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## Interventions and Management

1. Arch Phys Med Rehabil. 2013 Sep 18. pii: S0003-9993(13)00911-8. doi: 10.1016/j.apmr.2013.08.245. [Epub ahead of print]

**Diffusion Tensor Imaging Study of the Response to Constraint-Induced Movement Therapy of Children with Hemiparetic Cerebral Palsy and Adults with Chronic Stroke.**

Rickards T, Sterling C, Taub E, Perkins-Hu C, Gauthier L, Graham M, Griffin A, Davis D, Mark VW, Uswatte G.

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**OBJECTIVE:** To investigate the relationship of white matter integrity and path of the corticospinal tract (CST) on arm function before and after Constraint-Induced Movement (CI) therapy in children with hemiparetic cerebral palsy (CP) and adults with chronic stroke. **DESIGN:** Study 1 used a multiple-baseline pre/post design. Study 2 was a randomized controlled trial. **SETTING:** Outpatient rehabilitation laboratory. **PARTICIPANTS:** Study 1 included 10 children ( $3.2 \pm 1.7$  years) with hemiparetic CP. Study 2 included 26 adults with chronic stroke ( $65.4 \pm 13.6$  years) who received either CI therapy or a comparison therapy. **INTERVENTIONS:** Children in Study 1 received CI therapy for 3.5 hours/day for 15 consecutive weekdays. Adults in Study 2 received either CI therapy or a comparison therapy for 3.5 hours for 10 consecutive weekdays. **MAIN OUTCOME MEASURES:** Diffusion tensor imaging was performed to quantify white matter integrity. Motor ability was assessed in children using the PMAL-R and PAFT and in adults with the MAL and WMFT. **RESULTS:** Participants in both studies improved in real-world arm function and motor capacity. Children and adults with disrupted/displaced CSTs and children with reduced FA values were worse on pre-treatment tests of motor function than participants with unaltered CSTs. However, neither integrity (FA) nor distorted or disrupted path of the CST affected motor improvement following treatment. **CONCLUSION:** Participants who had reduced integrity, displacement or interruption of their CST performed worse on pre-treatment motor testing. However, this had no effect on their ability to benefit from CI therapy. The results for children and adults are consistent with one another.

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**2. Hum Mov Sci. 2013 Sep 18. pii: S0167-9457(13)00102-4. doi: 10.1016/j.humov.2013.08.007. [Epub ahead of print]**

**Dynamic touch is affected in children with cerebral palsy.**

Ocarino JM, Fonseca ST, Silva PL, Gonçalves GG, Souza TR, Mancini MC.

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Children with developmental disorders such as cerebral palsy have limited opportunities for effortful interactions with objects and tools. The goal of the study was to investigate whether children with cerebral palsy have deficits in their ability to perceive object length by dynamic touch when compared to typically developing children. Fourteen children with typical development and 12 children with cerebral palsy were asked to report the length of hand-held rods after wielding them out of sight. Multilevel regression models indicated that I1 (maximum principal moment of inertia) was a significant predictor of perceived length - LP ( $p < .0001$ ). The effect of I1 on LP was significantly different among children ( $p = .001$ ) and the presence of cerebral palsy (group factor) partially explained such variance ( $p = .002$ ). In addition, accuracy and reliability of the length judgments made by children with cerebral palsy were significantly lower than the typically developing children ( $p < .05$ ). Theoretical and clinical implications of these results were identified and discussed.

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**3. Braz J Phys Ther. 2013 Aug 23;17(4):359-66. doi: 10.1590/S1413-35552013005000105. Epub 2013 Aug 23.**

**Assessment of gait in toddlers with normal motor development and in hemiplegic children with mild motor impairment: a validity study [Article in English, Portuguese]**

Figueiredo PR, Silva PL, Avelar BS, Chagas PS, Oliveira LC, Mancini MC.

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**BACKGROUND:** The optimization of gait performance is an important goal in the rehabilitation of children with cerebral palsy (CP) who present a prognosis associated with locomotion. Gait analysis using videos captured by digital cameras requires validation. **OBJECTIVE:** To evaluate the validity of a method that involves the analysis of videos captured using a digital camera for quantifying the temporal parameters of gait in toddlers with normal motor development and children with CP. **METHOD:** Eleven toddlers with normal motor development and eight children with spastic hemiplegia who were able to walk without assistive devices were asked to walk through a space contained in the visual field of two instruments: a digital camera and a three-dimensional motion analysis system, Qualisys Pro-Reflex. The duration of the stance and swing phases of gait and of the entire gait cycle were calculated by analyzing videos captured by a digital camera and compared to those obtained by Qualisys Pro-Reflex, which is considered a highly accurate system. **RESULTS:** The Intraclass Correlation Coefficient (ICC) demonstrated excellent agreement ( $ICC > 0.90$ ) between the two procedures for all measurements, except for the swing phase of the normal toddlers ( $ICC = 0.35$ ). The standard error of measurement was less than 0.02 seconds for all measures. **CONCLUSIONS:** The results reveal similarities between the two instruments, suggesting that digital cameras can be valid instruments for quantifying two temporal parameters of gait. This congruence is of clinical and scientific relevance and validates the use of digital cameras as a resource for helping the assessment and documentation of the therapeutic effects of interventions targeted at the gait of children with CP.

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**4. Gait Posture. 2013 Sep 2. pii: S0966-6362(13)00469-4. doi: 10.1016/j.gaitpost.2013.08.014. [Epub ahead of print]**

**Which functional impairments are the main contributors to pelvic anterior tilt during gait in individuals with cerebral palsy?**

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While past investigations focused on describing pelvic motion patterns in the frontal and transversal plane, the sagittal plane "double bump" pattern commonly found in children with cerebral palsy was only rarely investigated, especially concerning the underlying pathology. 375 ambulatory (GMFCS I-III) patients with bilateral spastic cerebral palsy were included in this study. Gait and clinical data (ROM, strength, spasticity) were classified in two different ways: (a) into two groups of normal and enhanced mean anterior pelvic tilt and (b) into two groups of moderate and excessive ROM in pelvic tilt. The results reveal that increased mean pelvic tilt is mainly associated with gait features of reduced hip extension and increased pelvic and trunk obliquity ROM but with increased knee ROM. In the clinical exam this corresponds to a smaller passive knee extension deficit and reduced knee flexor strength. It seems that flexors to extensors strength imbalance at the knee is a major feature why mean pelvic position is tilted anterior whereas maximum passive hip extension is of minor importance. Contrarily, excessive sagittal pelvic ROM is associated with increased knee flexion at initial contact and reduced knee ROM. Furthermore, Duncan-Ely- and Tardieu-tests show both increased values in this group with excessive pelvic range of motion indicating for spastic rectus femoris activation. The results of our study indicate that the two gait variables are influenced by different specific mechanisms which are now described for the first time. Since the pelvis plays a central role during gait, these findings should be considered when planning single event multilevel surgery in patients with cerebral palsy.

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**5. Hip Int. 2013 Sep 20:0. doi: 10.5301/hipint.5000051. [Epub ahead of print]**

**Discrimination of abnormal gait parameters due to increased femoral anteversion from other effects in cerebral palsy.**

Akalan NE, Temelli Y, Kuchimov S.

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The effects of increased femoral anteversion (IFA) on gait pattern have a complex relationship with other orthopaedic and neurological abnormalities of cerebral palsy (CP). The aim of this study was to differentiate the effects of IFA from other factors in CP. The four groups in this study included: 15 typically developing children (Group: TDC) (age:  $9.7 \pm 0.5$ ); 14 TDC with IFA ( $7.5 \pm 1.7$ ) (Group: TDC-IFA); 8 CP participants with IFA (age:  $6.3 \pm 1.7$ ) (Group: CP IFA); and 10 CP participants with nearly normal femoral anteversion (age:  $10.3 \pm 4.7$ ) (Group: CP-NFA). Altered peak knee-extension angle and stance-time, increased internal hip-rotation, internal foot-progression ( $p \leq 0.05$ ) were influenced by IFA in both groups of CP-NFA and TDC-IFA. For the TDC groups; pelvic-rotation increased and peak knee and hip-extension, knee flexion-moment, peak knee-power generation in late-stance decreased among children with IFA ( $p \leq 0.05$ ). For CP children; anterior pelvic-tilt, hip-flexion and peak knee-extension, hip power-absorption and generation, and peak knee power-absorption (K3) increased and peak knee-flexion was delayed by IFA ( $p \leq 0.05$ ). Therefore, IFA effects are different in CP and TDC. Peak knee-extension angle increased in TDC and decreased in CP with IFA. Besides the well known gait parameters related to IFA which are increased internal hip-rotation and foot-progression angle, it is recognised that peak knee-extension and stance-time are also influenced. Therefore, before muscle lengthening, femoral derotational osteotomy should be considered in the early stages of growth in CP to improve pelvic stability and the knee extensor mechanism.

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**6. Qual Life Res. 2013 Sep 24. [Epub ahead of print]****Qualitative development of the 'Questionnaire on Pain caused by Spasticity (QPS),' a pediatric patient-reported outcome for spasticity-related pain in cerebral palsy.**

Geister TL, Quintanar-Solares M, Martin M, Aufhammer S, Asmus F.

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**PURPOSE:** To develop a patient-reported outcome measure for spasticity-related pain in children/adolescents (age 2-17 years) with cerebral palsy (CP), the 'Questionnaire on Pain caused by Spasticity (QPS).' **METHODS:** Using a semi-structured interview guide, concept elicitation interviews on spasticity-related pain in upper and lower limbs were conducted in 21 children and caregiver pairs. Data were used to modify initial QPS modules and develop six draft modules, which were subsequently refined and finalized in four consecutive cognitive interview waves (12 children and caregiver pairs). **RESULTS:** To accommodate the broad range in the children's communication skills, QPS child/adolescent modules were developed in both interviewer-administered and self-administered formats. With the additional parent modules, three QPS modules were developed for each of the upper and lower limb applications. Information gained from the parent/caregiver modules complements the child/adolescent assessment. Parents report observed signs and frequency of pain in the same situations used to capture the child/adolescent reports of pain severity (e.g., rest, usual daily activities, active mobilization, and physically difficult activities). Participating children/adolescents and parents/caregivers reported that the final QPS instruments were comprehensive, relevant to the child's spasticity-related experience, and easy to understand and complete. **CONCLUSIONS:** The QPS is a novel instrument for the assessment of spasticity-related pain in children/adolescents with CP that was developed with direct patient input. Its modules allow the use of this instrument in children/adolescents with varied levels of impairment and communication skills.

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**7. Zhongguo Zhong Xi Yi Jie He Za Zhi. 2013 Jul;33(7):924-6.****Effect of acupuncture combined language training on cerebral palsy children with language retardation [Article in Chinese]**

Zou XY, Yu ZH, He YM, Yang H, Dong XL.

Children's Rehabilitation Center, First People's Hospital of Chengdu, Chengdu 610017, China.

**OBJECTIVE:** To observe effects of acupuncture combined speech therapy for cerebral palsy children with linguistic retardation. **METHODS:** Totally 132 cerebral palsy children were randomly assigned to the speech training group (Group A, 44 cases) and the routine acupuncture combined speech training group (Group B, 44 cases), and the acupuncture combined speech training group (Group C, 44 cases). Patients in Group A received one to one training including game therapy, therapy of communication attitudes, and so on. Those in the other two groups were needled at Baihui (GV20), Sishencong (EX-HN1), the first language zone, the second language zone, and the third language zone. Those in Group B were treated with electric needling and then speech training. Those in Group C were treated with language training, while needling with needle maintaining for 40 min. All patients were treated once daily, 5 times per week, 20 times as one course of treatment, 6 courses in total. The efficacy was assessed using S-S phonetic speech developmental retardation examination (CRRC version). The development quotient (DQ) was observed referring to the Gesell intellectual development scale before treatment, after 3 and 6 treatment courses. **RESULTS:** Compared with Group A (the total effective rate: 51.3%, DQ value: 58.1 +/- 13.3), better effects were obtained in Group B (the total effective rate: 77.5%, DQ value: 60.4 +/- 13.5) and Group C (the total effective rate: 81.0%, DQ value: 64.0 +/- 11.6) (all  $P < 0.05$ ). There was no statistical difference in the total effective rate or post-treatment DQ value between Group B and Group C ( $P > 0.05$ ). **CONCLUSION:** Acupuncture combined speech therapy showed obvious effects on cerebral palsy children with linguistic retardation.

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## Prevention and Cure

8. *J Pediatr.* 2013 Oct;163(4):961-967.e3. doi: 10.1016/j.jpeds.2013.04.034. Epub 2013 May 30.

### Neurodevelopmental outcome of extremely low birth weight infants with *Candida* infection.

Adams-Chapman I, Bann CM, Das A, Goldberg RN, Stoll BJ, Walsh MC, Sánchez PJ, Higgins RD, Shankaran S, Watterberg KL, Duara S, Miller NA, Heyne RJ, Peralta-Carcelen M, Goldstein RF, Steichen JJ, Bauer CR, Hintz SR, Evans PW, Acarregui MJ, Myers GJ, Vohr BR, Wilson-Costello DE, Pappas A, Vaucher YE, Ehrenkranz RA, McGowan EC, Dillard RG, Fuller J, Benjamin DK Jr; Eunice Kennedy Shriver National Institutes of Child Health and Human Development Neonatal Research Network.

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**OBJECTIVE:** *Candida* remains an important cause of late-onset infection in preterm infants. Mortality and neurodevelopmental outcome of extremely low birth weight (ELBW) infants enrolled in the *Candida* study were evaluated based on infection status. **STUDY DESIGN:** ELBW infants born at Eunice Kennedy Shriver National Institute of Child Health and Human Development Neonatal Research Network (NRN) centers between March 2004 and July 2007 who were screened for suspected sepsis were eligible for inclusion in the *Candida* study. Primary outcome data for neurodevelopmental impairment (NDI) or death were available for 1317 of the 1515 infants (87%) enrolled in the *Candida* study. The Bayley Scales of Infant Development-II or -III was administered at 18 months' adjusted age. A secondary comparison was performed with 864 infants enrolled in the NRN Generic Database during the same cohort who were never screened for sepsis and therefore not eligible for the *Candida* study. **RESULTS:** Among ELBW infants enrolled in the *Candida* study, 31% with *Candida* and 31% with late-onset non-*Candida* sepsis had NDI at 18 months. Infants with *Candida* sepsis and/or meningitis had an increased risk of death and were more likely to have the composite outcome of death and/or NDI compared with uninfected infants in adjusted analysis. Compared with infants in the NRN registry never screened for sepsis, overall risk for death were similar but those with *Candida* infection were more likely to have NDI (OR 1.83, 95% CI 1.01-3.33, P = .047). **CONCLUSIONS:** In this cohort of ELBW infants, those with infection and/or meningitis were at increased risk for death and/or NDI. This risk was highest among those with *Candida* sepsis and/or meningitis.

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9. *J Perinat Med.* 2013 Sep 24:1-6. doi: 10.1515/jpm-2013-0137. [Epub ahead of print]

### Influence of antenatal magnesium sulfate application on cord blood levels of brain-derived neurotrophic factor in premature infants.

Bachnas MA, Mose JC, Effendi JS, Andonotopo W.

**Aim:** To investigate the influence of antenatal magnesium sulfate (MgSO<sub>4</sub>) application on cord blood brain-derived neurotrophic factor (BDNF) levels - the first-line neuroprotection for preventing cerebral palsy in prematurely born infants. **Subjects and methods:** A randomized controlled trial was conducted by observing 72 pregnant women who were divided into three groups: group I (preterm pregnancy with MgSO<sub>4</sub>), group II (preterm pregnancy without MgSO<sub>4</sub>), and group III (full-term pregnancy as control group). Groups I and II were selected by block permutation randomization on subjects. Inclusion criteria consisted of preterm pregnancy at 34 weeks of gestation or less who were in labor or having planned terminations and receiving antenatal corticosteroids. Exclusion criteria consisted of previous complications caused by MgSO<sub>4</sub>, previous history of antenatal MgSO<sub>4</sub> application in the current pregnancy infant was born before 4 h administration of MgSO<sub>4</sub> or unborn more than 72 h after maximum course of antenatal MgSO<sub>4</sub> of 24 h, prolonged antenatal MgSO<sub>4</sub> treatment (>24 h), refusal to participate, and emergent adverse events during the study. Group I was given intravenous MgSO<sub>4</sub>; initial dose was 4 g, which was maintained at 1 g/h up to maximum of 24 h. Meanwhile, groups II and III were not given any special treatment. BDNF was examined by ELISA by taking 5 mL cord blood sample shortly after birth. The result was statistically measured by ANOVA. **Results:** The cord blood BDNF levels in premature infants with antenatal MgSO<sub>4</sub> was significantly higher than in premature infants without antenatal MgSO<sub>4</sub> (11,568 vs. 5027 pg/mL, P=0.000).

Moreover, the result was statistically comparable to full-term infants (11,568 vs. 13,300 pg/mL,  $P=0.085$ ).

Conclusion: The application of antenatal MgSO<sub>4</sub> in preterm delivery increased cord blood BDNF levels, which could have a potential role on fetal neuroprotection. Further investigation is needed.

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#### 10. Mol Biol Rep. 2013 Sep 25. [Epub ahead of print]

##### **Genetic association study of adaptor protein complex 4 with cerebral palsy in a Han Chinese population.**

Wang H, Xu Y, Chen M, Shang Q, Sun Y, Zhu D, Wang L, Huang Z, Ma C, Li T, He L, Xing Q, Zhu C.

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Adaptor protein complex 4 (AP-4) plays a key role in vesicle formation, trafficking, and sorting processes that are critical for brain development and function. AP-4 consists of four subunits encoded by the AP4E1, AP4B1, AP4M1, and AP4S1 genes. A number of studies have pointed to the involvement of AP-4-mediated vesicular trafficking pathways in the etiology of cerebral palsy (CP), the most notable of which are the causative mutations that have recently been identified in each of the AP-4 genes in different CP families. We postulated, therefore, that variations in AP-4 genes might influence an individual's susceptibility to CP. In the present study, 16 SNPs were genotyped among 517 CP patients and 502 healthy controls from the Han Chinese population. We systematically analyzed the association of the AP4E1, AP4B1, AP4M1, and AP4S1 genes with CP on the basis of clinical characteristics. No significant associations were found between these variants and the overall risk of CP. Subgroup analysis showed that rs1217401 of AP4B1 was significantly associated with CP as a sequela of hypoxic-ischemic encephalopathy (HIE) (CP + HIE) (allele:  $p = 0.042151$ ; genotype:  $p = 4.46 \times 10^{-6}$ ). Our results indicate that the 16 variants studied in the genes of the four subunits of AP-4 have no detectable effects on the overall susceptibility to CP, but AP4B1 appears to be a susceptibility gene for CP + HIE in the Han Chinese population.

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