

Monday 22 February 2010

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. *Ann Biomed Eng.* 2010 Feb 17. [Epub ahead of print]

How Crouch Gait Can Dynamically Induce Stiff-Knee Gait.

van der Krogt MM, Bregman DJ, Wisse M, Doorenbosch CA, Harlaar J, Collins SH.

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Children with cerebral palsy frequently experience foot dragging and tripping during walking due to a lack of adequate knee flexion in swing (stiff-knee gait). Stiff-knee gait is often accompanied by an overly flexed knee during stance (crouch gait). Studies on stiff-knee gait have mostly focused on excessive knee muscle activity during (pre) swing, but the passive dynamics of the limbs may also have an important effect. To examine the effects of a crouched posture on swing knee flexion, we developed a forward-dynamic model of human walking with a passive swing knee, capable of stable cyclic walking for a range of stance knee crouch angles. As crouch angle during stance was increased, the knee naturally flexed much less during swing, resulting in a 'stiff-knee' gait pattern and reduced foot clearance. Reduced swing knee flexion was primarily due to altered gravitational moments around the joints during initial swing. We also considered the effects of increased push-off strength and swing hip flexion torque, which both increased swing knee flexion, but the effect of crouch angle was dominant. These findings demonstrate that decreased knee flexion during swing can occur purely as the dynamical result of crouch, rather than from altered muscle function or pathoneurological control alone.

PMID: 20162360 [PubMed - as supplied by publisher]

2. *Dev Med Child Neurol.* 2010 Feb 12. [Epub ahead of print]

Thickened saliva after effective management of drooling with botulinum toxin A.

Erasmus CE, VAN Hulst K, VAN DEN Hoogen FJ, VAN Limbeek J, Roeleveld N, Veerman EC, Rotteveel JJ, Jongerius PH.

Department of Paediatric Neurology, Radboud University Nijmegen Medical Centre/Donders Institute for Brain, Cognition and Behaviour, the Netherlands.

Aim: The aim of this study was to evaluate the rheological properties of saliva after submandibular botulinum toxin type A (BoNT-A) injections. **Method:** We enrolled 15 children (11 males and six females; age range 3-17y, mean age 9y 10mo) diagnosed with spastic (n=9) or dyskinetic (n=6) quadriplegic cerebral palsy (CP); Gross Motor Function Classification System level IV or V; and two children with intellectual disability (IQ <70) who experienced moderate to severe drooling. Salivary flow rate and drooling quotient were measured at baseline and at different times after BoNT-A injections up to 24 weeks. The mucin concentration of saliva was analysed before and after

BoNT-A treatment. Results: Both submandibular salivary flow rate (baseline 0.38mL/min; 24wks after injection 0.26mL/min) and drooling quotient (baseline 42.5%; 24wks 28.80%) were substantially reduced, with a concomitant increase in mucin concentration within 8 weeks after BoNT-A injection (from 0.612 to 1.830U/mL). The parents of nine children observed thickened saliva. Swallowing and chewing were problematic in seven children. Two of these children needed treatment with mucolytics because of pooling of thickened saliva in the throat. Interpretation: When making decisions about the use of BoNT-A, the risk of problems with masticatory and swallowing functions as a result of thickening of saliva after BoNT-A treatment should be taken into account.

PMID: 20163435 [PubMed - as supplied by publisher]

3. Dev Med Child Neurol. 2010 Feb 12. [Epub ahead of print]

Precision and content range of a parent-reported item bank assessing lower extremity and mobility skills in children with cerebral palsy.

Gorton Iii GE, Watson K, Tucker CA, Tian F, Montpetit K, Haley SM, Mulcahey MJ.

Shriners Hospitals for Children, Springfield, MA, USA.

Aim: The aim of this study was to determine the psychometric properties, content range, and measurement precision of a lower extremity physical functioning and mobility skills item bank (LE85) in children with cerebral palsy (CP). **Method:** Lower extremity functioning and mobility skill items were administered to 308 parents of children (169 males, 139 females; mean age 10y 8mo, SD 4y) with spastic CP (145 diplegia, 73 hemiplegia, 89 quadriplegia; [for one person type of CP was unknown]) classified using the Gross Motor Function Classification System (75 level I, 91 level II, 79 level III, 37 level IV, 26 level V). Additional legacy measures were administered to assess concurrent validity. Psychometric characteristics, differential item functioning, content range, and score precision were examined. **Results:** The LE85 had acceptable psychometric properties. Content range matched the ability range of the sample population and exceeded legacy measures with minimal differential item functioning. The LE85 had good correlation with the Paediatric Outcomes Data Collection Instrument, Functional Independence Measure for Children, Gillette Functional Assessment Questionnaire, and Paediatric Quality of Life Inventory - CP module (range $r=0.63-0.86$). Precision of the LE85 and 10-item simulated computer adaptive test scores outperformed legacy measures. **Interpretation:** The LE85 appears to be suitable to administer as a computer adaptive test to measure lower extremity physical functioning and mobility in children with CP.

PMID: 20163428 [PubMed - as supplied by publisher]

4. Arch Phys Med Rehabil. 2010 Feb;91(2):178-183.

The Business Case for Adult Disability Care Coordination.

Palsbo SE, Diao G.

Center for the Study of Chronic Illness and Disability, George Mason University, Fairfax, VA.

OBJECTIVE: To analyze the financial performance of a care coordination program. **DESIGN:** The study used a retrospective pretest, posttest design of 245 beneficiaries. Physical impairment ranged from slight to severe. **SETTING:** Minnesota Disability Health Options (MnDHO), a capitated Medicaid program. **PARTICIPANTS:** Medicaid beneficiaries ages 18 to 64 with physical disabilities arising from multiple sclerosis, cerebral palsy, spinal cord injury, or brain injury. **INTERVENTIONS:** Not applicable. **MAIN OUTCOMES MEASURES:** Change in expenditures, rate of return, and utilization. **RESULTS:** Mean MnDHO monthly expenditures including care coordination increased by a factor of 1.75 ($P<.001$) over the previous expenditures. Increasing age has a multiplier effect on increased expenditures. Hospitalization rates were unchanged, but the average cost per admission and average length of stay dropped significantly ($P=.017$, $P=.032$, respectively). For people enrolled at least 3 years, annual reductions in medical costs more than paid for the added cost of care coordination, but the savings in Year 3 were about 20% of the savings in the first 2 years. **CONCLUSIONS:** Care coordination leads to higher program expenditures for enrollees with moderate physical impairments who encounter access problems, but has little impact on enrollees who are already getting 24-hour care. There is some evidence of adverse selection bias. MnDHO's disability care coordination may not be financially sustainable over the long term. Copyright © 2010 American Congress of Rehabilitation

tion Medicine. Published by Elsevier Inc. All rights reserved.

PMID: 20159118 [PubMed - as supplied by publisher]

5. Acta Orthop Belg. 2009 Dec;75(6):808-14.

Does tendon lengthening surgery affect muscle tone in children with cerebral palsy?

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The objective of this study was to determine if surgical lengthening of the hamstrings and gastrocnemius/Achilles complex affects muscle tone in patients with cerebral palsy. The question was if the dynamic component of muscle length changes after orthopedic surgery. A retrospective study was performed on ambulatory children with cerebral palsy who underwent either hamstring lengthening or gastrocnemius/Achilles tendon lengthening. A total of 135 consecutive patients with an average age of 13 years were included in the study. A single random side was selected for children with bilateral surgery and the affected limb was analyzed for those undergoing unilateral surgery. The popliteal angle measurement was performed with a quick and slow stretch, as well as the ankle dorsiflexion, and measurements were made using a goniometer. The difference (delta ml) between initial grab with fast stretch and end of range (EOR) with slow stretch was used as a measure of spasticity. The Bohannon modification of the Ashworth score was also assessed. Postoperatively, 18 degrees popliteal angle improvement in end-of-range and 32 degrees improvement in quick stretch in the hamstrings group were noted, with change in slow stretch, quick stretch and delta ml (comparison between quick and slow stretch) being significant at $p < .0001$. In the triceps surae group, 14 degrees ankle dorsiflexion improvement in end-of-range, and 18 degrees improvement in quick stretch were noted postoperatively, with change in slow stretch, quick stretch and delta ml at $p < .0001$, $p < .0001$, and $p < .0180$ respectively. Ashworth scale was reduced by at least one grade in 89% of subjects in the hamstring group and 78% of subjects in the triceps surae group of the children with preoperative Ashworth 3 and above.

PMID: 20166364 [PubMed - in process]

6. Aust J Physiother. 2009;55(4):291; author reply 292.

Should we change practice?

Lancaster A, Mudge A, Wu J, Lewis J, Bau K.

Comment on:

Aust J Physiother. 2009;55(2):81-7.

PMID: 19929779 [PubMed - indexed for MEDLINE]

Epidemiology / Aetiology / Diagnosis & Early Treatment

Please note: *This is not yet a comprehensive outline of cerebral palsy prevention literature. It is expected that more research will be included when the search terms are expanded to include key terms other than "cerebral palsy". It is a work-in-progress and it will be expanded in coming months.*

7. *Pediatr Neurol.* 2010 Mar;42(3):231-233.

Grade IV Fetal Intracranial Hemorrhage With Good Cognitive Function.

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Fewer than 200 cases of prenatally diagnosed magnetic resonance imaging-confirmed fetal intracranial hemorrhage have been reported. Children surviving grade IV fetal intracranial hemorrhage usually manifest severe impairments, including mental retardation. We report on a child with a grade IV intracranial hemorrhage diagnosed by in utero ultrasound at 28 weeks of gestation, and confirmed by fetal magnetic resonance imaging at 29 weeks of gestation. At age 27 months, she has a ventriculoperitoneal shunt and exhibits hemiplegic cerebral palsy, but without seizures, and with normal cognitive function and excellent verbal ability. We discuss how perinatal care may have contributed to her good outcome. Copyright © 2010 Elsevier Inc. All rights reserved.

PMID: 20159437 [PubMed - as supplied by publisher]

8. *BMC Pregnancy Childbirth.* 2010 Feb 18;10(1):8. [Epub ahead of print]

Antenatal allopurinol for reduction of birth asphyxia induced brain damage (ALLO-Trial); a randomized double blind placebo controlled multicenter study.

Kaandorp JJ, Benders MJ, Rademaker CM, Torrance HL, Oudijk MA, de Haan TR, Bloemenkamp KW, Rijken M, van Pampus MG, Bos AF, Porath MM, Bambang Oetomo S, Willekes C, Gavilanes AD, Wouters MG, van Elburg RM, Huisjes AJ, Bakker SC, van Meir CA, von Lindern J, Boon J, de Boer IP, Rijnders RJ, Jacobs CJ, Uiterwaal CS, Mol BW, Visser GH, van Bel F, Derks JB.

BACKGROUND: Hypoxic-ischaemic encephalopathy is associated with development of cerebral palsy and cognitive disability later in life and is therefore one of the fundamental problems in perinatal medicine. The xanthine-oxidase inhibitor allopurinol reduces the formation of free radicals, thereby limiting the amount of hypoxia-reperfusion damage. In case of suspected intra-uterine hypoxia, both animal and human studies suggest that maternal administration of allopurinol immediately prior to delivery reduces hypoxic-ischaemic encephalopathy. **METHODS:** The proposed trial is a randomized double blind placebo controlled multicenter study in pregnant women at term in whom the foetus is suspected of intra-uterine hypoxia. Allopurinol 500 mg IV or placebo will be administered antenatally to the pregnant woman when foetal hypoxia is suspected. Foetal distress is being diagnosed by the clinician as an abnormal or non-reassuring foetal heart rate trace, preferably accompanied by either significant ST-wave abnormalities (as detected by the STAN-monitor) or an abnormal foetal blood scalp sampling (pH < 7.20). Primary outcome measures are the amount of S100B (a marker for brain tissue damage) and the severity of oxidative stress (measured by isoprostane, neuroprostane, non protein bound iron and hypoxanthine), both measured in umbilical cord blood. Secondary outcome measures are neonatal mortality, serious composite neonatal morbidity and long-term neurological outcome. Furthermore pharmacokinetics and pharmacodynamics will be investigated. We expect an inclusion of 220 patients (110 per group) to be feasible in an inclusion period of two years. Given a suspected mean value of S100B of 1.05 ug/L (SD 0.37 ug/L) in the placebo group this trial has a power of 90% (alpha 0.05) to detect a mean value of S100B of 0.89 ug/L (SD 0.37 ug/L) in the 'allopurinol-treated' group (z-test 2-sided). Analysis will be by intention to treat and it allows for one interim analysis. **DISCUSSION:** In this trial we aim to answer the question whether antenatal allopurinol administration reduces hypoxic-ischaemic encephalopathy in neonates exposed to foetal hypoxia. Trial registration number Clinical Trials, protocol registration system: NCT00189007.

PMID: 20167117 [PubMed - as supplied by publisher]

9. *Pediatr Neurol.* 2010 Mar;42(3):177-180.

CP or Not CP? A Review of Diagnoses in a Cerebral Palsy Register.

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The purpose of this study was to document the inaccuracy rate of diagnosis of cerebral palsy recorded on the South Australian Cerebral Palsy Register. A total of 402 children born in South Australia from 1993 to 2002 and notified to the Register as having cerebral palsy were identified through the Register database, and 21 children (5.2%) were later identified to have a noncerebral palsy diagnosis. Of these, 5 had either a metabolic or a neurodegenerative disorder and 2 had a syndromic disorder (1 Joubert syndrome and 1 Sotos syndrome); the remaining 14 children had one of the following final diagnoses: developmental delay, gross motor delay, perinatal myositis, spinal subdural and subarachnoid arteriovenous malformation, and Erb's palsy. In 16 of 21 children (76%), the diagnosis was changed at 5 years of age or older. Studies based on population registers may need to take into account the possibility of misclassification, estimated to be at least 5.2% in this study. A complete clinical assessment at the time of diagnosis followed by regular reassessment would enable the clinician to exclude children with alternative diagnoses, which has important implications for clinical management and research based on cerebral palsy registers. Crown Copyright © 2010. Published by Elsevier Inc. All rights reserved.

PMID: 20159426 [PubMed - as supplied by publisher]

10. *Dev Med Child Neurol.* 2010 Feb 12. [Epub ahead of print]

Predictors of cerebral palsy in very preterm infants: the EPIPAGE prospective population-based cohort study.

Beaino G, Khoshnood B, Kaminski M, Pierrat V, Marret S, Matis J, Ledésert B, Thiriez G, Fresson J, Rozé JC, Zupan-Simunek V, Arnaud C, Burguet A, Larroque B, Bréart G, Ancel PY; for the EPIPAGE Study Group.

INSERM, UMR S953, Epidemiological Research Unit on Perinatal Health and Women's and Children's Health, Hôpital Tenon, Paris, France.

Aim: The aim of this study was to assess the independent role of cerebral lesions on ultrasound scan, and several other neonatal and obstetric factors, as potential predictors of cerebral palsy (CP) in a large population-based cohort of very preterm infants. **Method:** As part of EPIPAGE, a population-based prospective cohort study, perinatal data and outcome at 5 years of age were recorded for 1812 infants born before 33 weeks of gestation in nine regions of France in 1997. **Results:** The study group comprised 942 males (52%) and 870 females with a mean gestational age of 30 weeks (SD 2wks; range 24-32wks) and a mean birthweight of 1367g (SD 393g; range 450-2645g). CP was diagnosed at 5 years of age in 159 infants (prevalence 9%; 95% confidence interval [CI] 7-10%), 97 males and 62 females, with a mean gestational age of 29 weeks (SD 2wks; range 24-32wks) and a mean birthweight of 1305g (SD 386g; range 500-2480g). Among this group, 67% walked without aid, 14% walked with aid, and 19% were unable to walk. Spastic, ataxic, and dyskinetic CP accounted for 89%, 7%, and 4% of cases respectively. The prevalence of CP was 61% among infants with cystic periventricular leukomalacia, 50% in infants with intraparenchymal haemorrhage, 8% in infants with grade I intraventricular haemorrhage, and 4% in infants without a detectable cerebral lesion. After controlling for cerebral lesions and obstetric and neonatal factors, only male sex (odds ratio [OR] 1.52; 95% CI 1.03-2.25) and preterm premature rupture of membranes or preterm labour (OR 1.72; 95% CI 0.95-3.14) were predictors of the development of CP in very preterm infants. **Interpretation:** Cerebral lesions were the most important predictor of CP in very preterm infants. In addition, infant sex and preterm premature rupture of membranes or preterm labour were also independent predictors of CP.

PMID: 20163431 [PubMed - as supplied by publisher]

11. Front Neuroengineering. 2010 Feb 8;2:18.**Bridging the Divide between Neuroprosthetic Design, Tissue Engineering and Neurobiology.**

Leach JB, Achyuta AK, Murthy SK.

Department of Chemical and Biochemical Engineering, University of Maryland Baltimore, MD, USA.

Neuroprosthetic devices have made a major impact in the treatment of a variety of disorders such as paralysis and stroke. However, a major impediment in the advancement of this technology is the challenge of maintaining device performance during chronic implantation (months to years) due to complex intrinsic host responses such as gliosis or glial scarring. The objective of this review is to bring together research communities in neurobiology, tissue engineering, and neuroprosthetics to address the major obstacles encountered in the translation of neuroprosthetics technology into long-term clinical use. This article draws connections between specific challenges faced by current neuroprosthetics technology and recent advances in the areas of nerve tissue engineering and neurobiology. Within the context of the device-nervous system interface and central nervous system implants, areas of synergistic opportunity are discussed, including platforms to present cells with multiple cues, controlled delivery of bioactive factors, three-dimensional constructs and in vitro models of gliosis and brain injury, nerve regeneration strategies, and neural stem/progenitor cell biology. Finally, recent insights gained from the fields of developmental neurobiology and cancer biology are discussed as examples of exciting new biological knowledge that may provide fresh inspiration toward novel technologies to address the complexities associated with long-term neuroprosthetic device performance.

PMID: 20161810 [PubMed - in process]

12. J Pediatr. 2010 Jan;156(1):49-53.e1.**Outcomes at age 2 years of infants < 28 weeks' gestational age born in Victoria in 2005.**

Doyle LW, Roberts G, Anderson PJ; Victorian Infant Collaborative Study Group.

Collaborators (18) Callanan C, Carse E, Charlton MP, Davey MA, Davis N, Duff J, Hunt R, de Luca C, Hayes M, Hutchinson E, Kelly E, McDonald M, Opie G, Stewart M, Ung L, Watkins A, Williamson A, Woods H. Newborn Services, Royal Women's Hospital, Melbourne, Australia. lwd@unimelb.edu.au

OBJECTIVE: To determine the survival rates and neurosensory outcomes of infants born at gestational age 22-27 weeks in the state of Victoria in 2005 and compare these data with those for similar infants born in the 1990s. **STUDY DESIGN:** This was a population-based study of all extremely preterm (22-27 weeks' gestational age) live births in Victoria in 2005 free of lethal anomalies and randomly selected term controls. Survival and quality-adjusted survival rates at age 2 years were determined relative to the controls, and results were compared with regional extremely preterm cohorts born in 1991-92 and 1997. **RESULTS:** Of 270 very preterm live births in 2005, 172 (63.7%) survived to 2 years, not significantly different from the survival rate of 69.6% for those born in 1997. Rates of severe developmental delay and severe disability were lower than in the very preterm survivors born in 1997. Quality-adjusted survival rates in the extremely preterm cohorts rose from 42.1% in 1991-92 to 55.1% in 1997, but did not increase in 2005 (53.4%). **CONCLUSIONS:** Survival rates for infants born at 22-27 weeks' gestational age have not increased since the late 1990s, but the neurosensory outcome in survivors has improved.

PMID: 19783004 [PubMed - indexed for MEDLINE]

13. Obstet Gynecol. 2009 Nov;114(5):1115-20.**Periventricular leukomalacia and placental histopathologic abnormalities.**

Maleki Z, Bailis AJ, Argani CH, Askin FB, Graham EM.

From the 1 Department of Pathology and 2 Department of Gynecology & Obstetrics, Division of Maternal-Fetal Medicine, Johns Hopkins University School of Medicine, Baltimore, Maryland.

OBJECTIVE: To estimate whether there are placental histopathologic abnormalities associated with neonatal periventricular leukomalacia (PVL), a major precursor of cerebral palsy. **METHODS:** This is a case-control study of 167 neonates born between 23 and 34 weeks of gestation diagnosed with PVL by head ultrasonography within 6 weeks of birth, and 167 control neonates without neurologic morbidity matched by gestational age. Placentas for both case neonates and control neonates were reviewed by two perinatal pathologists who were blinded to neonatal course. **RESULTS:** Neonates with PVL were significantly more likely to have positive neonatal blood (28.7%, 16.8%, $P=.001$) and cerebrospinal fluid (14.4%, 4.8%, $P=.007$) cultures. The ratio of placental weight to birth weight did not differ between groups, but neonates with PVL had significantly more chronic diffuse capsular deciduitis (20.4%, 10.8%, $P=.02$) and capsular decidual plasma cells (8.4%, 2.4%, $P=.02$). Conditional logistic regression adjusting for birth weight and the presence of multiple gestation in the identification of PVL showed a significant increase for diffuse capsular deciduitis ($P=.02$) and capsular decidual plasma cells ($P=.03$). **CONCLUSION:** Periventricular leukomalacia has a significant but weak association with chronic diffuse capsular deciduitis and the presence of capsular decidual plasma cells, evidence of chronic infection but not histologic acute chorioamnionitis. **LEVEL OF EVIDENCE:** II.

PMID: 20168115 [PubMed - in process]