapy, Rotterdam, the Netherlands.

PMID: 21244415 [PubMed - in process]

**4. Dev Med Child Neurol. 2011 Feb;53(2):102-3. doi: 10.1111/j.1469-8749.2010.03851.x. Epub 2010 Dec 17.**

**Bone density and size in ambulatory children with cerebral palsy.**

Henderson R.

University of North Carolina, Department of Orthopaedics, Chapel Hill, NC, USA.

PMID: 21244407 [PubMed - in process]

**5. Dev Med Child Neurol. 2010 Nov;52(11):1070. doi: 10.1111/j.1469-8749.2010.03782.x. Epub 2010 Sep 15.**

**The terms diplegia, quadriplegia, and hemiplegia should be phased out.**

Hurvitz EA, Brown SH.

Comment on:

Dev Med Child Neurol. 2010 Jun;52(6):508-9.

PMID: 20846158 [PubMed - indexed for MEDLINE]

**6. Dev Neurorehabil. 2011;14(1):15-21.**

**Using motion interactive games to promote physical activity and enhance motor performance in children with cerebral palsy.**

Sandlund M, Lindh Waterworth E, Häger C.

Department of Community Medicine and Rehabilitation, Umeå University, Umeå, Sweden.

Objective: To explore the feasibility of using low-cost motion interactive games as a home-based intervention for children with cerebral palsy (CP). Methods: Fourteen children with CP, 6-16 years old, practiced with the EyeToy

for PlayStation2® in their homes during 4 weeks. Outcome measures were physical activity monitors, Movement Assessment Battery for Children-2 (mABC-2), Bruininks-Oseretsky Test of Motor Proficiency (sub-test 5 : 6), 1 Minute Walk Test and gaming diaries. Results: Motivation for practice and compliance of training were high. The children's physical activity increased during the intervention and activity monitors were feasible to use, although data loss may be a concern. According to mABC-2 the children's motor performance improved, but there were both floor and ceiling effects. The two additional motor tests showed only non-significant progress. Conclusion: It is highly feasible to use motion interactive games in home rehabilitation for children with CP. Specific motor effects need to be further explored.

PMID: 21241174 [PubMed - in process]

## **7. Gait Posture. 2011 Jan 17. [Epub ahead of print]**

### **Calculating gait kinematics using MR-based kinematic models.**

Scheys L, Desloovere K, Spaepen A, Suetens P, Jonkers I.

Medical Image Computing (Radiology - ESAT/PSI), University Hospital Leuven Campus, Gasthuisberg, Herestraat 4, B-3000 Leuven, Belgium; Department of Kinesiology, FABER/K.U.Leuven, Tervuursevest 101, B-3000 Leuven, Belgium.

Rescaling generic models is the most frequently applied approach in generating biomechanical models for inverse kinematics. Nevertheless it is well known that this procedure introduces errors in calculated gait kinematics due to: (1) errors associated with palpation of anatomical landmarks, (2) inaccuracies in the definition of joint coordinate systems. Based on magnetic resonance (MR) images, more accurate, subject-specific kinematic models can be built that are significantly less sensitive to both error types. We studied the difference between the two modelling techniques by quantifying differences in calculated hip and knee joint kinematics during gait. In a clinically relevant patient group of 7 pediatric cerebral palsy (CP) subjects with increased femoral anteversion, gait kinematics were calculated using (1) rescaled generic kinematic models and (2) subject-specific MR-based models. In addition, both sets of kinematics were compared to those obtained using the standard clinical data processing workflow. Inverse kinematics, calculated using rescaled generic models or the standard clinical workflow, differed largely compared to kinematics calculated using subject-specific MR-based kinematic models. The kinematic differences were most pronounced in the sagittal and transverse planes (hip and knee flexion, hip rotation). This study shows that MR-based kinematic models improve the reliability of gait kinematics, compared to generic models based on normal subjects. This is the case especially in CP subjects where bony deformations may alter the relative configuration of joint coordinate systems. Whilst high cost impedes the implementation of this modeling technique, our results demonstrate that efforts should be made to improve the level of subject-specific detail in the joint axes determination.

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PMID: 21247765 [PubMed - as supplied by publisher]

## **8. Health Expect. 2011 Jan 18. doi: 10.1111/j.1369-7625.2010.00652.x. [Epub ahead of print]**

### **Consulting parents about the design of a randomized controlled trial of osteopathy for children with cerebral palsy.**

Edwards V, Wyatt K, Logan S, Britten N.

Research Fellow in Child Health Senior Lecturer in Child Health Cerebra Professor of Paediatric Epidemiology Professor of Applied Healthcare Research, Cerebra Research Unit, Peninsula Medical School, University of Exeter, Exeter, UK.

Background: Although the UK Department of Health has advocated the involvement of service users and carers in health research for several years, there is little evidence about their contribution to the design of randomized controlled trials (RCTs). Objective: To demonstrate how consulting parents about the design of a study, including which outcomes to use, led to the design and successful delivery of a RCT of osteopathy for children with cerebral palsy (CP). Design Semi-structured interviews were carried out with 20 parents of children with CP and other neurological

conditions, asking them to choose between four different trial designs, to talk about noticeable changes in their child's condition and their views about payment for trial treatment. Setting and participants: The parents interviewed were all members of Cerebra, a charity for 'brain-injured' children and young people. All interviews were carried out at the parents' homes. Results: Parents had mixed views about possible trial designs; however, a waitlist design which allowed all children eventually to receive the treatment emerged as a clear favourite. Parents did not focus on isolated outcomes, but suggested a range of factors relevant to their child's quality of life. They expressed a clear preference for the costs of treatment to be funded by the trial. Conclusions: Involvement of parents helped design a trial which was acceptable to families and addressed outcomes that mattered to them. By consulting parents about the design of the research, the subsequent trial achieved excellent recruitment and retention rates.

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PMID: 21244590 [PubMed - as supplied by publisher]

### **9. J Am Acad Orthop Surg. 2010 Dec;18(12):739-48.**

#### **Revision spine surgery to manage pediatric deformity.**

Kim HJ, Cunningham ME, Boachie-Adjei O.

Hospital for Special Surgery, New York, NY, USA.

Revision deformity surgery in the growing child is a complex clinical problem. Excellent outcomes can be obtained with meticulous patient evaluation followed by well-planned and well-executed treatment. A multidisciplinary team is crucial to a satisfactory overall outcome. Diagnosis of failed index spine fusion requires a thorough patient history and physical examination, careful patient assessment, and imaging between the index procedure and the presentation for revision and confirmatory testing that validates the diagnosis. Revision surgery may include irrigation and débridement, implant removal, or revision spine fusion with deformity correction. Correction may require either an anterior approach or a posterior approach with osteotomy. For best results, the planned revision must address the mechanism of the failure of the index procedure. If the symptoms or observations are not explained by the diagnosis, then alternative etiologies should be considered.

PMID: 21119140 [PubMed - indexed for MEDLINE]

### **10. J Am Podiatr Med Assoc. 2011 Jan-Feb;101(1):59-69.**

#### **Clinical assessment of ankle joint dorsiflexion: a review of measurement techniques.**

Gatt A, Chockalingam N.

Podiatry Department, Faculty of Health Sciences, University of Malta, Msida, Malta.

Ankle dorsiflexion measurement is important for clinical and research use. With so much evidence on the unreliability of goniometric measurements, a systematic review was performed to investigate various alternative techniques for measuring ankle dorsiflexion in the nonneurologic patient. All of the major databases were queried electronically to identify studies that used any method of ankle dorsiflexion measurement in the nonneurologic subject. Keywords included ankle dorsiflexion NOT cerebral palsy NOT stroke, the latter to exclude neurologic conditions. In 755 studies that used some form of ankle joint dorsiflexion measurement, ten different techniques were identified that included various apparatuses designed specifically for this purpose. Reliability testing of these techniques involved test-retest trials with small student populations as subjects, which returned high intraclass correlation coefficient scores. However, their methodological quality would have benefitted from the use of an actual patient population and comparison with a reference standard. When validating ankle dorsiflexion measurement techniques, actual patient populations should be used, otherwise papers would score poorly on methodological quality assessment. Standardizing patient position, foot posture, amount of moment applied, and reference landmarks will ensure that various trial results can be compared directly.

PMID: 21242472 [PubMed - in process]

**11. J Appl Biomech. 2010 Nov;26(4):512-5.****Detecting postoperative change in children with cerebral palsy: net nondimensional versus body mass oxygen normalization.**

Svehlík M, Slabý K, Trc T, Radvanský J.

Orthopaedic Department for Children and Adults, Charles University Prague, 2nd Medical School, Czech Republic.

The aim of the study is to investigate whether the net nondimensional oxygen utilization scheme is able to detect postoperative improvement in the energy cost of walking in children with cerebral palsy and to compare it with a body mass normalization scheme. We evaluated 10 children with spastic cerebral palsy before and 9 months after equinus deformity surgery. Participants walked at a given speed of 2 km/hr and 3 km/hr on a treadmill. Oxygen utilization was measured, and mass relative VO<sub>2</sub> and net nondimensional VO<sub>2</sub> were calculated. Coefficient of variation was used for the description of variability among subjects. Postoperatively, gait kinematics normalized and the mass relative VO<sub>2</sub> and net nondimensional VO<sub>2</sub> showed significant improvement. Net nondimensional VO<sub>2</sub> is able to detect postoperative improvement with smaller variability among subjects than body mass related normalization in children with cerebral palsy.

PMID: 21245512 [PubMed - in process]

**12. J Bone Joint Surg Am. 2011 Jan;93(2):150-8.****Reliability of physical examination in the measurement of hip flexion contracture and correlation with gait parameters in cerebral palsy.**

Lee KM, Chung CY, Kwon DG, Han HS, Choi IH, Park MS.

Department of Orthopaedic Surgery, Seoul National University Bundang Hospital, 300 Gumi-Dong, Bundang-Gu, Sungnam, Kyungki 463-707, South Korea. pmsmed@gmail.com.

**BACKGROUND:** This study was undertaken to determine the validity and reliability of the physical examination tests commonly used to measure hip flexion contracture in patients with cerebral palsy who are able to walk. **METHODS:** Thirty-six consecutive patients (twenty-two male and fourteen female patients), with a mean age (and standard deviation) of  $9.8 \pm 3.9$  years, who had cerebral palsy (level I, II, or III on the Gross Motor Function Classification System) and thirty-seven children without cerebral palsy (nineteen male and eighteen female subjects), with a mean age of  $10.0 \pm 3.0$  years, were enrolled prospectively for this study. Hip flexion contracture was determined by three physical examination tests: the Thomas test, the prone hip extension test (the Staheli test), and the hamstring shift test. Three-dimensional gait analysis was performed in all subjects. The interobserver reliabilities of the three physical examination tests were determined with use of three observers. Convergent validity was assessed by evaluating the relationships between the findings on physical examination and kinematic and kinetic gait variables (maximum hip extension during stance and hip flexor index) and three-dimensional modeled psoas lengths. **RESULTS:** The Thomas test showed the highest intraclass correlation coefficient (0.501 in patients and 0.207 in controls) and the smallest mean absolute difference ( $5.8^\circ$  in patients and  $1.2^\circ$  in controls). The Staheli test was found to be the most valid method in the patient group ( $r = 0.568$  with hip flexor index), whereas the Thomas test was the most valid in the control group ( $r = 0.526$  with maximum hip extension in stance, and  $r = 0.532$  with the hip flexor index). The hamstring shift test had the lowest intraclass correlation coefficient and the lowest convergent validity. **CONCLUSIONS:** While the Thomas test showed the highest intraclass correlation coefficient and the smallest mean absolute difference, the Staheli test was the most valid method for detecting hip flexion contractures in patients with cerebral palsy. Although the Staheli test cannot be used for intraoperative assessment, we recommend that this test be included in preoperative physical examinations to determine the role of a hip flexion contracture in the abnormal gait of patients with cerebral palsy.

PMID: 21248212 [PubMed - in process]

**13. J Neural Eng. 2011 Jan 19;8(1):016005. [Epub ahead of print]****Nerve lesioning with direct current.**

Ravid EN, Gan LS, Todd K, Prochazka A.

Spastic hypertonus (muscle over-activity due to exaggerated stretch reflexes) often develops in people with stroke, cerebral palsy, multiple sclerosis and spinal cord injury. Lesioning of nerves, e.g. with phenol or botulinum toxin is widely performed to reduce spastic hypertonus. We have explored the use of direct electrical current (DC) to lesion peripheral nerves. In a series of animal experiments, DC reduced muscle force by controlled amounts and the reduction could last several months. We conclude that in some cases controlled DC lesioning may provide an effective alternative to the less controllable molecular treatments available today.

PMID: 21248380 [PubMed - as supplied by publisher]

**14. J Paediatr Child Health. 2011 Jan 18. doi: 10.1111/j.1440-1754.2010.01950.x. [Epub ahead of print]****Levetiracetam in children and adolescents with epilepsy and hemiplegic cerebral palsy.**

Harbord MG.

Paediatrics Department, Flinders Medical Centre, Bedford Park, South Australia, Australia.

**Aim:** To monitor the effect of adding levetiracetam in paediatric patients with hemiplegic cerebral palsy and uncontrolled epilepsy. **Methods:** A case series of eight patients with hemiplegic cerebral palsy whose focal seizures were not adequately controlled by their current anticonvulsants were monitored after levetiracetam was added to their medications. If there was a 50% reduction in seizure frequency, then the other anticonvulsants were discontinued. Prolonged follow-up occurred for a minimum of 2 years. **Results:** There were seven males and one female whose ages ranged from 4 years to 17 years. All had focal onset seizures, while seven also had secondarily generalised tonic clonic seizures. Levetiracetam resulted in at least a 50% reduction in seizure frequency in seven, with no change in one. Three were able to wean successfully to monotherapy and remained seizure free for over 2 years. They had a prior history of infrequent seizures, one to six per year. Those who continued to require multiple anticonvulsants had a prior history of more frequent seizures, 6-50/year. Levetiracetam was well tolerated, and none ceased this because of side effects. **Conclusion:** Levetiracetam is likely to be an effective anticonvulsant in children and adolescents with hemiplegic cerebral palsy and infrequent but persistent focal seizures.

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PMID: 21244554 [PubMed - as supplied by publisher]

**15. J Radiol. 2010 Dec;91(12-C2):1352-1359.****Presentation of a handicap, impairment and disability: the example of cerebral palsy. [Article in French]**

Heran F, Gastal A.

Fondation Rothschild service d'imagerie, 25 rue Manin 75019, Paris, France.

This article, co-authored by a functional therapist and a neuroradiologist, proposes a definition as well as a general overview of epidemiological, legal and clinical concerns related to the handicap followed by a more in-depth study of subjects with cerebral palsy or other brain motor handicap. This patient population contains an increasing number of adults. The effects of aging and the increased incidence of lethal malignancies in this population will be reviewed. The role of imaging in the management of these patients, its key features and related pitfalls are discussed. Finally, the role of MR imaging of the brain in patients with cerebral palsy is discussed with emphasis on the relation between lesion type and impairment, imaging characteristics and injury mechanism.

PMID: 21242933 [PubMed - as supplied by publisher]

**16. J Surg Orthop Adv. 2010 Winter;19(4):196-9.****Open versus percutaneous tendo-achilles lengthening in spastic cerebral palsy with equines deformity of the foot in children.**

Jaddue DA, Abbas MA, Sayed-Noor AS.

Department of Orthopaedic Surgery, Al-Kindy Teaching Hospital, Baghdad, Iraq.

The purpose of this study was to compare open to percutaneous tendo-achilles lengthening (TAL) as treatment for equinus deformity (ED) in children with cerebral palsy (CP). Eighteen ambulatory spastic CP children (28 feet) with isolated primary fixed ED were randomized to these two methods and prospectively followed up 7 to 18 months postoperatively (mean 11 months). The study found that the percutaneous TAL gave shorter operative time, shorter hospitalization period, better active dorsal and plantarflexion abilities, better parent satisfaction, and lower complication rate. It was concluded that percutaneous TAL seemed to be superior to the open TAL regarding the studied parameters.

PMID: 21244805 [PubMed - in process]

**17. Res Dev Disabil. 2011 Jan 15. [Epub ahead of print]****Emergent literacy activities, instructional adaptations and school absence of children with cerebral palsy in special education.**

Peeters M, de Moor J, Verhoeven L.

Science Hub, Institute for Science Innovation and Society, Radboud University, the Netherlands.

The goal of the present study was to get an overview of the emergent literacy activities, instructional adaptations and school absence of children with cerebral palsy (CP) compared to normally developing peers. The results showed that there were differences between the groups regarding the amount of emergent literacy instruction. While time dedicated to storybook reading and independent picture-book reading was comparable, the children with CP received fewer opportunities to work with educational software and more time was dedicated to rhyming games and singing. For the children with CP, the level of speech, intellectual, and physical impairments were all related to the amount of time in emergent literacy instruction. Additionally, the amount of time reading precursors is trained and the number of specific reading precursors that is trained is all related to skills of emergent literacy.

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PMID: 21242056 [PubMed - as supplied by publisher]

**18. Rev Med Chir Soc Med Nat Iasi. 2010 Jul-Sep;114(3):748-52.****Clinico-radiologic correlations in cerebral palsy [Article in Romanian]**

Grigore I, Diaconu G.

Facultatea de Medicină, Doctorand al Universității de Medicină Si Farmacie Gr. T. Popa Iași.

The aim of this study was to determine clinico-radiologic correlations, using cranial magnetic resonance imaging (IRM)/computed tomographic exam (CT), in cerebral palsy (CP). MATERIAL AND METHOD: We studied 129 children (86 males, 43 females; aged 2-18 years) diagnosed with different types of CP. Computed tomographic examinations was performed in 100 (77.52%) of children and IRM in 29 (22.48%). RESULTS: In 19 (14.72%) children the neuroimaging exam was normal. At 110 (85.28%) patients the IRM/CT showed different types of abnormalities. The most common neuroimaging findings was ventriculomegaly (38 cases), followed by focal infarct (28 cases), periventricular leukomalacia (17 cases), cortical and cortical/subcortical atrophy (13 cases), basal ganglia lesions (12 cases) and cortical migration and organization problems (12 cases). The CT/IRM abnormalities was associated in 65.45% of cases with mental retardation and 44.54% presented epileptic seizures. In CP neuroimaging findings

are common, but variable and IRM/CT change correlates with neurological assessment. **CONCLUSION:** Patients with CP and mental retardation or/and epilepsy were more likely to have obvious CT/IRM changes.

PMID: 21243802 [PubMed - in process]

#### 19. *Acta Ortop Mex.* 2010 Sep-Oct;24(5):331-7.

##### **Neuromotor assessment of patients with spastic cerebral palsy treated with orthopedic surgery at the National Rehabilitation Institute [Article in Spanish]**

Piana AR, Viñals CL, Del Valle MC, Arellano MS, Redón AT, Peralta SC, León SL.

Servicio de Parálisis Cerebral y Estimulación Temprana perteneciente a la División de Rehabilitación Pediátrica del Instituto Nacional de Rehabilitación. andreapiana@yahoo.com

**BACKGROUND:** Cerebral palsy (CP) is a static neurologic condition resulting from a brain lesion occurring before the completion of brain development. The goal of management is not cure, but increasing patients' functionality and improving their capabilities and maintaining their locomotion, cognitive development, social interaction and independence. The best results are obtained with an early and intensive management that includes physical and occupational therapy, medical and surgical treatments, mechanical aids and the management of concomitant conditions. **OBJECTIVE:** To assess the neuromotor improvement in patients with spastic CP after surgical treatment at the National Rehabilitation Institute.

**PATIENTS AND METHODS:** Patients with a diagnosis of spastic CP who presented at the Pediatric Rehabilitation outpatient service were referred to the Joint CP Clinic from January 2007 to January 2008, and underwent surgical treatment of the pelvic limbs. They were assessed 3 times and underwent neuromotor tests with gross motor function measure (GMFM), which was rated with the gross motor function classification system (GMFCS). **RESULTS:** Most of the patients had improvement in the muscle tone and contracture assessments as well as in the GMFM, and their self-mobility increased one level. **CONCLUSIONS:** Significant improvements were seen in the muscle tone and contractures after surgery; the GMFM and the self-mobility levels in the GMFCS also improved. Multiple level surgery together with a postoperative physical therapy program results in considerable improvements in the gross motor function measure of patients with spastic CP.

PMID: 21246805 [PubMed - in process]

## Epidemiology / Aetiology / Diagnosis & Early Treatment

#### 20. *Acta Paediatr.* 2011 Jan 18. doi: 10.1111/j.1651-2227.2011.02136.x. [Epub ahead of print]

##### **The risk of psychiatric disorders in individuals born prematurely in Denmark from 1974 to 1996.**

Mathiasen R, Hansen BM, Forman JL, Kessing LV, Greisen G.

Department of Neonatology, Copenhagen University Hospital, Rigshospitalet, Copenhagen, Denmark Department of Biostatistics, University of Copenhagen, Copenhagen, Denmark Department of Psychiatry, Copenhagen University Hospital, Rigshospitalet, Copenhagen, Denmark.

**Aim:** To investigate the risk of developing psychiatric disorders in individuals born prematurely (born before 37 weeks of gestation). **Methods:** The study is a longitudinal register-based study including all live-born individuals in Denmark from 1974 to 1996. Poisson regression models including well-known confounders were used to investigate the rate ratio of psychiatric disorders at the age of 11-34 years in the individuals born prematurely. **Results:** A total of 1,545,641 individuals were born from 1974 to 1996. Of these, 1,348,106 live-born individuals constituted the study cohort. Rate ratios of psychiatric disorders, in total, increased in proportion to the degree of prematurity. The rate ratio of major psychiatric disorder was increased in individuals born with a gestational age below 28 weeks compared to persons born with a gestational age of 39-45 weeks (RR = 1.88 (95% CI: 1.25-2.83)). Similarly, the rate ratios of minor psychiatric disorder (RR = 1.63 (95% CI: 1.29-2.06)) and psychotropic drugs purchased (RR =

1.35 (95% CI: 0.98-1.86)) were increased. Conclusion: The risk of minor as well as major psychiatric disorders during adolescence and young adulthood increases in proportion to the degree of prematurity. The relative risk, however, is small compared to the risks of cerebral palsy or low intelligence.

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PMID: 21244484 [PubMed - as supplied by publisher]

## 21. BMC Pediatr. 2011 Jan 17;11(1):6. [Epub ahead of print]

### **NeOProm: Neonatal Oxygenation Prospective Meta-analysis Collaboration study protocol.**

Askie LM, Brocklehurst P, Darlow BA, Finer N, Schmidt B, Tarnow-Mordi W, Neoprom NC.

**BACKGROUND:** The appropriate level of oxygenation for extremely preterm neonates (<28 weeks' gestation) to maximise the greatest chance of survival, without incurring significant morbidity, remains unknown. Infants exposed to lower levels of oxygen (targeting oxygen saturations of <90%) in the first weeks of life are at increased risk of death, cerebral palsy, patent ductus arteriosus, pulmonary vascular resistance and apnoea, whilst those maintained in higher levels of oxygen (targeting oxygen saturations of greater than or equal to 90%) have been reported to have greater rates of morbidity including retinopathy of prematurity and chronic lung disease. In order to answer this clinical dilemma reliably, large scale trial evidence is needed. **METHODS:** To detect a small but important 4% increase in death or severe disability in survivors, over 5000 neonates would need to be recruited. As extreme prematurity affects 1% of births, such a project undertaken by one trial group would be prohibitively lengthy and expensive. Hence, the Neonatal Oxygenation Prospective Meta-analysis (NeOProm) Collaboration has been formed. A prospective meta-analysis (PMA) is one where studies are identified, evaluated, and determined to be eligible before the results of any included studies are known or published, thereby avoiding some of the potential biases inherent in standard, retrospective meta-analyses. This methodology provides the same strengths as a single large-scale multicentre randomised study whilst allowing greater pragmatic flexibility. The NeOProm Collaboration protocol (NCT01124331) has been agreed prior to the results of individual trials being available. This includes pre-specifying the hypotheses, inclusion criteria and outcome measures to be used. Each trial will first publish their respective results as they become available and the combined meta-analytic results, using individual patient data, will be published when all trials are complete. The primary outcome to be assessed is a composite outcome of death or major disability at 18 months - 2 years corrected age. Secondary outcomes include several measures of neonatal morbidity. The size of the combined dataset will allow the effect of the interventions to be explored more reliably with respect to pre-specified patient- and intervention-level characteristics. **DISCUSSION:** Results should be available by 2014.

PMID: 21235822 [PubMed - as supplied by publisher]

## 22. Exp Neurol. 2011 Jan 12. [Epub ahead of print]

### **Effects of Fetal Exposure to Lipopolysaccharide, Perinatal Anoxia and Sensorimotor Restriction on Motor Skills and Musculoskeletal tissue: Implications for an Animal Model of Cerebral Palsy.**

Stigger F, Felizzola AL, Kronbauer GA, Couto GK, Achaval M, Marcuzzo S.

Programa de Pós-Graduação em Neurociências, Instituto de Ciências Básicas da Saúde, Universidade Federal do Rio Grande do Sul, RS, Brazil; Laboratório de Histofisiologia Comparada, Departamento de Ciências Morfológicas, Instituto de Ciências Básicas da Saúde, Universidade Federal do Rio Grande do Sul, RS, Brazil.

Cerebral palsy (CP) is a disorder of locomotion, posture and movement that can be caused by prenatal, perinatal or postnatal insults during brain development. An increased incidence of CP has been correlated to perinatal asphyxia and maternal infections during gestation. The effects of maternal exposure to low doses of bacterial endotoxin (lipopolysaccharide, LPS) on motor behavior and hind leg muscle morphology were examined in young adult rats. Prenatal exposure to LPS was also studied in association with perinatal anoxia (PA) and /or combined with subsequent sensorimotor restriction (SR) and all possible combinations of the three conditions. Rats exposed to LPS, PA and SR alone or combined (LPS+PA, LPS+SR, PA+SR, LPS+PA+SR) showed deficits in balance and coordination when tested on the Rotarod. The SR groups, with or without other insults, (SR, LPS+SR, PA+SR, LPS+PA+SR)

exhibited the greatest motor deficits, characterized by the reduced ability to perform the horizontal ladder and suspended bar tests on postnatal day 29 (P29) and P45. Histological assessment revealed substantial morphological alterations in the slow ankle extensor soleus muscle of all SR rats. Soleus myofibers presented a reduction in cross-sectional area (CSA), an increase in sarcomere length and a decrease in sarcomere density. The CSA of the fast flexor tibialis anterior muscle was only decreased by the association of all treatments (LPS, PA, SR), but no differences were found in sarcomere length and density when compared to control. A slow-to-fast fiber type transition was only observed in the soleus and tibialis anterior muscles in the SR groups. These results suggest that exposure to LPS during the prenatal period, PA, SR alone or in combination have various degrees of consequences on motor behavior and muscle morphology. These data corroborate the concept that early experience-dependent movements play the most important role in shaping motor behavior and that reduced or anomalous sensorimotor experience can contribute to the development of aberrant motor behavior and muscle morphology.

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### 23. PLoS One. 2011 Jan 13;6(1):e16211.

#### **Murine cytomegalovirus infection of neural stem cells alters neurogenesis in the developing brain.**

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**BACKGROUND:** Congenital cytomegalovirus (CMV) brain infection causes serious neuro-developmental sequelae including: mental retardation, cerebral palsy, and sensorineural hearing loss. But, the mechanisms of injury and pathogenesis to the fetal brain are not completely understood. The present study addresses potential pathogenic mechanisms by which this virus injures the CNS using a neonatal mouse model that mirrors congenital brain infection. This investigation focused on, analysis of cell types infected with mouse cytomegalovirus (MCMV) and the pattern of injury to the developing brain. **METHODOLOGY/PRINCIPAL FINDINGS:** We used our MCMV infection model and a multi-color flow cytometry approach to quantify the effect of viral infection on the developing brain, identifying specific target cells and the consequent effect on neurogenesis. In this study, we show that neural stem cells (NSCs) and neuronal precursor cells are the principal target cells for MCMV in the developing brain. In addition, viral infection was demonstrated to cause a loss of NSCs expressing CD133 and nestin. We also showed that infection of neonates leads to subsequent abnormal brain development as indicated by loss of CD24(hi) cells that incorporated BrdU. This neonatal brain infection was also associated with altered expression of Oct4, a multipotency marker; as well as down regulation of the neurotrophins BDNF and NT3, which are essential to regulate the birth and differentiation of neurons during normal brain development. Finally, we report decreased expression of doublecortin, a marker to identify young neurons, following viral brain infection.

**CONCLUSIONS:** MCMV brain infection of newborn mice causes significant loss of NSCs, decreased proliferation of neuronal precursor cells, and marked loss of young neurons.

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