

Monday 1 August 2011

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

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## Interventions and Management

### 1. Clin Rehabil. 2011 Jul 27. [Epub ahead of print]

**Responsiveness of Goal Attainment Scaling in comparison to two standardized measures in outcome evaluation of children with cerebral palsy.**

Steenbeek D, Gorter JW, Ketelaar M, Galama K, Lindeman E.

Revant Rehabilitation Centre Breda and Partner of NetChild, Network for Childhood Disability Research in the Netherlands, The Netherlands.

**Objectives:** To assess the responsiveness of Goal Attainment Scaling compared with the Pediatric Evaluation of Disability Inventory (PEDI) and the 66-item Gross Motor Function Measure (GMFM-66) in multidisciplinary rehabilitation practice. **Design:** Observational study. Pretest-posttest design. **Subjects/patients:** Twenty-three children with cerebral palsy, aged 2-13 years. **Methods:** Goal Attainment Scaling, PEDI and GMFM-66 assessments were performed before and after six months of treatment. Physical, occupational and speech therapists constructed and scored 6-point Goal Attainment Scaling scales meeting predetermined criteria, describing the main functional goal per discipline. The contents of the three measures were compared using International Classification of Functioning, Disability and Health child and youth version (ICF-CY) codes. Spearman's rho correlations between Goal Attainment Scaling change scores per discipline and change scores obtained with the PEDI functional skills scales and GMFM-66 were calculated. Complete goal attainment was compared with significant change in terms of the standardized measures. **Results:** Twenty per cent of the Goal Attainment Scaling items were not covered by items of the PEDI or the GMFM-66. Inconclusive correlations were found between Goal Attainment Scaling and PEDI change scores ( $r$  0.28-0.64). Even after exclusion of the non-corresponding items, correlations were moderate ( $r$  0.57-0.73). Of 39/64 Goal Attainment Scaling scales scored as complete goal attainment, 16 individual PEDI scores did not show change on the corresponding scale. Low correlation was found between Goal Attainment Scaling change scores and GMFM-66 change scores. **Conclusion:** Goal Attainment Scaling, PEDI and GMFM-66 were complementary in their ability to measure individual change over time in children with cerebral palsy. Using only the standardized instruments could have caused many individual rehabilitation goals actually attained being missed in the outcome evaluation.

PMID: 21795404 [PubMed - as supplied by publisher]

## 2. Am J Clin Nutr. 2011 Jul 27. [Epub ahead of print]

### Measuring body composition and energy expenditure in children with severe neurologic impairment and intellectual disability.

Rieken R, van Goudoever JB, Schierbeek H, Willemsen S, Calis EA, Tibboel D, Evenhuis HM, Penning C.

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**BACKGROUND:** Accurate prediction equations for estimating body composition and total energy expenditure (TEE) in children with severe neurologic impairment and intellectual disability are currently lacking. **OBJECTIVE:** The objective was to develop group-specific equations to predict body composition by using skinfold-thickness measurements and bioelectrical impedance analysis (BIA) and to predict TEE by using data on mobility, epilepsy, and muscle tone. **DESIGN:** Measures of body composition with the use of skinfold-thickness measurements (percentage of body fat) and BIA (total body water) were compared with those from isotope dilution (reference method) by using intraclass correlation coefficients (ICCs) and Bland and Altman limits of agreement analyses. With the use of the same methods, the outcomes of cerebral palsy-specific TEE equations were compared with those of the doubly labeled water method (reference method). Group-specific regression equations were developed by using forward-stepwise-multiple-correlation-regression analyses. **RESULTS:** Sixty-one children with a mean ( $\pm$ SD) age of  $10.1 \pm 4.3$  y (32 boys) were studied. A new equation based on the sum of 4 skinfold-thickness measurements did not improve agreement ( $n = 49$ ; ICC = 0.61), whereas the newly developed BIA equation-which includes tibia length as an alternative for standing height-did improve agreement ( $n = 61$ ; ICC = 0.96, SEE = 1.7 kg,  $R(2) = 0.92$ ). The newly developed TEE equation, which uses body composition, performed better ( $n = 52$ ; ICC = 0.87, SEE = 180 kcal,  $R(2) = 0.77$ ) than did the equation of Schofield ( $n = 52$ ; ICC = 0.82, SEE = 207 kcal,  $R(2) = 0.69$ ). **CONCLUSIONS:** Current cerebral palsy-specific equations for measuring body composition and energy expenditure are inaccurate. BIA is more accurate at assessing nutritional status in this population than is the measurement of skinfold thickness. The newly developed TEE equation, which uses body composition, provides a reasonable estimate of energy expenditure in these children despite its variability.

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## 3. Strategies Trauma Limb Reconstr. 2011 Jul 22. [Epub ahead of print]

### Guided growth for correction of knee flexion deformity: a series of four cases.

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Fixed knee flexion deformity can present as an insidious and significant problem in diverse etiologies, most commonly in cerebral palsy. Traditional surgical intervention has included posterior capsulotomy and supracondylar femoral osteotomy, both of which carry significant associated morbidity and risks. In the skeletally immature patient, guided growth may be used to correct or substantially diminish the deformity. We are presenting our early experience encompassing four subjects who completed instrumented gait analysis both prior to and after distal femoral anterior guided growth (hemiepiphysiodesis). Changes in gait and function resulting from surgery in each individual are reported. Outcomes indicate improved knee range of motion and alleviation of crouch at the knee with secondary improvements in the ankle, hip and pelvis. Three subjects with initially slow gait velocity improved to within normal limits by demonstrating increased stride length. A measure of overall gait kinematics showed improvements in all limbs. Anterior guided growth (hemiepiphysiodesis) of the distal femur resulted in positive quantitative changes in all four patients, though degree and types of changes were

variable in this small series. Encouraged by these findings, we now prefer guided growth to extension supracondylar osteotomy for the skeletally immature patient with fixed knee flexion deformity.

PMID: 21785910 [PubMed - as supplied by publisher]

**4. Dev Med Child Neurol. 2011 Jul 26. doi: 10.1111/j.1469-8749.2011.04061.x. [Epub ahead of print]**

**Coordination of fingertip forces in object transport during gait in children with hemiplegic cerebral palsy.**

Prabhu SB, Diermayr G, Gysin P, Gordon AM.

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PMID: 21790557 [PubMed - as supplied by publisher]

**5. Zhen Ci Yan Jiu. 2011 Jun;36(3):215-9.**

**Randomized controlled clinical trials for acupuncture treatment of spastic cerebral palsy children by bilateral horizontal puncturing from Yuzhen (BL 9) to Tianzhu (BL 10). [Article in Chinese]**

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**OBJECTIVE:** To observe the effect of acupuncture of the body surface projection region of the pyramidal decussation on spastic cerebral palsy (CP) so as to explore an effective therapy for it. **METHODS:** A total of 120 CP infant patients were randomized into control group (treated with modern rehabilitation training, n = 60) and acupuncture group (treated with acupuncture combined with modern rehabilitation training, n = 60). Four acupuncture needles were penetrated subcutaneously through the region between Yuzhen (BL 9) and Tianzhu (BL 10) equidistantly (the superficial projection region of the pyramidal decussation), once daily for 3 months. The modified Ashworth rating, gross motor function measure (GMFM)-88 scores and synthetic function scale were adopted to assess the therapeutic effect after the treatment. **RESULTS:** After the treatment, of the 59 and 58 CP children in the control and acupuncture groups, 17 (28.81%) and 26 (44.83%) experienced marked improvement in their symptoms, 33 (55.84%) and 27 (46.55%) had an improvement, 9 (15.25%) and 5 (8.62%) failed in the treatment, with the total effective rates being 84.75% and 91.38%, respectively. The effective rate of the acupuncture group was significantly superior to that of the control group (P < 0.05). The scores of modified Ashworth rating and GMFM-88 of the control group were significantly lower than those of the acupuncture group after the treatment (P < 0.05). **CONCLUSION:** Acupuncture combined with modern rehabilitation training is effective in the treatment of CP children patients.

PMID: 21793388 [PubMed - in process]

**6. Eur J Paediatr Neurol. 2011 Jul 21. [Epub ahead of print]**

**What could predict effectiveness of Botulinum Toxin to treat drooling: A search for evidence of discriminatory factors on the level of body functions or structures.**

Erasmus CE, van Hulst K, Scheffer AR, van Limbeek J, van den Hoogen FJ, Rotteveel JJ, Jongerius PH.

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Department of Paediatric Neurology, Nijmegen, The Netherlands.

**BACKGROUND:** The treatment of drooling is important to families that experience the daily impact and research to elucidate clinical factors that play a role in the outcome of drooling treatment should be encouraged. **AIM:** To define clinical factors that influence therapy outcome of submandibular Botulinum Toxin (BoNT-A) injections for drooling. **METHODS:** Prospectively collected data of 128 children with cerebral palsy were evaluated; 80 spastic and 48 dyskinetic movement disorder, mostly Gross Motor Function Classification System III and higher; over 70% had an IQ <70. In addition, 23 fully ambulant children with exclusively intellectual disability were treated for drooling by ultrasound-guided injections of BoNT-A into the submandibular glands. Salivary flow rates and drooling quotients were measured at baseline and at 8 weeks after injection. Extensive information about the oral motor performance was gathered. Successful clinical response was defined as a 50% reduction of the baseline Drooling Quotient; 85 children were responsive to BoNT-A and 66 children unresponsive. **RESULTS:** Five nominated clinical factors that possibly could influence saliva reduction (head position, lip seal, voluntary control over the tongue, control of voluntary movement functions, and mental age) did not influence the responsiveness to BoNT-A. **INTERPRETATION:** Other variables need to be considered to predict the outcome of BoNT-A treatment. This article describes the first attempt to reveal the contribution of body functions and structures to the outcome of BoNT-A submandibular injections.

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## 7. Clin Linguist Phon. 2011 Jul 25. [Epub ahead of print]

### Testing the language of German cerebral palsy patients with right hemispheric language organization after early left hemispheric damage.

Schwilling E, Krägeloh-Mann I, Konietzko A, Winkler S, Lidzba K.

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Language functions are generally represented in the left cerebral hemisphere. After early (prenatally acquired or perinatally acquired) left hemispheric brain damage language functions may be salvaged by reorganization into the right hemisphere. This is different from brain lesions acquired in adulthood which normally lead to aphasia. Right hemispheric reorganized language (RL) is not associated with obvious language deficits. In this pilot study we compared a group of German-speaking patients with left hemispheric brain damage and RL with a group of matched healthy controls. The novel combination of reliable language lateralization as assessed by neuroimaging (functional magnetic resonance imaging) and specific linguistic tasks revealed significant differences between patients with RL and healthy controls in both language comprehension and production. Our results provide evidence for the hypothesis that RL is significantly different from normal left hemispheric language. This knowledge can be used to improve counselling of parents and to develop specific therapeutic approaches.

PMID: 21787139 [PubMed - as supplied by publisher]

## 8. J Formos Med Assoc. 2011 Aug;110(8):527-36.

### Developmental profiles and temperament patterns in children with spastic cerebral palsy: relationships with subtypes and severity.

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Graduate Institute of Early Intervention, Department of Physical Therapy, Chang Gung University, Taoyuan, Taiwan; Department of Physical Medicine and Rehabilitation, Chang Gung Memorial Hospital, Linkou, Taiwan.

**BACKGROUND/PURPOSE:** Elucidating developmental profiles and temperament patterns in children with cerebral palsy (CP) could help clinicians elaborate more flexible strategies for treating these children. This study investigated the developmental profiles and temperament patterns in children with spastic CP (sCP) of different subtypes and severities. **METHODS:** One hundred and five children, aged 3-6 years, with sCP and 66 children with typical development (TD) were analyzed. Children with sCP were classified into spastic diplegia (SD; n = 60), and spastic quadriplegia (SQ; n = 45) groups. Motor severity was classified via the Gross Motor Function Classification System (GMFCS). Development quotients (DQs) of eight domains and temperament scores of nine dimensions were evaluated. **RESULTS:** The SQ group had lower DQs in all developmental functions than the SD group ( $p < 0.01$ ). The DQ distributions of developmental profiles showed the same trend in SD and SQ groups, and both groups displayed lowest DQs in the gross motor domain. The SQ group was less adaptable and approachable than the TD group ( $p < 0.05$ ), and both sCP groups had lower attention span and persistence and a higher threshold of responsiveness than the TD group ( $p < 0.05$ ). Correlation analysis showed that GMFCS levels were highly related to all developmental functions ( $r < -0.54$ ,  $p < 0.01$ ) and weakly related to some temperament dimensions in children with sCP. **CONCLUSION:** The subtype and severity of sCP were associated with developmental profiles in children with sCP. Temperament patterns were different between SD and SQ groups, but only weakly related to motor deficit. These data could allow clinicians to anticipate the developmental profiles and temperament patterns and plan appropriate therapeutic strategies for children with sCP.

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## 9. Arch Dis Child. 2011 Jul 27. [Epub ahead of print]

### Cardiovascular dysfunction in infants with neonatal encephalopathy.

Armstrong K, Franklin O, Sweetman D, Molloy EJ.

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Severe perinatal asphyxia with hypoxic ischaemic encephalopathy occurs in approximately 1-2/1000 live births and is an important cause of cerebral palsy and associated neurological disabilities in children. Multiorgan dysfunction commonly occurs as part of the asphyxial episode, with cardiovascular dysfunction occurring in up to a third of infants. This narrative paper attempts to review the literature on the importance of early recognition of cardiac dysfunction using echocardiography and biomarkers such as troponin and brain type natriuretic peptide. These tools may allow accurate assessment of cardiac dysfunction and guide therapy to improve outcome.

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## Prevention and Cure

10. Dev Neurosci. 2011 Jul 28. [Epub ahead of print]

### Magnitude of [C]PK11195 Binding Is Related to Severity of Motor Deficits in a Rabbit Model of Cerebral Palsy Induced by Intrauterine Endotoxin Exposure.

Kannan S, Saadani-Makki F, Balakrishnan B, Chakraborty P, Janisse J, Lu X, Muzik O, Romero R, Chugani DC.

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Intrauterine inflammation is known to be a risk factor for the development of periventricular leukomalacia (PVL) and cerebral palsy. In recent years, activated microglial cells have been implicated in the pathogenesis of PVL and in the development of white matter injury. Clinical studies have shown the increased presence of activated microglial cells diffusely throughout the white matter in brains of patients with PVL. In vitro studies have reported that activated microglial cells induce oligodendrocyte damage and white matter injury by release of inflammatory cytokines, reactive nitrogen and oxygen species and the production of excitotoxic metabolites. PK11195 [1-(2-chlorophenyl)-N-methyl-N-(1-methylpropyl)-3-isoquinoline carboxamide] is a ligand that is selective for the 18-kDa translocator protein expressed on the outer mitochondrial membrane of activated microglia and macrophages. When labeled with carbon-11, [(11)C]PK11195 can effectively be used as a ligand in positron emission tomography (PET) studies for the detection of activated microglial cells in various neuroinflammatory and neurodegenerative conditions. In this study, we hypothesized that the magnitude of [(11)C]-(R)-PK11195 uptake in the newborn rabbit brain, as measured using a small-animal PET scanner, would match the severity of motor deficits resulting from intrauterine inflammation-induced perinatal brain injury. Pregnant New Zealand white rabbits were intrauterinely injected with endotoxin or saline at 28 days of gestation. Kits were born spontaneously at 31 days and underwent neurobehavioral testing and PET imaging following intravenous injection of the tracer [(11)C]-(R)-PK11195 on the day of birth. The neurobehavioral scores were compared with the change in [(11)C]PK11195 uptake over the time of scanning, for each of the kits. Upon analysis using receiver operating characteristic curves, an optimal combined sensitivity and specificity for detecting abnormal neurobehavioral scores suggestive of cerebral palsy in the neonatal rabbit was noted for a positive change in [(11)C]PK11195 uptake in the brain over time on PET imaging (sensitivity of 100% and area under the curve of >0.82 for all parameters tested). The strongest agreements were noted between a positive uptake slope - indicating increased [(11)C]PK11195 uptake over time - and worsening scores for measures of locomotion (indicated by hindlimb movement, forelimb movement, circular motion and straight-line motion; Cohen's  $\kappa$  >0.75 for each) and feeding (indicated by ability to suck and swallow and turn the head during feeding; Cohen's  $\kappa$  >0.85 for each). This was also associated with increased numbers of activated microglia (mean ratio  $\pm$  SD of activated to total microglia:  $0.96 \pm 0.16$  in the endotoxin group vs.  $0.13 \pm 0.08$  in controls;  $p < 0.001$ ) in the internal capsule and corona radiata. Our findings indicate that the magnitude of [(11)C]PK11195 binding measured in vivo by PET imaging matches the severity of motor deficits in the neonatal rabbit. Molecular imaging of ongoing neuroinflammation in the neonatal period may be helpful as a screening biomarker for detecting patients at risk of developing cerebral palsy due to a perinatal insult.

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11. J Pediatr. 2011 Jul 26. [Epub ahead of print]

**Cytokines and Neurodevelopmental Outcomes in Extremely Low Birth Weight Infants.**

Carlo WA, McDonald SA, Tyson JE, Stoll BJ, Ehrenkranz RA, Shankaran S, Goldberg RN, Das A, Schendel D, Thorsen P, Skogstrand K, Hougaard DM, Oh W, Laptook AR, Duara S, Fanaroff AA, Donovan EF, Korones SB, Stevenson DK, Papile LA, Finer NN, O'Shea TM, Poindexter BB, Wright LL, Ambalavanan N, Higgins RD; Eunice Kennedy Shriver National Institute of Child Health and Human Development Neonatal Research Network.

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**OBJECTIVE:** To determine if selected pro-inflammatory and anti-inflammatory cytokines and/or mediators of inflammation reported to be related to the development of cerebral palsy (CP) predict neurodevelopmental outcome in extremely low birth weight infants. **STUDY DESIGN:** Infants with birth weights  $< 1000$  g ( $n = 1067$ ) had blood samples collected at birth and on days  $3 \pm 1$ ,  $7 \pm 1$ ,  $14 \pm 3$ , and  $21 \pm 3$  to examine the association between cytokines and neurodevelopmental outcomes. The analyses were focused on 5 cytokines (interleukin [IL]  $1\beta$ ; IL-8; tumor necrosis factor- $\alpha$ ; regulated upon activation, normal T-cell expressed, and secreted (RANTES); and IL-2) reported to be most predictive of CP in term and late preterm infants. **RESULTS:** IL-8 was higher on days 0-4 and subsequently in infants who developed CP compared with infants who did not develop CP in both unadjusted and adjusted analyses. Other cytokines (IL-12, IL-17, tumor necrosis factor- $\beta$ , soluble IL  $1\alpha$ , macrophage inflammatory protein  $1\beta$ ) were found to be altered on days 0-4 in infants who developed CP. **CONCLUSIONS:** CP in former preterm infants may, in part, have a late perinatal and/or early neonatal inflammatory origin.

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