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Interventions and Management

1. BMC Pediatr. 2013 Oct 28;13(1):175. [Epub ahead of print]

Intrathecal baclofen treatment in dystonic cerebral palsy: a randomized clinical trial: the IDYS trial.

Bonouvrié LA, Becher JG, Vles JS, Boeschoten K, Soudant D, de Groot V, van Ouwerkerk WJ, Strijers RL, Foncke E, Geytenbeek J, van de Ven PM, Teernstra O, Vermeulen RJ.

BACKGROUND: Dystonic cerebral palsy is primarily caused by damage to the basal ganglia and central cortex. The daily care of these patients can be difficult due to dystonic movements. Intrathecal baclofen treatment is a potential treatment option for dystonia and has become common practice. Despite this widespread adoption, high quality evidence on the effects of intrathecal baclofen treatment on daily activities is lacking and prospective data are needed to judge the usefulness and indications for dystonic cerebral palsy. The primary aim of this study is to provide level one clinical evidence for the effects of intrathecal baclofen treatment on the level of activities and participation in dystonic cerebral palsy patients. Furthermore, we hope to identify clinical characteristics that will predict a beneficial effect of intrathecal baclofen in an individual patient. **Methods/design:** A double blind placebo-controlled multi-center randomized clinical trial will be performed in 30 children with dystonic cerebral palsy. Patients aged between 4 and 25 years old with a confirmed diagnosis of dystonic cerebral palsy, Gross Motor Functioning Classification System level IV or V, with lesions in the cerebral white matter, basal ganglia or central cortex and who are eligible for intrathecal baclofen treatment will be included. Group A will receive three months of continuous intrathecal baclofen treatment and group B will receive three months of placebo treatment, both via an implanted pump. After this three month period, all patients will receive intrathecal baclofen treatment, with a follow-up after nine months. The primary outcome measurement will be the effect on activities of and participation in daily life measured by Goal Attainment Scaling. Secondary outcome measurements on the level of body functions include dystonia, spasticity, pain, comfort and sleep-related breathing disorders. Side effects will be monitored and we will study whether patient characteristics influence outcome. **DISCUSSION:** The results of this study will provide data for evidence-based use of intrathecal baclofen in dystonic cerebral palsy.

Trial registration: Nederlands Trial Register: NTR3642.

[PMID: 24165282](#) [PubMed - as supplied by publisher] [Free full text \(Provisional PDF\)](#)

2. Braz J Phys Ther. 2013 Oct;17(5):458-63. doi: 10.1590/S1413-35552012005000113. Epub 2013 Oct 21.

Gross Motor Function Classification System Expanded & Revised (GMFCS E & R): reliability between therapists and parents in Brazil.

Silva DB, Pfeifer LI, Funayama CA.

Universidade de São Paulo, Faculdade de Medicina de Ribeirão Preto, Ribeirão PretoSPBrazil.

BACKGROUND: Several studies have demonstrated the importance of using the Gross Motor Function Classification System (GMFCS) to classify gross motor function in children with cerebral palsy, but the reliability of the expanded and revised version has not been examined in Brazil (GMFCS E & R). **OBJECTIVE:** To determine the intra- and inter-rater reliability of the Portuguese-Brazil version of the GMFCS E & R applied by therapists and compare to classification provided by parents of children with cerebral palsy. **METHOD:** Data were obtained from 90 children with cerebral palsy, aged 4 to 18 years old, attending the neurology or rehabilitation service of a Brazilian hospital. Therapists classified the children's motor function using the GMFCS E & R and parents used the Brazilian Portuguese version of the GMFCS Family Report Questionnaire. Intra- and inter-rater reliability was obtained through percentage agreement and Cohen's unweighted Kappa statistics (k). The Chi-square test was used to identify significant differences in the classification of parents and therapists. **RESULTS:** Almost perfect agreement was reached between the therapists [K=0.90 (95% confidence interval 0.83-0.97)] and intra-raters (therapists) with K=1.00 [95% confidence interval (1.00-1.00)], $p < 0.001$. Agreement between therapists and parents was substantial (k=0.716, confidence interval 0.596-0.836), though parents classify gross motor impairment more severely than therapists ($p=0.04$). **CONCLUSIONS:** The Portuguese version of the GMFCS E & R is reliable for use by parents and therapists. Parents tend to classify their children's limitations more severely, because they know their performance in different environments.

[PMID: 24173347](#) [PubMed - in process] [Free full text](#)

3. Disabil Rehabil. 2013 Oct 25. [Epub ahead of print]

Walking activity patterns in youth with cerebral palsy and youth developing typically.

Bjornson KF, Zhou C, Stevenson R, Christakis D, Song K.

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Purpose: To describe daily walking stride rate patterns of young children with cerebral palsy (CP) as compared to a typically developing youth (TDY) cohort relative to age and functional level. **Method:** A cross-sectional comparison cohort study compared 209 youth with CP with 368 TDY aged 2-13 years. Youth with CP had Gross Motor Function Classification System (GMFCS) levels I-III with 60% bilateral involvement and 79% spastic. Five days of StepWatch data were averaged and classified into low, moderate and high stride rates. Group differences were examined by t-test and analysis of variance. **Results:** Children with CP walk significantly less each day than TDY ($F = 245$, $p \leq 0.001$) and differ by GMFCS ($F = 1.51$, $p < 0.001$). TDY walk a similar number of strides in low and moderate stride rates each day while youth with CP do not. TDY attained high stride rates (>60 strides/min) for 8 min/d with levels I-III at 4.0, 3.2 and 0.53 min/d, respectively. **Conclusions:** The relative relationship of walking intensity levels within total daily stride activity differs for youth with CP as compared to TDY. The influence of functional walking ability on walking stride activity levels and intensity does not appear to differ significantly across age groups. Implications for Rehabilitation Limitation in the ability to attain moderate stride-rate intensity, regardless of total number of strides taken each day for ambulatory youth with CP, is a potential area of focus for intervention. Understanding of stride activity levels and intensity in youth with CP may be employed to focus rehabilitation strategies to enhance habitual walking activity. Community-based stride rate data has potential as an effectiveness outcome for rehabilitation strategies focused on walking (i.e. orthopedic surgery, orthoses and injections therapies).

[PMID: 24160855](#) [PubMed - as supplied by publisher]

4. Prosthet Orthot Int. 2013 Oct 25. [Epub ahead of print]**Validation of the activPAL activity monitor in children with hemiplegic gait patterns resultant from cerebral palsy.**

McAloon MT, Hutchins S, Twiste M, Jones R, Forchtner S.

UNIPOD - United National Institute for Prosthetics & Orthotics Development, University of Salford, Salford, UK.

Background: Current investigation of treatment outcomes by clinicians is currently hampered by a lack of clinically viable tools. The use of activity monitors specifically validated for a population could help resolve this situation. Objectives: The purpose of the study was to validate an activity monitor for monitoring children with cerebral palsy. The study was designed to validate the duration of time spent sitting, standing and walking and the number of steps taken when being measured by the activPAL activity monitor. Study design: A validation study was undertaken. Methods: Observations of participants were carried out while completing a specifically designed activity course using video footage, which were then compared to the output from the activity monitor. Results: The activity monitor was found to be valid for the time spent standing and walking, the number of steps taken and the number of transitions. Conclusions: The results demonstrated that the monitor may prove useful to clinicians as a measurement outcome device for children with hemiplegic gait patterns resultant from cerebral palsy. However, the sensitivity of the device is variable, and further investigations are necessary to confirm it would also be able to detect minor changes after interventions. Clinical relevance: The monitor may provide clinicians with a simplistic tool that is easily utilised, to enable audit exercises of current and future treatments.

[PMID: 24163328](#) [PubMed - as supplied by publisher]

5. Neurosurg Focus. 2013 Nov;35(5):E6. doi: 10.3171/2013.8.FOCUS13294.**Selective dorsal rhizotomy for spasticity not associated with cerebral palsy: reconsideration of surgical inclusion criteria.**

Gump WC, Mutchnick IS, Moriarty TM.

Division of Pediatric Neurosurgery, Norton Neuroscience Institute and Kosair Children's Hospital; and.

Children with spastic diplegia from cerebral palsy (CP) experience measurable improvement in their spasticity and motor function following selective dorsal rhizotomy (SDR). The role of this operation in the treatment of other spasticity causes is less well defined. A literature review was undertaken to survey outcomes from SDRs performed outside the CP population. Multiple sclerosis was the most common diagnosis found, accounting for 74 of 145 patients described. Selective dorsal rhizotomies have also been reported in patients with traumatic brain and spinal cord injuries, ischemic and hemorrhagic stroke, neurodegenerative disease, hypoxic encephalopathy, and other causes of spasticity. Outcomes from surgery are generally described as favorable, although postoperative assessments and follow-up times are not standardized across reports. Long-term outcomes are sparsely reported. Larger numbers of patients and more detailed outcomes data have the potential to form a basis for expanding the inclusion criteria for SDR.

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6. Spine J. 2013 Oct 23. pii: S1529-9430(13)01446-0. doi: 10.1016/j.spinee.2013.07.484. [Epub ahead of print]**Bilateral rib-to-pelvis Eiffel Tower VEPTR construct for children with neuromuscular scoliosis: a preliminary report.**

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BACKGROUND CONTEXT: Neuromuscular scoliosis could develop at a young age and progress beyond skeletal

maturity. An early spinal fusion arrests growth of the spine and thorax, risking the development of secondary thoracic insufficiency syndrome. Vertical expandable prosthetic titanium rib (VEPTR) is a fusionless technique aiming at correction of the deformity with preservation of growth potential. PURPOSE: To demonstrate the preliminary results of the use of VEPTR in an Eiffel Tower construct in children with neuromuscular scoliosis in regard to coronal and sagittal profiles, space available for the lungs (SAL), and spinal growth. The report lists the complications we faced during the follow-up of 1.33 years after the index procedure. STUDY DESIGN: A retrospective analysis of prospectively collected data of a case series. PATIENT SAMPLE: Twenty nonambulatory children (mean 8.9 years) with neuromuscular scoliosis. Their primary diagnoses were myelomeningocele in seven, cerebral palsy in three, spinal muscular atrophy in two, myopathies in three, arthrogryposis in one, and syndromic scoliosis in four patients. METHODS: All 20 patients received percutaneous rib-to-pelvis VEPTR implantation. Mean operative time was 2 hours, and mean hospital stay was 12 days. None of them needed blood transfusion. They underwent 20 primary implantations and 39 lengthenings. OUTCOME MEASURES: The patients were assessed based on physiologic measures, that is, the radiographic improvement of their scoliosis, SAL, pelvic tilt, spinal height, and sagittal and coronal decompensation. RESULTS: At the latest follow-up, thoracolumbar curvature improved significantly ($65.7^{\circ} \pm 20.5^{\circ}$ to $49.9^{\circ} \pm 15.7^{\circ}$), as did lumbar curvature ($61.6^{\circ} \pm 19.5^{\circ}$ to $35^{\circ} \pm 21.2^{\circ}$), thoracic (17.2 ± 2.3 to 20 ± 2.3 cm) and lumbar spinal height (9.9 ± 1.7 to 11.9 ± 1.8 cm), SAL (86.5 ± 8.9 to 97 ± 10), pelvic obliquity ($12.5^{\circ} \pm 8^{\circ}$ to $5.2^{\circ} \pm 5.2^{\circ}$), and the iliolumbar angle ($15^{\circ} \pm 8^{\circ}$ to $10.06^{\circ} \pm 7.1^{\circ}$). Nine patients suffered complications in the form of proximal cradle migration (five), implant breakage (five), deep wound infection (three), and dislodged iliac hooks (two). CONCLUSIONS: Early results of VEPTR for neuromuscular scoliosis are encouraging. Follow-up till skeletal maturity will best determine future indications.

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7. Disabil Rehabil. 2013 Oct 28. [Epub ahead of print]

Environmental needs and facilitators available for children and adolescents with cerebral palsy: adaptation and validation of the European Child Environment Questionnaire (ECEQ) Spanish version.

Badia M, Orgaz B, Gómez-Vela M, Longo E.

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Purpose: The objective of this study is to present the process of translating, adapting and validating the European Child Environment Questionnaire (ECEQ) in the Spanish context. Method: The participants were 200 parents of children and adolescents with cerebral palsy (CP) aged 8-18 years, from seven regions in Spain. The adaptation of the ECEQ original version was carried out through the translation and back translation into Spanish. Construct validity was assessed by Factor analysis, Rasch model, and analysing group differences in need and availability of environmental features (EFs) according to level GMFCS. Results: We obtained a high rate of parental response. The ECEQ Spanish version contains 59 items and we identified four domains: Products and technology - home, school and community - services, systems and policies, support and relations, and Attitudes. Seventeen items were dropped as they did not fit well into plausible domains. Construct validity in terms of distinguishing between groups with expected for both need and availability. Conclusion: The ECEQ Spanish version was more appropriate to assess the needs of and access to EFs in the following domains: Products and technology and services, systems and policies, and it proved less appropriate for the support and relations, and attitudes domains. Implications for Rehabilitation Identification of barriers and environmental facilitators are key aspects to ensure the participation of children and adolescents with CP. The ECEQ is a useful tool for identifying needs and availability of the environmental features for children and adolescents with CP in Spain. This tool contains 59 items that are consistent with ICF framework. The Spanish version of ECEQ provides valuable information, which could be helpful to guide public services and organization services in order to optimize participation of children and adolescents with CP.

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8. Spec Care Dentist. 2013 Nov;33(6):280-5. doi: 10.1111/j.1754-4505.2012.00306.x. Epub 2012 Nov 20.

The relationship between nurses' oral hygiene and the mouth care of their patients.

Ashkenazi M, Yaish Y, Yitzhak M, Sarnat H, Rakocz M.

Formerly, Senior Lecturer in Pediatric Dentistry, The Maurice and Gabriela Goldschleger School of Dental Medicine, Tel-Aviv University, Tel-Aviv, Israel; Currently, Pediatric Dentistry Dental Clinic, Petach-Tikva, Israel.

To investigate the extent to which a relationship may exist between nurses' own oral hygiene and their commitment and capability of following instructions for tooth brushing with conventional and triple-headed toothbrushes, to cerebral palsy (CP) children. The study included 43 individuals with CP and their 44 nurses. A structured questionnaire was designed to assess I. Demographic characteristics of the nurses II. Nurses' knowledge and maintenance of their own oral-hygiene and that of their CP patients. Nurses' ability to follow instruction for tooth-brushing was evaluated and scored using the TB-PS-I/Ashkenazi index following the first brushing, as well as on a recall visit one month later. More nurses (72.7%) reported routine tooth-brushing in the morning than in the evening (40.9%). Most nurses (73%) reported not flossing their teeth at all, and more than half reported visiting their dentist only when they suffer pain. A positive correlation was found between the nurses' knowledge of preventive oral measures and their compliance with their own oral hygiene and with that of their CP patients. Similarly, a positive correlation was found between nurses' receiving previous instruction for correct oral hygiene and their maintenance of their patients' oral hygiene. Institutions for CP patients should disseminate information on oral hygiene to staff, as a means of increasing their maintenance of their patients' oral health.

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9. Spec Care Dentist. 2013 Nov;33(6):275-9. doi: 10.1111/j.1754-4505.2012.00304.x. Epub 2012 Dec 26.

A study on the eruption timing of permanent dentition in patients with cerebral palsy.

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PURPOSE: This study aimed to determine the average eruption time and sequence of permanent teeth in patients with cerebral palsy (CP) and to compare the results with the established norms for Iranian subjects. **METHODS:** This cross-sectional study comprised of 207 individuals with CP, 96 boys and 111 girls, ranging from 6 to 19 years. The average age at eruption of permanent teeth, excluding third molars, was given as the mean (\pm SD) and median in years for each gender. A table of percentiles of the eruption time was also determined. Comparisons were made using t-test at a significance level of 0.05. **RESULTS:** The sequence of eruption in children with CP was almost similar to the normal. With the exception of the second premolar and the second molar, tooth eruption was advanced in girls compared with boys. There was no difference between the left and right sides of each arch. Mandibular teeth had an earlier eruption time than maxillary teeth except for the second premolar. In general, eruption times of children with CP were later (1-33 months) than those reported previously for healthy children. **CONCLUSIONS:** Despite the almost similar sequence of eruption, a high tendency to delayed eruption of permanent dentition was observed in children with CP.

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10. Int J Lang Commun Disord. 2013 Nov;48(6):689-702. doi: 10.1111/1460-6984.12042. Epub 2013 Aug 1.

Investigation of practices to support the complex communication needs of children with hearing impairment and cerebral palsy in a rural district of Kenya: a case series.

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BACKGROUND: Rehabilitation services are scarce in low-income countries, where under-representation of some specialist professions has led to the role extension of others. An example of this can be found in Kilifi in Kenya where the role of speech and language therapy has been taken on by occupational therapists and teachers. **AIMS:** To investigate the communication practices used by these professional groups to support children with complex communication needs in a rural part of Kenya and to explore the ways in which this might be seen to facilitate or obstruct improved communication by asking the following questions: What are the critical features of interactional discourse in practitioner-child dyads with caregiver-child dyads providing a natural comparison? What communicative modalities and practice techniques are invoked? And how does this information relate to extending professional roles? **METHODS & PROCEDURES:** An in-depth, descriptive study of a case series was conducted in a school for deaf children and the occupational therapy department of a district general hospital. A mixed methodology was used involving naturalistic observation and applied linguistics analysis. A convenience sample was established comprising six practitioner-child dyads assigned to partnership types: (A) three children with hearing impairment and their teachers; and (B) three children with cerebral palsy and their occupational therapists. As a natural comparator, the same three children in B were also observed with their mothers (partnership type C). Dyadic interaction was video recorded on three occasions. The video data were sampled, transcribed into standard orthography and translated. Codes were applied to determine turn structure, linguistic move types and communicative modalities. Sequential analysis was conducted on the move types. **OUTCOMES & RESULTS:** Partnership type A dyads showed a fairly even turn distribution between teacher and child. A common pattern was teacher-initiated Instruct and Model/Prompt, followed by child response in the form of an Action. The most frequently used modality was Sound Production and Hands-on-Articulators, which corresponded to articulation drill practice. Partnership type B dyads revealed a tendency towards adult domination of turns. The majority of adult-initiated moves required no response from the child. The practice technique Hands-on-Articulators involved manipulating the oral musculature of the child. Partnership type C dyads showed resonances of type B dyads, although focused more on Motor-Action in relation to task performance. **CONCLUSIONS & IMPLICATIONS:** The assignment of speech and language therapy duties to teachers and occupational therapists has resulted in suboptimal practice for children with complex communication needs.

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[PMID: 24165365](#) [PubMed - in process]

11. Dev Med Child Neurol. 2013 Oct;55(10):965-6. doi: 10.1111/dmcn.12179. Epub 2013 May 30.

Motivation and paediatric interventions: is it a predisposition, a mechanism for change, or an outcome?

Ziviani J, Poulsen A, King G, Johnson D.

Health and Rehabilitation Sciences, The University of Queensland and Children's Health Queensland, Brisbane, Qld, Australia.

Comment on

Evidence for outcomes of motivational rehabilitation interventions for children and adolescents with cerebral palsy: an American Academy for Cerebral Palsy and Developmental Medicine systematic review. [Dev Med Child Neurol. 2013]

[PMID: 23721157](#) [PubMed - indexed for MEDLINE]

12. Int J Urol. 2013 Oct 29. doi: 10.1111/iju.12287. [Epub ahead of print]

Sacral neuromodulation is an effective option for non-obstructive urinary retention in men with cerebral palsy.

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[PMID: 24168169](#) [PubMed - as supplied by publisher]

13. J Neurosci Rural Pract. 2013 Aug;4(Suppl 1):S40-4. doi: 10.4103/0976-3147.116446.

Elementary school enrolment and its determinants among children with cerebral palsy in Thiruvananthapuram district, Kerala, India.

Anish TS, Ramachandran R, Sivaram P, Mohandas S, Sasidharan A, Sreelakshmi PR.

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CONTEXT: There is enough documented evidence to prove the benefits of early and appropriate initiation of education among children with cerebral palsy (CP). AIM: To find out the proportion of children with CP who are enrolled for some kind of formal education and to study the determinants of the same. SETTING AND DESIGN: This cross sectional study was done among children, attending the special clinics at government medical college, Thiruvananthapuram. MATERIALS AND METHODS: Children between 3 and 12 years of age diagnosed with CP were subjects for the study. STATISTICAL ANALYSIS USED: Enrollment for any form of formal education was the major outcome variable. The factors associated with initiation of formal education were tested using Chi-square test or Fischer's exact test. Independent association of each factor was evaluated through binary logistic Regression analysis. RESULTS AND CONCLUSIONS: The mean (SD) age of the children (n = 86) was 5.7 (2.3) years with forty-six (53.5%) of them being girls. Diplegia was the commonest limb abnormality found. Fifty-two (60.5%) children were undergoing some kind of schooling. Those children who were less dependent physically and those who had achieved better language development were regular school goers. After binary logistic regression the ability of a child to speak in sentences (P = 0.008) and ambulatory level of the child (P = 0.019) were factors which favored, whereas delay in attaining the adaptive developmental milestone of transferring objects from one hand to another (P = 0.014) was found to be detrimental for school enrollment.

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Prevention and Cure

14. Cell Transplant. 2012 Mar 27. [Epub ahead of print]

[No title available]

Sharma A, Gokulchandran N, Chopra G, Kulkarni P, Lohia M, Badhe P, Jacob VC.

Neurological disorders such as muscular dystrophy, cerebral palsy and injury to the brain and spine currently, have no known definitive treatments or cures. A study was carried out on seventy one children suffering from such incurable neurological disorders and injury. They were intrathecally and intra-muscularly administered autologous bone marrow-derived mononuclear cells. Assessment after transplantation showed neurological improvements in muscle power and a shift on assessment scales such as FIM and Brooke and Vignos scale. Further, imaging and electrophysiological studies also showed significant changes in selective cases. On an average follow up of 15 months 1 month, overall 97% muscular dystrophy cases showed subjective and functional improvement, with 2 of them also showing changes on MRI and 3 on EMG. One hundred percent of the spinal cord injury cases showed improvement with respect to muscle strength, urine control, spasticity etc. Eighty five percent of cases of cerebral palsy cases showed improvements out of which 75% reported improvement in muscle tone and 50% in speech

among other symptoms. Eighty eight percent of cases of other incurable neurological disorders such as autism, Retts Syndrome, Giant Axonal Neuropathy etc also showed improvement. No significant adverse events were noted. The results show that this treatment is safe, efficacious and also improves the quality of life of children with incurable neurological disorders and injury.

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15. Childs Nerv Syst. 2013 Nov 1. [Epub ahead of print]

Stem cells for brain repair in neonatal hypoxia-ischemia.

Chicha L, Smith T, Guzman R.

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Neonatal hypoxic-ischemic insults are a significant cause of pediatric encephalopathy, developmental delays, and spastic cerebral palsy. Although the developing brain's plasticity allows for remarkable self-repair, severe disruption of normal myelination and cortical development upon neonatal brain injury are likely to generate life-persisting sensory-motor and cognitive deficits in the growing child. Currently, no treatments are available that can address the long-term consequences. Thus, regenerative medicine appears as a promising avenue to help restore normal developmental processes in affected infants. Stem cell therapy has proven effective in promoting functional recovery in animal models of neonatal hypoxic-ischemic injury and therefore represents a hopeful therapy for this unmet medical condition. Neural stem cells derived from pluripotent stem cells or fetal tissues as well as umbilical cord blood and mesenchymal stem cells have all shown initial success in improving functional outcomes. However, much still remains to be understood about how those stem cells can safely be administered to infants and what their repair mechanisms in the brain are. In this review, we discuss updated research into pathophysiological mechanisms of neonatal brain injury, the types of stem cell therapies currently being tested in this context, and the potential mechanisms through which exogenous stem cells might interact with and influence the developing brain.

[PMID: 24178233](#) [PubMed - as supplied by publisher]

16. Front Neurosci. 2013 Oct 24;7:194.

Stem cell therapy to protect and repair the developing brain: a review of mechanisms of action of cord blood and amnion epithelial derived cells.

Castillo-Melendez M, Yawno T, Jenkin G, Miller SL.

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In the research, clinical, and wider community there is great interest in the use of stem cells to reduce the progression, or indeed repair brain injury. Perinatal brain injury may result from acute or chronic insults sustained during fetal development, during the process of birth, or in the newborn period. The most readily identifiable outcome of perinatal brain injury is cerebral palsy, however, this is just one consequence in a spectrum of mild to severe neurological deficits. As we review, there are now clinical trials taking place worldwide targeting cerebral palsy with stem cell therapies. It will likely be many years before strong evidence-based results emerge from these trials. With such trials underway, it is both appropriate and timely to address the physiological basis for the efficacy of stem-like cells in preventing damage to, or regenerating, the newborn brain. Appropriate experimental animal models are best placed to deliver this information. Cell availability, the potential for immunological rejection, ethical, and logistical considerations, together with the propensity for native cells to form teratomas, make it unlikely that embryonic or fetal stem cells will be practical. Fortunately, these issues do not pertain to the use of human amnion epithelial cells (hAECs), or umbilical cord blood (UCB) stem cells that are readily and economically obtained from the placenta and umbilical cord discarded at birth. These cells have the potential for transplantation to the newborn where brain injury is diagnosed or even suspected. We will explore the novel characteristics of hAECs and undifferentiated UCB cells, as well as UCB-derived endothelial progenitor cells (EPCs) and mesenchymal stem cells (MSCs), and how immunomodulation and anti-inflammatory properties are principal mechanisms of action that are common to these cells, and which in turn may ameliorate the cerebral hypoxia and inflammation that are final pathways in the pathogenesis of perinatal brain injury.

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17. Neurosci Lett. 2013 Oct 28. pii: S0304-3940(13)00951-8. doi: 10.1016/j.neulet.2013.10.047. [Epub ahead of print]

CST recovery in pediatric hemiplegic patients; Diffusion tensor tractography study.

Baek SO, Jang SH, Lee E, Kim S, Hah JO, Park YH, Lee JM, Son SM.

Department of Physical Medicine and Rehabilitation, College of Medicine, Yeungnam University.

Many diffusion tensor imaging (DTI) studies have reported an association between corticospinal tract (CST) injury and motor dysfunction. In this study, we investigated CST recovery in 29 pediatric patients with clinical hemiplegia using DTI. We measured the fractional anisotropy (FA), apparent diffusion coefficient (ADC), and asymmetric anisotropy (AA) of both CSTs. The patients were classified into three groups according to severity of CST disruption of the more affected hemisphere. DTI was followed up for 9.34 ± 2.07 months after initial evaluation. The FA value of the more affected CST showed a significant decrease compared to the opposite side at initial and follow up evaluation, respectively ($p < 0.05$). The FA value of both CSTs showed a significant increase at follow up compared to the initial evaluation, while more changes were observed on the more affected side, compared with the less affected side ($p < 0.05$). AA showed a significant decrease at follow up, and showed significant correlation with interval change of FA value of the more affected side, not with that of the less affected side ($r = 0.543$, $p < 0.05$). 19 patients showed change of CST integrity. In the current study, the results of DTI showed recovery of the CST and provided radiologic evidence for a scientific basis of brain plasticity in pediatric patients.

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18. J Perinat Med. 2013 Oct 30:1-3. doi: 10.1515/jpm-2013-0134. [Epub ahead of print]

Origin of the long-term variability and acceleration of FHR studied for the prevention of cerebral palsy in fetal hypoxia and general insults.

Maeda K.

Aims: The development of fetal heart rate (FHR) variability and acceleration, and their loss in the hypoxic brain damage and cerebral palsy (CP) is investigated. **Methods:** FHR, movements in physiologic sinusoidal FHR and fetal movements were studied by actocardiogram. **Results:** Periodic fetal respiratory movements evoked moderate FHR variation similar to medium variability. Small fetal movements provoked FHR variability, and large fetal movement burst developed the acceleration. The brain centers should be midbrain for variability and acceleration. FHR variability and acceleration develop by the reaction of fetal brain to fetal movements. As severe organic fetal brain damage could develop through fetal hypoxia in the loss of variability, early delivery before the loss of variability will prevent infantile CP. As the abnormal FHR would be developed by fetal brain damage in non-hypoxic fetal insults, early delivery before the loss of variability could also prevent the brain damage in viral and bacterial infections.

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19. Neuroimage (Amst). 2013 Mar 22;2:440-7. doi: 10.1016/j.nicl.2013.03.006.

Diffuse reduction of white matter connectivity in cerebral palsy with specific vulnerability of long range fiber tracts.

Englander ZA, Pizoli CE, Batrachenko A, Sun J, Worley G, Mikati MA, Kurtzberg J, Song AW.

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Cerebral palsy (CP) is a heterogeneous group of non-progressive motor disorders caused by injury to the developing fetal or infant brain. Although the defining feature of CP is motor impairment, numerous other neurodevelopmental disabilities are associated with CP and contribute greatly to its morbidity. The relationship between brain structure and neurodevelopmental outcomes in CP is complex, and current evidence suggests that motor and developmental outcomes are related to the spatial pattern and extent of brain injury. Given that multiple disabilities are frequently associated with CP, and that there is increasing burden of neurodevelopmental disability with increasing motor severity, global white matter (WM) connectivity was examined in a cohort of 17 children with bilateral CP to test the hypothesis that increased global WM damage will be seen in the group of severely affected (Gross Motor Function Classification Scale (GMFCS) level of IV) as compared to moderately affected (GMFCS of II or III) individuals. Diffusion tensor tractography was performed and the resulting fibers between anatomically defined brain regions were quantified and analyzed in relation to GMFCS levels. Overall, a reduction in total WM connectivity throughout the brain in severe versus moderate CP was observed, including but not limited to regions associated with the sensorimotor system. Our results also show a diffuse and significant reduction in global inter-regional connectivity between severity groups, represented by inter-regional fiber count, throughout the brain. Furthermore, it was also observed that there is a significant difference ($p = 0.02$) in long-range connectivity in patients with severe CP as compared to those with moderate CP, whereas short-range connectivity was similar between groups. This new finding, which has not been previously reported in the CP literature, demonstrates that CP may involve distributed, network-level structural disruptions.

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Advancing critical care medicine with stem cell therapy and hypothermia for cerebral palsy.

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With limited clinical trials on stem cell therapy for adult stroke underway, the assessment of efficacy also needs to be considered for neonatal hypoxic-ischemic brain injury, considering its distinct symptoms. The critical nature of this condition leads to establishment of deficits that last a lifetime. Here, we will highlight the progress of current translational research, commenting on the critical nature of the disease, stem cell sources, the use of hypothermia, safety and efficacy of each treatment, modes of action, and the possibility of combination therapy. With this in mind, we reference translational guidelines established by a consortium of research partners called Stem cell Therapeutics as an Emerging Paradigm for Stroke (STEPS). The guidelines of STEPS are directed toward evaluating outcomes of cell therapy in adult stroke; however, we identify the overlapping pathology, as we believe that these guidelines will serve well in the investigation of neonatal hypoxic-ischemic therapy. Finally, we discuss emerging treatments and a case report, altogether suggesting that the potential for these treatments to be used in synergy has arrived and the time for advancing stem cell use in combination with hypothermia for cerebral palsy is now.

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