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Interventions and Management

1. *J Rehabil Med.* 2013 May 21;45(1):14-23. doi: 10.2340/16501977-1082.

Psychometric evidence of spasticity measurement tools in cerebral palsy children and adolescents: A systematic review.

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Objective: To conduct a systematic review using validated critical appraisal scales to analyze both the quality and content of the psychometric evidence of spasticity measurement tools in cerebral palsy children and adolescents. **Data Sources:** The literature search was performed in 3 databases (Pubmed, CINAHL, Embase) up to March 2012. **Study Selection:** To be retained for detailed review, studies had to report on at least one psychometric property of one or many spasticity assessment tool(s) used to evaluate cerebral palsy children and adolescents. **Data Extraction:** Two raters independently reviewed admissible articles using a critical appraisal scale and a structured data extraction form. **Data Synthesis:** A total of 19 studies examining 17 spasticity assessment tools in cerebral palsy children and adolescents were reviewed. None of the reviewed tools demonstrated satisfactory results for all psychometric properties evaluated, and a major lack of evidence concerning responsiveness was emphasized. However, neurophysiological tools demonstrated the most promising results in terms of reliability and discriminating validity. **Conclusions:** This systematic review revealed insufficient psychometric evidence for a single spasticity assessment tool to be recommended over the others in pediatric and adolescent populations.

[PMID: 23689503](#) [PubMed - in process]

2. *Ann Rehabil Med.* 2013 Apr;37(2):167-74. doi: 10.5535/arm.2013.37.2.167. Epub 2013 Apr 30.

Reliability and Applicability of the Bayley Scale of Infant Development-II for Children With Cerebral Palsy.

Lee JH, Lim HK, Park E, Song J, Lee HS, Ko J, Kim M.

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OBJECTIVE: To obtain reliability and applicability of the Korean version Bayley Scale of Infant Development-II (BSID-II) in evaluating the developmental status of children with cerebral palsy (CP). **METHODS:** The inter-rater reliability of BSID-II scores from 68 children with CP (46 boys and 22 girls; mean age, 32.54±16.76 months; age range, 4 to 78 months) was evaluated by 10 pediatric occupational therapists. Patients were classified in several ways according to age group, typology, and the severity of motor impairment by the level of the Gross Motor Function Classification System (GMFCS). The measures were performed by video analysis, and the results of intraclass correlation (ICC) were obtained for each of the above classifications. To evaluate the clinical applicability of BSID-II for CP, its correlation with the Gross Motor Function Measure (GMFM), which has been known as the standard motor assessment for CP, was investigated. **RESULTS:** ICC was 0.99 for the Mental scale and 0.98 for the Motor scale in all subjects. The values of ICC ranged from 0.92 to 0.99 for each age group, 0.93 to 0.99 for each typology, and 0.99 to 1.00 for each GMFCS level. A strong positive correlation was found between the BSID-II Motor raw score and the GMFM total score ($r=0.84$, $p<0.001$), and a moderate correlation was observed between the BSID-II Mental raw score and the GMFM total score ($r=0.65$, $p<0.001$). **CONCLUSION:** The Korean version of BSID-II is a reliable tool to measure the functional status of children with CP. The raw scores of BSID-II showed a great correlation with GMFM, indicating validity of this measure for children with CP on clinical basis.

[PMID: 23705110](#) [PubMed - in process] PMID: PMC3660476

3. Eur J Appl Physiol. 2013 May 22. [Epub ahead of print]

Passive stiffness of the gastrocnemius muscle in athletes with spastic hemiplegic cerebral palsy.

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The passive properties of the muscle-tendon unit are regularly assessed in individuals with cerebral palsy (CP). However, no information is available on the passive properties of adult muscle, and whether any differences exist between the paretic and control muscles. Eleven ambulant male athletes with spastic hemiplegic CP (21.2 ± 3.0 years) and controls without neurological impairment (age = 21.8 ± 2.2 years) completed two and one passive stretch session, respectively. During each session, the ankle was passively dorsiflexed until end range of motion (ROM), whilst recording passive ankle angle, torque and gastrocnemius medialis (GM) myotendinous junction (MTJ) displacement. In addition, GM cross-sectional area (CSA) and length were measured. Subsequently, in vivo stress and strain were determined to calculate elastic modulus. Passive stiffness, MTJ displacement and ROM of the paretic GM were not different from the control muscles. However, the elastic modulus of the paretic GM was two times stiffer than the control GM muscles. In conclusion, athletes with CP exhibit absolute passive muscle stiffness similar to the controls; however, the elastic modulus of the CP muscle was significantly greater. Therefore, throughout the same ROM a smaller GM CSA in CP athletes has to dissipate larger relative torque compared to the control muscles, consequently causing the muscle to elongate to the same extent as the non-paretic muscle under stretch.

[PMID: 23689294](#) [PubMed - as supplied by publisher]

4. Paediatr Anaesth. 2013 May 18. doi: 10.1111/pan.12187. [Epub ahead of print]

Peri-operative pain management in children with cerebral palsy: comparative efficacy of epidural vs systemic analgesia protocols.

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INTRODUCTION: Selective Dorsal Rhizotomy (SDR) is the only surgical intervention with class I evidence supporting permanent reduction in spasticity for children with cerebral palsy (Paediatr Anaesth, 12, 2002, 296; Neurosurg Focus, 21, 2006, e2). Postoperatively, adequate analgesia can be difficult to achieve (J Neurosurg, 105, 2006, 8; Childs Nerv Syst, 17, 2001, 556; Paediatr Neurosurg, 43, 2007, 107; Anesth Analg, 79, 1994, 340; Reg

Anesth Pain Med, 24, 1999, 438; *Pediatr Anesth*, 19, 2009, 1213). This study examines a novel regimen utilizing the combination of epidurally infused ropivacaine - hydromorphone and scheduled ketorolac. This regimen was compared to a protocol utilizing systemic fentanyl and diazepam. **METHODS:** Following IRB approval, 31 patients receiving epidural analgesia were compared with 41 patients who received systemic analgesia. All surgeries were performed by one surgeon with standardized anesthetic and nursing care. Studied outcomes included: pain scores; episodes of severe pain; nausea, itching; oxygen desaturation; and ICU admission. Data were analyzed using Mann-Whitney U-test, CHI square, and Fisher exact test where indicated with $P < 0.05$ considered significant. **RESULTS:** Studied groups had similar demographics, biometrics and disease burdens. Patients in the epidural group had statistically and clinically significant reductions in peak recorded pain scores for each 4-h period in the first 24 postoperative hours. Severe pain (score >5) was markedly reduced in the epidural group with 9% of epidural patients vs. 68% of systemic patients experiencing at least one episode. Fewer epidural patients experienced oxygen desaturation during the first two postoperative days (6.5% vs. 41%, 6.5% vs. 39%). **CONCLUSION:** Epidural analgesia resulted in substantial improvements in pain control and safety. The data supports the superiority of a multimodal analgesia approach centered on epidural analgesia. A similar protocol should be considered following simple laminectomies or procedures associated with lower-extremity muscle spasm.

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[PMID: 23682965](#) [PubMed - as supplied by publisher]

5. Value Health. 2013 May;16(3):A41. doi: 10.1016/j.jval.2013.03.232. Epub 2013 May 3.

Using questionnaire design to explore reporting differences for spasticity related pain in children and adolescents with cerebral palsy.

Quintanar-Solares M, Martin ML, Bryant AJ, Ascoytia CM, Asmus F, Geister TL.

Health Research Associates, Inc., Seattle, WA, USA.

[PMID: 23694347](#) [PubMed - in process]

6. Gait Posture. 2013 May 14. pii: S0966-6362(13)00199-9. doi: 10.1016/j.gaitpost.2013.04.010. [Epub ahead of print]

Spatio-temporal parameters and lower-limb kinematics of turning gait in typically developing children.

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Turning is a requirement for most locomotor tasks; however, knowledge of the biomechanical requirements of successful turning is limited. Therefore, the aims of this study were to investigate the spatio-temporal and lower-limb kinematics of 90° turning. Seventeen typically developing children, fitted with full body and multi-segment foot marker sets, having performed both step (outside leg) and spin (inside leg) turning strategies at self-selected velocity, were included in the study. Three turning phases were identified: approach, turn, and depart. Stride velocity and stride length were reduced for both turning strategies for all turning phases ($p < 0.03$ and $p < 0.01$, respectively), while stance time and stride width were increased during only select phases ($p < 0.05$ and $p < 0.01$, respectively) for both turn conditions compared to straight gait. Many spatio-temporal differences between turn conditions and phases were also found ($p < 0.03$). Lower-limb kinematics revealed numerous significant differences mainly in the coronal and transverse planes for the hip, knee, ankle, midfoot, and hallux between conditions ($p < 0.05$). The findings summarized in this study help explain how typically developing children successfully execute turns and provide greater insight into the biomechanics of turning. This knowledge may be applied to a clinical setting to help improve the management of gait disorders in pathological populations, such as children with cerebral palsy.

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[PMID: 23684101](#) [PubMed - as supplied by publisher]

7. Pediatr Phys Ther. 2013 May 16. [Epub ahead of print]**Forefoot Mobility in Ankle and Foot Orthoses: Effect on Gait of Children With Cerebral Palsy.**

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BACKGROUND AND PURPOSE: Typical gait requires flexibility in the ankle and foot. During gait, it is critical that the ankle dorsiflex and the toes extend. The purpose of this report is to demonstrate that when foot orthoses block critical movement undesirable compensations that may interfere with gait can appear. **CASE DESCRIPTION:** Three children with spastic cerebral palsy demonstrate the effect on gait when the blocks attributable to the orthoses were removed. **INTERVENTION:** All children received electrical stimulation and used foot orthoses. **OUTCOMES:** Internal hip rotation and toe walking occurred when orthoses blocked digit extension. A block may be small and unnoticed but can still influence gait and force the child to compensate for the loss of mobility.

[PMID: 23685740](#) [PubMed - as supplied by publisher]

8. BMJ Case Rep. 2013 May 22;2013. pii: bcr2013009717. doi: 10.1136/bcr-2013-009717.**A greenstick fracture of the patella: a unique fracture in CP crouch gait.**

Elhassan Y, Mahon J, Kiernan D, O'Brien T.

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We report a greenstick fracture of the patella in an ambulant boy with diplegic cerebral palsy (CP). The boy was known to have knee crouch which was documented in our gait laboratory. Greenstick fractures usually occur in the long bones of children and are caused by a bending force. This is the first report of a patellar greenstick fracture and provides a unique insight into the propagation of patellar fractures in CP crouch.

[PMID: 23704454](#) [PubMed - in process]

9. J Int Med Res. 2013 May 21. [Epub ahead of print]**Botulinum toxin-A with and without rehabilitation for the treatment of spastic cerebral palsy.**

Jianjun L, Shurong J, Weihong W, Yan Z, Fanyong Z, Nanling L.

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OBJECTIVE: To determine the efficacy of botulinum toxin-A (BTX-A) nerve block, with and without rehabilitation, in the treatment of spastic cerebral palsy. **METHODS:** Patients (aged 1-23 years) with spastic cerebral palsy underwent nerve block with BTX-A, followed by 2h/day rehabilitation (experimental group) or <2h/day rehabilitation (control group). Muscle tension and motor function were evaluated pre-block using the Modified Ashworth Scale (MAS) and gross motor function measure (GMFM), respectively. MAS was assessed weekly to determine duration of action of BTX-A; GMFM was assessed at 1 year post-block. **RESULTS:** There were no significant differences between the experimental group (n=120) and the control group (n=124) in age, body weight, pre-block MAS or GMFM, or BTX-A duration of action. MAS was significantly improved in both groups at 1 month post-block. At 1 year post-block, GMFM was significantly improved in both groups, with a significantly greater improvement seen in the experimental group compared with the control group. **CONCLUSION:** BTX-A block improved muscle tension and motor function. Rehabilitation training, following the block, resulted in greater improvements to motor function than block alone.

[PMID: 23696596](#) [PubMed - as supplied by publisher]

10. Anesth Analg. 2013 May 17. [Epub ahead of print]**A Retrospective Identification of Gastroesophageal Reflux Disease as a New Risk Factor for Surgical Site Infection in Cerebral Palsy Patients After Spine Surgery.**

Chidambaran V, Gentry C, Ajuba-Iwuji C, Sponsellar PD, Ain M, Lin E, Zhang X, Klaus SA, Njoku DB.

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BACKGROUND: Neuromuscular scoliosis is a known risk factor for surgical site infection (SSI) after spinal fusion, with reported infection rates as high as 11.2%. Although risk factors such as antibiotic timing have been previously addressed, our objective was to identify intrinsic risk factors for SSI in cerebral palsy (CP) patients with neuromuscular scoliosis. We hypothesized that CP patients who develop SSI after spine fusion would have a risk profile similar to those who develop nosocomial infection. **METHODS:** We retrospectively analyzed records from patients with CP who developed infections after spinal fusion from January 1998 until July 2008, who were identified by our Infection Control Officer using National Nosocomial Infection Surveillance System criteria (N = 34). Demographically and procedurally matched controls without infection were identified from our spine database (N = 37). We compared these groups for gastroesophageal reflux disease (GERD), use of gastric acid inhibitors, presence of preoperative decubitus ulcer, previous infection, and postoperative ventilation. Multivariable logistic regression was then performed to assess the relative contributions of the predictors to "deep infection" and "any infection." **RESULTS:** Of 30 evaluable infected patients, 70% had incisional SSI. Although many of the infections were polymicrobial, the most common pathogens identified were Gram-negative bacilli. Many significant predictors were identified by univariable logistic regression for any infection and deep infection. Multivariable logistic regression found a significant effect only for GERD (odds ratio, 6.4; 95% confidence interval, 1.9-21.3; P = 0.002) for any infection, whereas the effect of therapy with gastric acid inhibitors did not reach statistical significance (odds ratio, 6.1 [95% confidence interval, 0.84-44.6]; P = 0.07). No significant interaction between the 2 factors was detected. Among our controls and infected patients altogether, 46.3% had GERD. **CONCLUSIONS:** We show that GERD increases the risk for infection in CP patients after spine fusion. Prospective multicenter studies are necessary to further validate the predictive value of this risk factor.

[PMID: 23687234](#) [PubMed - as supplied by publisher]

11. J Korean Acad Nurs. 2013 Apr;43(2):247-55. doi: 10.4040/jkan.2013.43.2.247.**Effects of Abdominal Meridian Massage with Aroma Oils on Relief of Constipation among Hospitalized Children with Brain related Disabilities [Article in Korean]**

Nam MJ, Bang Yle, Kim TI.

Department of Nursing, Daejeon Health Science College, Daejeon, Korea.

PURPOSE: This study was done to evaluate the effects of 3 times/week and 5 times/week abdominal meridian massage with aroma oils (AMMAO) on the relief of constipation among hospitalized children with disabilities involving the brain lesions (cerebral palsy, epilepsy, and others). **METHODS:** The participants were 33 hospitalized children with a disability involving the brain (15 were in the 5 times/week of AMMAO group and 18 were in the 3 times/week of AMMAO group). Data were collected from March 21 to May 1, 2011. Chi-square test, t-test, and repeated measures ANOVA with SPSS 18.0 were used to evaluate the effects of AMMAO. **RESULTS:** While there was no significant difference between the two groups, there was a significant difference within groups between baseline and the end of the intervention period for the following, frequency of suppository use or enemas, amount of stool, and number of bowel movements. **CONCLUSION:** The results of this study indicate that AMMAO is an effective nursing intervention in relief of constipation for hospitalized children with a disability involving the brain. Therefore it is recommended that AMMAO be used in clinical practice as an effective nursing intervention for relief of constipation to these children.

[PMID: 23703602](#) [PubMed - in process]

12. Toxins (Basel). 2013 May 21;5(5):1010-31. doi: 10.3390/toxins5051010.

Sialorrhea: anatomy, pathophysiology and treatment with emphasis on the role of botulinum toxins.

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Sialorrhea or excessive drooling is a major issue in children with cerebral palsy and adults with neurodegenerative disorders. In this review, we describe the clinical features, anatomy and physiology of sialorrhea, as well as a review of the world literature on medical treatment using Yale University's search engine; including but not limited to Medline and Erasmus. Level of drug efficacy is defined according to the guidelines of American Academy of Neurology. Current medical management is unsatisfactory. Topical agents (scopolamine and tropicamide) and oral agents (glycopyrolate) combined render a level B evidence (probably effective); however, this treatment is associated with troublesome side effects. Double-blind and placebo-controlled studies of botulinum toxin (BoNT) provide a level A evidence for type B (two class I studies; effective and established) and both overall and individual B level of evidence for OnabotulinumtoxinA (A/Ona) and AbobotulinumtoxinA (A/Abo); these are probably effective. For IncobotulinumtoxinA (A/Inco), the level of evidence is U (insufficient) due to lack of blinded studies. Side effects are uncommon; transient and comparable between the two types of toxin. A clinical note at the end of this review comments on fine clinical points. Administration of BoNTs into salivary glands is currently the most effective way of treating sialorrhea.

[PMID: 23698357](#) [PubMed - in process]

13. Rev Paul Pediatr. 2013 Mar;31(1):51-57.

Functional performance of children with cerebral palsy from high and low socioeconomic status [Article in English, Portuguese]

Assis-Madeira EA, Carvalho SG, Blascovi-Assis SM.

Faculdade de Tecnologia e Ciências, Vitória da Conquista, BA, Brasil.

OBJECTIVE: To investigate the influence of socioeconomic status on the functional performance of children with cerebral palsy. **METHODS:** Cross-sectional quantitative study of 49 children diagnosed with cerebral palsy from a convenience sample. Children of both genders aged three to seven and a half years were studied. They were classified according to the level of severity of cerebral palsy based on the Gross Motor Function Classification System. Participants were organized in two groups considering their high or low socioeconomic status, according to the Brazilian Economic Classification Criteria. Functional performance was assessed by the Pediatric Evaluation of Disability Inventory. The Student's t-test was applied for independent samples in order to compare means between groups. **RESULTS:** Socioeconomic status did not affect functional performance of children with mild cerebral palsy. Those with moderate cerebral palsy and low socioeconomic status presented lower social function scores ($p=0.027$) than those with high socioeconomic status. Children with severe cerebral palsy with low socioeconomic status presented worse performance in self-care skills ($p=0.021$) and mobility ($p=0.005$). These children were more dependent regarding mobility ($p=0.015$) than those with high socioeconomic status. **CONCLUSIONS:** Socioeconomic status may influence the development process of children with cerebral palsy and must be considered as a risk factor in educational and health practices aimed at this population.

[PMID: 23703044](#) [PubMed - as supplied by publisher]

14. Scientific World Journal. 2013 Apr 3;2013:468402. doi: 10.1155/2013/468402. Print 2013.**Mental health in children with cerebral palsy: does screening capture the complexity?**

Bjorgaas HM, Elgen I, Boe T, Hysing M.

Department of Paediatric Habilitation, Stavanger University Hospital, Postboks 8100, 4068 Stavanger, Norway ;
Department of Clinical Medicine, University of Bergen, Postboks 7800, 5020 Bergen, Norway.

Introduction. Children with cerebral palsy (CP), one of the most common childhood neurological disorders, often have associated medical and psychological symptoms. This study assesses mental health problems compared to population controls and the ability of a mental health screening tool to predict psychiatric disorders and to capture the complexity of coexisting symptoms. **Methods.** Children with CP (N = 47) were assessed according to DSM-IV criteria using a psychiatric diagnostic instrument (Kiddie-SADS) and a mental health screening questionnaire (SDQ). Participants from the Bergen Child Study, a large epidemiological study, served as controls. **Results.** Children with CP had significantly higher means on all problem scores including impact scores. Two in three children scored above 90th percentile cutoff on Total Difficulties Score (TDS), and 57% met criteria for a psychiatric disorder, yielding a sensitivity of 0.85 and a specificity of 0.55. Mental health problems coexisted across symptom scales, and peer problems were highly prevalent in all groups of psychiatric disorders. **Conclusion.** A high prevalence of mental health problems and cooccurrence of symptoms were found in children with CP compared to controls. Screening with SDQ detects mental health problems, but does not predict specific disorders in children with CP. ADHD is common, but difficult to diagnose due to complexity of symptoms. Mental health services integrated in regular followup of children with CP are recommended due to high prevalence and considerable overlap of mental health symptoms.

[PMID: 23690745](#) [PubMed - in process] PMCID: PMC3654290

15. Clin Neurophysiol. 2013 May 15. pii: S1388-2457(13)00270-8. doi: 10.1016/j.clinph.2013.02.118. [Epub ahead of print]**On the control of brain-computer interfaces by users with cerebral palsy.**

Daly I, Billinger M, Laparra-Hernández J, Aloise F, García ML, Faller J, Scherer R, Müller-Putz G.

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OBJECTIVE: Brain-computer interfaces (BCIs) have been proposed as a potential assistive device for individuals with cerebral palsy (CP) to assist with their communication needs. However, it is unclear how well-suited BCIs are to individuals with CP. Therefore, this study aims to investigate to what extent these users are able to gain control of BCIs. **METHODS:** This study is conducted with 14 individuals with CP attempting to control two standard online BCIs (1) based upon sensorimotor rhythm modulations, and (2) based upon steady state visual evoked potentials. **RESULTS:** Of the 14 users, 8 are able to use one or other of the BCIs, online, with a statistically significant level of accuracy, without prior training. Classification results are driven by neurophysiological activity and not seen to correlate with occurrences of artifacts. However, many of these users' accuracies, while statistically significant, would require either more training or more advanced methods before practical BCI control would be possible. **CONCLUSIONS:** The results indicate that BCIs may be controlled by individuals with CP but that many issues need to be overcome before practical application use may be achieved. **SIGNIFICANCE:** This is the first study to assess the ability of a large group of different individuals with CP to gain control of an online BCI system. The results indicate that six users could control a sensorimotor rhythm BCI and three a steady state visual evoked potential BCI at statistically significant levels of accuracy (SMR accuracies; mean±STD, 0.821±0.116, SSVEP accuracies; 0.422±0.069).

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16. Comput Methods Programs Biomed. 2013 May 20. pii: S0169-2607(13)00134-X. doi: 10.1016/j.cmpb.2013.04.012. [Epub ahead of print]

Design of virtual keyboard using blink control method for the severely disabled.

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In this paper, a human-machine interface with the concept of "blink control" is proposed. The human-machine interface is applied to an assistive device, namely "blink scanning keyboard", which is designed specifically for the severely physical disabled and people suffering from motor neuron diseases or severe cerebral palsy. The pseudo electromyography (EMG) signal of blinking eyes could be acquired by wearing a Bluetooth headset with one sensor on the forehead and the other three on the left ear of the user. Through a conscious blink, a clear and immediate variation will be formed in the pseudo EMG signal from the users' forehead. The occurrence of this variation in pseudo EMG signal could be detected and filtered by the algorithms proposed in this paper, acting like a trigger to activate the functions integrated in the scanning keyboard. The severely physical and visual disabled then can operate the proposed design by simply blinking their eyes, thus communicating with outside world.

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[PMID: 23702128](#) [PubMed - as supplied by publisher]

17. Turk J Pediatr. 2013 Jan-Feb;55(1):8-15.

Changing views of cerebral palsy over 35 years: the experience of a center.

Tosun A, Gökben S, Serdaroglu G, Polat M, Tekgöl H.

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In this study, it was aimed to evaluate the demographic and clinical characteristics of cerebral palsy (CP) cases over a 35-year period. Findings of 442 patients with CP followed from 1995 to 2006 (Group 2) were compared with 208 patients with CP followed between 1972 and 1994 (Group 1) in the same pediatric neurology division. Ratios of both prematurity (38% vs. 17.7%) and very low birth weight (VLBW) infants (13.8% vs. 1.5%) significantly increased in Group 2. There was also a four-fold increase in cesarean delivery in Group 2 (42.3% vs. 9.6%). A significant increase in the rate of early diagnosis during the first year was also found in this group (56.9% vs. 39.4%). The rate of spastic diparesis cases has significantly increased (33.7% vs. 7.7%), while the rate of spastic tetraparesis cases has significantly decreased (63.5% vs. 37.3%). It was seen that preventable risk factors continue today.

[PMID: 23692827](#) [PubMed - in process]

18. Value Health. 2013 May;16(3):A39. doi: 10.1016/j.jval.2013.03.224. Epub 2013 May 3.

Conducting qualitative interviews in compromised child populations: cerebral palsy (CP) as a case study.

Bryant AJ, Quintanar-Solares M, Ascoytia CM, Martin ML, Asmus F, Geister TL.

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[PMID: 23694333](#) [PubMed - in process]

Prevention and Cure

19. An Pediatr (Barc). 2013 May 15. pii: S1695-4033(13)00155-0. doi: 10.1016/j.anpedi.2013.03.017. [Epub ahead of print]

Outcome at two years corrected age of a cohort of very low birth weight infants from hospitals within the neonatal SEN1500 network [Article in Spanish]

García P, San Feliciano L, Benito F, García R, Guzmán J, Salas S, Fernández C, Del Prado N, Ciprián D, Figueras J; hospitales pertenecientes a SEN1500.

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OBJECTIVE: To describe growth and neurodevelopmental status of 4,944 children who completed a follow-up at two years of corrected age out of the 10,456 newborns with weight =1500g born between the years 2002-2007 and discharged from hospitals within the network SEN1500. A total of 522 newborns were excluded as they had some type of malformation. The total number of children assessed represents the 49.76% of children discharged alive and without malformations. **METHODS:** A retrospective review was conducted using prospectively collected data in the SEN1500 database. We compared growth data at two years of corrected age according to birth weight and sex. Motor impairment, incidence of cerebral palsy, visual and hearing disabilities, and abnormal neurodevelopment for gestational age were analysed between groups. We studied the associations between cerebral palsy (CP) and perinatal factors. **RESULTS:** At 2 years of age 44.2% of children had a weight <2 SD for corrected age. Children with birth weight =1000g showed worse outcomes in growth. Some type of motor impairment was observed in 6.96% of the infants, and 4.56% of them were diagnosed with CP. The incidence was higher among males with birth weight =1000g. There was an incidence of 5.21% of visual disability, with 0.5% of children being blind in one or both eyes. Cerebral palsy was associated with retinopathy of prematurity, severe intraventricular haemorrhage, and periventricular leukomalacia, in particular cystic periventricular leukomalacia.

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20. Brain Dev. 2013 May 18. pii: S0387-7604(13)00156-3. doi: 10.1016/j.braindev.2013.04.007. [Epub ahead of print]

Preconditioning and post-treatment with cobalt chloride in rat model of perinatal hypoxic-ischemic encephalopathy.

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Background: Hypoxia-ischemia (HI)-induced perinatal encephalopathy is a major cause of acute mortality and chronic neurologic morbidities such as cerebral palsy, mental retardation, and epilepsy. As the essential transcription factor for the activation of hypoxia-inducible genes, hypoxia-inducible factor 1 alpha (HIF-1a) plays an important role in the pathophysiological response to the stress of HI brain damage. Whether HIF-1a activation promotes neuroprotection in HI tissues is controversial. **Methods:** The left common carotid artery of rats aged 7days was ligated under anesthesia. The pups were then exposed to hypoxia in a normobaric chamber filled with 8% oxygen and 92% nitrogen for 2.5h. In the sham control group, the left common carotid artery was exposed but was not ligated or exposed to hypoxia. To assess the time window for effective treatment, the HIF-1a inducer cobalt chloride (CoCl₂) was injected subcutaneously 1day before surgery, immediately or 1day after surgery. The brain tissues were harvested from the pups of each groups at 1, 2 and 7days after insult for HIF-1a protein and its target genes expression and for investigating the injury. Morris water maze tests were performed at postnatal 7weeks. **Results:** HIF-1a protein levels and its target genes vascular endothelial growth factor, heme oxygenase-1, and insulin-like growth factor 1 were markedly increased after intraperitoneal injection of CoCl₂ (60mg/kg). The target gene inducible nitric oxide synthase exhibited a biphasic time course. HI caused apoptosis and reduced capillary

density, which were ameliorated by CoCl₂. Both preconditioning with CoCl₂ 24h before HI and administration of CoCl₂ 24h after HI improved long-term reference memory compared with that in vehicle-injected littermate controls. Administration of CoCl₂ immediately after HI did not improve spatial working memory. Conclusions: CoCl₂ activates HIF-1 α and protects against brain damage in vivo. The time of administration could be used to manipulate the activity of HIF-1 α pathways and promote recovery.

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21. Eur J Hum Genet. 2013 May 22. doi: 10.1038/ejhg.2013.93. [Epub ahead of print]

Rare copy number variation in cerebral palsy.

McMichael G, Girirajan S, Moreno-De-Luca A, Gecz J, Shard C, Nguyen LS, Nicholl J, Gibson C, Haan E, Eichler E, Martin CL, MacLennan A.

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Recent studies have established the role of rare copy number variants (CNVs) in several neurological disorders but the contribution of rare CNVs to cerebral palsy (CP) is not known. Fifty Caucasian families having children with CP were studied using two microarray designs. Potentially pathogenic, rare (<1% population frequency) CNVs were identified, and their frequency determined, by comparing the CNVs found in cases with 8329 adult controls with no known neurological disorders. Ten of the 50 cases (20%) had rare CNVs of potential relevance to CP; there were a total of 14 CNVs, which were observed in <0.1% (<8/8329) of the control population. Eight inherited from an unaffected mother: a 751-kb deletion including FSCB, a 1.5-Mb duplication of 7q21.13, a 534-kb duplication of 15q11.2, a 446-kb duplication including CTNND2, a 219-kb duplication including MCPH1, a 169-kb duplication of 22q13.33, a 64-kb duplication of MC2R, and a 135-bp exonic deletion of SLC06A1. Three inherited from an unaffected father: a 386-kb deletion of 12p12.2-p12.1, a 234-kb duplication of 10q26.13, and a 4-kb exonic deletion of COPS3. The inheritance was unknown for three CNVs: a 157-bp exonic deletion of ACOX1, a 693-kb duplication of 17q25.3, and a 265-kb duplication of DAAM1. This is the first systematic study of CNVs in CP, and although it did not identify de novo mutations, has shown inherited, rare CNVs involving potentially pathogenic genes and pathways requiring further investigation. European Journal of Human Genetics advance online publication, 22 May 2013; doi:10.1038/ejhg.2013.93.

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Dexamethasone induces apoptosis of progenitor cells in the subventricular zone and dentate gyrus of developing rat brain.

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The use of dexamethasone in premature infants to prevent and/or treat bronchopulmonary dysplasia adversely affects neurocognitive development and is associated with cerebral palsy. The underlying mechanisms of these effects are multifactorial and likely include apoptosis. The objective of this study was to confirm whether dexamethasone causes apoptosis in different regions of the developing rat brain. On postnatal day 2, pups in each litter were randomly divided into the dexamethasone-treated (n=?91) or vehicle-treated (n=?92) groups. Rat pups in the dexamethasone group received tapering doses of dexamethasone on postnatal days 3-6 (0.5, 0.25, 0.125, and 0.06 mg/kg/day, respectively). Dexamethasone treatment significantly decreased the gain of body and brain weight and increased brain caspase-3 activity, DNA fragments, terminal deoxynucleotidyl transferase-mediated dUTP nick end labeling, and cleaved caspase-3-positive cells at 24 hr after treatment. Dexamethasone increased cleaved caspase-3-positive cells in the cortex, thalamus, hippocampus, cerebellum, dentate gyrus, and subventricular zone. Double-immunofluorescence studies show that progenitor cells in the subventricular zone and

dentate gyrus preferentially undergo apoptosis following dexamethasone exposure. These results indicate that dexamethasone-induced apoptosis in immature cells in developing brain is one of the mechanisms of its neurodegenerative effects in newborn rats. © 2013 Wiley Periodicals, Inc.

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Hyperthermia, Inflammation, and Perinatal Brain Injury.

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Hyperthermia at the time of or following a hypoxic-ischemic insult has been associated with adverse neurodevelopmental outcome. Moreover, an elevation in temperature during labor has been associated with a variety of other adverse neurologic sequelae such as neonatal seizures, encephalopathy, stroke, and cerebral palsy. These outcomes may be secondary to a number of deleterious effects of hyperthermia including an increase in cellular metabolic rate and cerebral blood flow alteration, release of excitotoxic products such as free radicals and glutamate, and hemostatic changes. There is also an association between chorioamnionitis at the time of delivery and cerebral palsy, which is thought to be secondary to cytokine-mediated injury. We review experimental and human studies demonstrating a link between hyperthermia and perinatal brain injury.

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