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Interventions and Management

1. BMC Neurol. 2016 Jun 2;16(1):86. doi: 10.1186/s12883-016-0582-7.

Evaluation of the effectiveness of robotic gait training and gait-focused physical therapy programs for children and youth with cerebral palsy: a mixed methods RCT.

Wiat L, Rosychuk RJ, Wright FV.

BACKGROUND: Robot assisted gait training (RAGT) is considered to be a promising approach for improving gait-related gross motor function of children and youth with cerebral palsy. However, RAGT has yet to be empirically demonstrated to be effective. This knowledge gap is particularly salient given the strong interest in this intensive therapy, the high cost of the technology, and the requirement for specialized rehabilitation centre resources. **METHODS:** This is a research protocol describing a prospective, multi-centre, concurrent mixed methods study comprised of a randomized controlled trial (RCT) and an interpretive descriptive qualitative design. It is a mixed methods study designed to determine the relative effectiveness of three physical therapy treatment conditions (i.e., RAGT, a functional physical therapy program conducted over-ground (fPT), and RAGT + fPT) on gait related motor skills of ambulatory children with cerebral palsy. Children with cerebral palsy aged 5-18 years who are ambulatory (Gross Motor Function Classification System Levels II and III) will be randomly allocated to one of four treatment conditions: 1) RAGT, 2) fPT, 3) RAGT and fPT combined, or 4) a maintenance therapy only control group. The qualitative component will explicate child and parent experiences with the interventions, provide insight into the values that underlie their therapy goals, and assist with interpretation of the results of the RCT.

[PMID: 27255908](#)

2. JMIR Serious Games. 2016 Jun 1;4(1):e9. doi: 10.2196/games.5528.

Development and Reliability Evaluation of the Movement Rating Instrument for Virtual Reality Video Game Play.

Levac D, Nawrotek J, Deschenes E, Giguere T, Serafin J, Bilodeau M, Sveistrup H.

BACKGROUND: Virtual reality active video games are increasingly popular physical therapy interventions for children with cerebral palsy. However, physical therapists require educational resources to support decision making about game selection to match individual patient goals. Quantifying the movements elicited during virtual reality active video game play can inform individualized game selection in pediatric rehabilitation. **OBJECTIVE:** The objectives of this study were to develop and evaluate the feasibility and reliability of the Movement Rating Instrument for Virtual Reality Game Play (MRI-VRGP). **METHODS:** Item generation occurred through an iterative process of literature review and sample videotape viewing. The MRI-VRGP includes 25 items quantifying upper extremity, lower extremity, and total body movements. A total of 176 videotaped 90-second game play sessions involving 7 typically developing children and 4 children with cerebral palsy were rated by 3 raters trained in MRI-VRGP use. Children played 8 games on 2 virtual reality and active video game systems.

Intraclass correlation coefficients (ICCs) determined intra-rater and interrater reliability. RESULTS: Excellent intrarater reliability was evidenced by ICCs of >0.75 for 17 of the 25 items across the 3 raters. Interrater reliability estimates were less precise. Excellent interrater reliability was achieved for far reach upper extremity movements (ICC=0.92 [for right and ICC=0.90 for left) and for squat (ICC=0.80) and jump items (ICC=0.99), with 9 items achieving ICCs of >0.70 , 12 items achieving ICCs of between 0.40 and 0.70, and 4 items achieving poor reliability (close-reach upper extremity-ICC=0.14 for right and ICC=0.07 for left) and single-leg stance (ICC=0.55 for right and ICC=0.27 for left). CONCLUSIONS: Poor video quality, differing item interpretations between raters, and difficulty quantifying the high-speed movements involved in game play affected reliability. With item definition clarification and further psychometric property evaluation, the MRI-VRGP could inform the content of educational resources for therapists by ranking games according to frequency and type of elicited body movements.

[PMID: 27251029](#)

3. Neurosurgery. 2016 May 27. [Epub ahead of print]

Combined Anterior and Posterior Lumbar Rhizotomy for Treatment of Mixed Dystonia and Spasticity in Children With Cerebral Palsy.

Abdel Ghany WA, Nada M, Mahran MA, Aboud A, Mahran MG, Aziz Nasef MA, Gaber M, Sabry T, Ibrahim MH, Taha MH.

BACKGROUND: Children with cerebral palsy (CP) can present with severe secondary dystonia with or without associated spasticity of their extremities. OBJECTIVE: To assess the outcomes of combined anterior and posterior lumbar rhizotomy for the treatment of mixed hypertonia in the lower extremities of children with CP. METHODS: Fifty children with CP were subjected to combined anterior and posterior lumbar rhizotomies in a prospective study. Clinical outcome measurements were recorded preoperatively and were evaluated at 2, 6, and 12 months postoperatively. The operative techniques were performed by laminotomy from L1-S1, and intraoperative monitoring was used in all cases. All patients underwent intensive postoperative physiotherapy programs. RESULTS: Changes in muscle tone, joint range of motion, and dystonia were significant ($P = .000$) at postoperative assessment visits. CONCLUSION: This study demonstrated the potential of combined anterior and posterior lumbar rhizotomies to improve activities of daily living in children with CP and with mixed spasticity and dystonia.

[PMID: 27244465](#)

4. Disabil Rehabil. 2016 May 30:1-7. [Epub ahead of print]

Treadmill training with an incline reduces ankle joint stiffness and improves active range of movement during gait in adults with cerebral palsy.

Lorentzen J, Kirk H, Fernandez-Lago H, Frisk R, Scharff Nielsen N, Jorsal M, Nielsen JB.

PURPOSE: We investigated if 30 min of daily treadmill training with an incline for 6 weeks would reduce ankle joint stiffness and improve active range of movement in adults with cerebral palsy (CP). METHODS: The study was designed as a randomized controlled clinical trial including 32 adults with CP (GMFCS 1-3) aged 38.1 SD 12 years. The training group ($n = 16$) performed uphill treadmill training at home daily for 30 min for 6 weeks in addition to their usual activities. Passive and reflex mediated stiffness and range of motion (ROM) of the ankle joint, kinematic and functional measures of gait were obtained before and after the intervention/control period. Intervention subjects trained 31.4 SD 10.1 days for 29.0 SD 2.3 min (total) 15.2 h. RESULTS: Passive ankle joint stiffness was reduced ($F = 5.1$; $p = 0.031$), maximal gait speed increased ($F = 42.8$, $p < 0.001$), amplitude of toe lift prior to heel strike increased ($F = 5.3$, $p < 0.03$) and ankle angle at heel strike was decreased ($F = 12.5$; $p < 0.001$) significant in the training group as compared to controls. CONCLUSION: Daily treadmill training with an incline for 6 weeks reduces ankle joint stiffness and increases active ROM during gait in adults with CP. Intensive gait training may thus be beneficial in preventing and reducing contractures and help to maintain functional gait ability in adults with CP. Implications for rehabilitation Uphill gait training is an effective way to reduce ankle joint stiffness in adult with contractures. 6 weeks of daily uphill gait training improves functional gait parameters such as gait speed and dorsal flexion during gait in adults with cerebral palsy.

[PMID: 27237772](#)

5. Clin Orthop Surg. 2016 Jun;8(2):187-93. doi: 10.4055/cios.2016.8.2.187. Epub 2016 May 10.

Effects of Soft Tissue Surgery on Pelvic and Hip Rotation in Patients with Spastic Diplegia: A Meta-Analysis.

Jung HJ, Yoon JY, Oh MK, Kim YC, Kim JH, Eom TW, Park KB.

BACKGROUND: There are several different opinions regarding the improvements seen on the transverse plane after soft tissue surgery alone in independently ambulant patients with cerebral palsy. We performed a meta-analysis using data from previous studies to identify the effects of soft tissue surgery alone on pelvic and hip rotation in children with spastic diplegia. **METHODS:** We conducted a pilot study to evaluate the improvement in pelvic and hip rotation after muscle-tendon lengthening surgery in children with spastic diplegia. We also searched EMBASE and PubMed and selected 2 previous studies using the same test conditions with kinematic data on the pelvis and hip joints. A meta-analysis of the results of these 3 studies, including this pilot study, was then performed. **RESULTS:** The meta-analysis results showed an external rotation decrease ($p = 0.005$) in the mean difference of pelvic rotation of -3.61 (95% confidence interval [CI], -6.13 to -1.09) and a mean difference in hip rotation of 6.60 (95% CI, 3.34 to 9.86), indicating a significant increase in the hip external rotation after surgery ($p < 0.001$). **CONCLUSIONS:** In independently community-ambulant pediatric patients with spastic diplegia, pelvic retraction and hip internal rotation could be improved after soft tissue surgery.

[PMID: 27247745](#)

6. Dev Med Child Neurol. 2016 May 31. doi: 10.1111/dmcn.13177. [Epub ahead of print]

Osteopenia of the hip joint in cerebral palsy - does this affect hip stability?

Rhodes J, Blanchard A.

[PMID: 27242195](#)

7. Acta Paediatr. 2016 Jun 2. doi: 10.1111/apa.13493. [Epub ahead of print]

Pain and hospital admissions are important factors associated with quality of life in non-ambulatory children.

Elema A, Zalmstra TA, Boonstra AM, Narayanan UG, Reinders-Messelink HA, V D Putten AA.

AIM: This was the first study to investigate the factors associated with health-related quality of life (HRQoL) in non-ambulatory children with cerebral palsy (CP), based on a HRQoL measure specifically developed for this population. **METHODS:** The Dutch version of the Caregiver Priorities and Child Health Index of Life with Disabilities (CPCHILD-DV) was used to measure HRQoL. It was completed by 66 parents of 47 boys and 19 girls with non-ambulatory CP aged between five and 18 years with gross motor function classification system (GMFCS) levels of IV and V. Factors measured were the child's motor and cognitive impairments, comorbidities, pain, parents' education and occupations and family structure. Multiple linear regression analyses were used to determine the significant factors and the relative contribution of these factors to the CPOCHILD-DV scores. **RESULTS:** The most important factors associated with poorer HRQoL scores were pain and hospital admissions in the previous six months. Other factors were: increased GMFCS level, feeding by gastrostomy tube, inability to communicate verbally, cognitive impairment, poor seizure control and higher parents' educational qualifications. **CONCLUSION:** Pain and hospital admissions were the most important factors that were negatively associated with HRQoL in non-ambulatory children with CP between five to 18 years. This article is protected by copyright. All rights reserved.

[PMID: 27250697](#)

8. Eur J Paediatr Neurol. 2016 May 11. pii: S1090-3798(16)30024-1. doi: 10.1016/j.ejpn.2016.05.001. [Epub ahead of print]

Bilateral transcervical submandibular gland excision for drooling: A study of the mature scar and long-term effects.

Delsing CP, Viergever T, Honings J, van den Hoogen FJ.

AIM: Several surgical techniques are available to treat drooling in neurologically disabled children and adolescents, with bilateral submandibular gland excision being the only transcervical procedure. External scars can be a reason to decline for this surgical approach. We investigated which factors influenced caregiver satisfaction by evaluating the long-term scar in relation to treatment outcome. **METHODS:** We identified a historical cohort, in which all neurologically disabled patients who underwent bilateral submandibular gland excision for drooling between January 2009 and December 2013 were identified (n = 41). The Patient and Observer Scar Assessment Scale (POSAS) was used to evaluate observer and clinician satisfaction. All included patients were contacted by telephone and completed a digital questionnaire that included digital images of the scars. **RESULTS:** Of the caregivers that responded the questionnaire 76% (19/25) were satisfied with the overall outcome. Twenty-four (96%) caregivers considered the scars acceptable. Caregiver satisfaction was not correlated to the appearance of scars, but was significantly correlated with the decrease in drooling severity on a visual analogue scale (p = 0.035) and decrease in lower respiratory tract infections (p = 0.042). **INTERPRETATION:** The appearance of scars does not influence satisfaction after bilateral submandibular gland excision for drooling. As expected, satisfaction is correlated to the treatment outcome.

[PMID: 27245880](#)

9. Int J Pediatr Otorhinolaryngol. 2016 Jun;85:33-9. doi: 10.1016/j.ijporl.2016.03.010. Epub 2016 Mar 19.

Managing children with sialorrhoea (drooling): Experience from the first 301 children in our saliva control clinic.

Montgomery J, McCusker S, Lang K, Grosse S, Mace A, Lumley R, Kubba H.

OBJECTIVES: Sialorrhoea (drooling) is defined as the involuntary escape of saliva from the mouth. It is considered normal in young children but may cause social problems in older children. Sialorrhoea is frequently seen in children with cerebral palsy, with rates between 10% and 58% and in other neurodevelopmental diseases. Management of these children can be challenging and often requires an individual and stepwise approach. This is a large case series of children managed at the saliva control clinic in Glasgow, Scotland. **METHODS:** A chart review of all children attending the saliva control clinic between 2006 and June 2012 was performed. This was to ensure that all children would have long term follow up (3 years minimum). Drooling severity was assessed on the child's first attendance at clinic, and at review following a treatment option, using the Teacher Drooling Scale (TDS). **RESULTS:** The total number of children attending this clinic was 301, of which 274 had adequate records for inclusion in the study. 176 (64%) were male. The mean age was 7.3 (median 5) years. In terms of development 35 (13%) of children were developing normally and 50 (18%) had general developmental delay. There were 105 (38%) children with cerebral palsy. The final management of sialorrhoea in these children was simple reassurance and advice for 34 (12%), speech and language therapy for 62 (23%) anticholinergics in 90 patients (33%), botox for 30 (11%) and surgery for 71 (26%) children. The rate of non-tolerance of anticholinergics is 30%; 90 of the 298 children tried on anticholinergics had side effects leading to the treatment being stopped. The average teachers drooling score was 4.24 before clinic and 1.59 after clinic. Satisfactory results were achieved in 215 (78%) of children. **CONCLUSION:** Our data illustrates that effective patient management requires all treatment options to be available, including speech therapy, medications, botulinum toxin and surgery. This is one of the larger case series of children attending a saliva control clinic.

[PMID: 27240493](#)

Prevention and Cure

10. Stem Cells *Transl Med.* 2016 May 31. pii: sctm.2015-0372. [Epub ahead of print]

Concise Review: Stem Cell Interventions for People With Cerebral Palsy: Systematic Review With Meta-Analysis.

Novak I, Walker K, Hunt RW, Wallace EM, Fahey M, Badawi N.

: Evidence for stem cells as a potential intervention for cerebral palsy is emerging. Our objective was to determine the efficacy and safety of stem cells for improving motor and cognitive function of people with cerebral palsy. Searches were conducted in October 2015 in CENTRAL, DARE, MEDLINE, and Cochrane Libraries. Randomized controlled trials and controlled clinical trials of stem cells for cerebral palsy were included. Two authors independently decided upon included trials, extracted data, quality, and risk of bias. The primary outcome was gross motor function. Secondary outcomes were cognitive function and adverse events (AEs). Effects were expressed as standardized mean differences (SMD) with 95% confidence intervals (CI), using a random-effects model. Five trials comprising 328 participants met inclusion criteria. Four cell types were studied: olfactory ensheathing, neural, neural progenitors, and allogeneic umbilical cord blood (UCBs). Transplantation procedures differed from central nervous system neurosurgical transplantation to intravenous/arterial infusion. Participants were followed short-term for only 6 months. Evidence of variable quality indicated a small statistically significant intervention effect from stem cells on gross motor skills (SMD 1.27; 95% CI 0.22, 2.33), with UCBs most effective. There were insufficient and heterogeneous data to compare cognitive effects. Serious AEs were rare ($n = 4/135$ [3%] stem cells; $n = 3/139$ [2%] controls). Stem cells appeared to induce short-term improvements in motor skills. Different types of stem cell interventions were compared, meaning the data were heterogeneous and are a study limitation. Further randomized controlled trials are warranted, using rigorous methodologies. SIGNIFICANCE: Stem cells are emerging as a scientifically plausible treatment and possible cure for cerebral palsy, but are not yet proven. The lack of valid animal models has significantly hampered the scope of clinical trials. Despite the state of current treatment evidence, parents remain optimistic about the potential improvements from stem cell intervention and feel compelled to exhaust all therapeutic options, including stem cell tourism. Receiving unproven therapies from unvalidated sources is potentially dangerous. Thus it is essential that researchers and clinicians stay up to date. A systematic review and meta-analysis summarizing and aggregating current research data may provide more conclusive evidence to inform treatment decision making and help direct future research.

[PMID: 27245364](#)

11. *Acta Paediatr.* 2016 May 31. doi: 10.1111/apa.13491. [Epub ahead of print]

Formal training in general movement assessment is required to effectively evaluate infants with perinatal asphyxia in outpatient settings.

Brown AK, Greisen G, Haugsted U, Jonsbo F.

AIM: General movement assessment (GMA) can help to identify children with a high risk of developing neurological dysfunction, such as cerebral palsy, and certified training is provided in this specialism. The aim of this study was to investigate the feasibility and reliability of using video recordings to assess GMA, in a busy Danish outpatient clinic. METHODS: The study comprised 30 term infants born with perinatal asphyxia, who were video recorded at three months. They were assessed by two certified GMA observers and re-assessed two weeks later. Inter-observer and intra-observer agreements were analysed using proportional agreement and nominal kappa statistics were used to calculate 95% confidence intervals (95% CI). RESULTS: We found substantial and almost perfect inter-observer and intra-observer reliability. Intra-observer agreement was 0.85 (95% CI: 0.65-1.00; $p < 0.0001$) and 0.85 (95% CI: 0.62-1.00; $p < 0.0001$) and inter-observer agreement was 0.71 (95% CI: 0.45-0.96; $p < 0.0001$) at time point one and 0.85 (95% CI: 0.63 -1.00; $p < 0.0001$) two weeks later. All video recordings were completed within our multidisciplinary outpatient clinic without delay. CONCLUSION: This study demonstrated the reliability of the GMA method in a busy multidisciplinary Danish paediatric outpatient setting, when assessors had been formally trained in the method and used it regularly. This article is protected by copyright. All rights reserved.

[PMID: 27240948](#)

12. BJOG. 2016 May 31. doi: 10.1111/1471-0528.14133. [Epub ahead of print]

Prolonged latency of preterm prelabour rupture of membranes and neurodevelopmental outcomes: a secondary analysis.

Drassinower D, Friedman AM, Običan SG, Levin H, Gyamfi-Bannerman C.

OBJECTIVE: To determine whether prolonged latency after preterm prelabour rupture of membranes (PPROM) is associated with an increased risk for adverse neurodevelopmental outcomes. **DESIGN:** This is a secondary analysis of the randomised controlled trial of magnesium sulphate for the prevention of cerebral palsy. **SETTING:** Multicentre trial. **POPULATION:** A total of 1305 women with PPRM were analysed, 1056 of whom had an interval of <3 weeks between diagnosis and delivery and 249 of whom had an interval of ≥3 weeks between diagnosis and delivery. **METHODS:** We evaluated whether the time interval between diagnosis of PPRM and delivery was associated with an increased risk for adverse neurodevelopmental outcomes. Latency was analysed as a continuous variable and categorised by weeks of latency. **MAIN OUTCOME MEASURES:** The primary outcome was motor and mental Bayley scores of <70 at 2 years of age. Secondary outcomes included motor and mental Bayley scores <85 and mean Bayley scores. Logistic regression was used to control for confounding factors. **RESULTS:** In the univariate analysis, motor and mental Bayley scores of <70 were similar in the <3 weeks (16.8 and 14.4%) and ≥3 weeks (15.3 and 14.1%) groups. In the regression analysis adjusting for confounding factors, PPRM for ≥3 weeks was an independent risk factor for motor (adjusted odds ratio (aOR) 2.12; 95% confidence interval, 95% CI 1.29-3.49) and mental (aOR 1.83, 95% CI 1.13-3.00) Bayley scores of <70. Neonatal sepsis, gestational age at delivery, maternal education, and race were significantly associated with neurodevelopmental outcomes. **CONCLUSIONS:** Whereas delivery at later gestational age is associated with improved prognosis for many outcomes, prolonged exposure to an intrauterine environment of PPRM is an independent risk factor for adverse neurodevelopmental outcomes.

[PMID: 27245741](#)

13. Case Rep Transplant. 2016;2016:1717426. doi: 10.1155/2016/1717426. Epub 2016 Apr 30.

First Autologous Cord Blood Therapy for Pediatric Ischemic Stroke and Cerebral Palsy Caused by Cephalic Molding during Birth: Individual Treatment with Mononuclear Cells.

Jensen A, Hamelmann E.

Intracranial laceration due to traumatic birth injury is an extremely rare event affecting approximately one newborn per a population of 4.5 million. However, depending on the mode of injury, the resulting brain damage may lead to lifelong sequelae, for example, cerebral palsy for which there is no cure at present. Here we report a rare case of neonatal arterial ischemic stroke and cerebral palsy caused by fetal traumatic molding and parietal depression of the head during delivery caused by functional cephalopelvic disproportion due to a "long pelvis." This patient was treated by autologous cord blood mononuclear cells (45.8 mL, cryopreserved, TNC 2.53×10^8) with a remarkable recovery. Active rehabilitation was provided weekly. Follow-up examinations were at 3, 18, 34, and 57 months. Generous use of neonatal head MRI in case of molding, craniofacial deformity, and a sentinel event during parturition is advocated to enhance diagnosis of neonatal brain damage as a basis for fast and potentially causative treatment modalities including autologous cord blood transplantation in a timely manner.

[PMID: 27239361](#)

14. Hum Brain Mapp. 2016 Jun 3. doi: 10.1002/hbm.23262. [Epub ahead of print]

Alterations in regional shape on ipsilateral and contralateral cortex contrast in children with unilateral cerebral palsy and are predictive of multiple outcomes.

Pagnozzi AM, Dowson N, Fiori S, Doecke J, Bradley AP, Boyd RN, Rose S.

Congenital brain lesions result in a wide range of cerebral tissue alterations observed in children with cerebral palsy (CP) that are associated with a range of functional impairments. The relationship between injury severity and functional outcomes, however, remains poorly understood. This research investigates the differences in cortical shape between children with congenital brain lesions and typically developing children (TDC) and investigates the correlations between cortical shape and functional outcome in a large cohort of patients diagnosed with unilateral CP. Using 139 structural magnetic resonance images, including 95 patients with clinically diagnosed CP and 44 TDC, cortical segmentations were obtained using a modified expectation maxi-

mization algorithm. Three shape characteristics (cortical thickness, curvature, and sulcal depth) were computed within a number of cortical regions. Significant differences in these shape measures compared to the TDC were observed on both the injured hemisphere of children with CP ($P < 0.004$), as well as on the apparently uninjured hemisphere, illustrating potential compensatory mechanisms in these children. Furthermore, these shape measures were significantly correlated with several functional outcomes, including motor, cognition, vision, and communication ($P < 0.012$), with three out of these four models performing well on test set validation. This study highlights that cortical neuroplastic effects may be quantified using MR imaging, allowing morphological changes to be studied longitudinally, including any influence of treatment. Ultimately, such approaches could be used for the long term prediction of outcomes and the tailoring of treatment to individuals. *Hum Brain Mapp*, 2016. © 2016 Wiley Periodicals, Inc.

[PMID: 27259165](#)

15. *Hum Brain Mapp*. 2016 Jun 3. doi: 10.1002/hbm.23276. [Epub ahead of print]

Using ventricular modeling to robustly probe significant deep gray matter pathologies: Application to cerebral palsy.

Pagnozzi AM, Shen K, Doecke JD, Boyd RN, Bradley AP, Rose S, Dowson N.

Understanding the relationships between the structure and function of the brain largely relies on the qualitative assessment of Magnetic Resonance Images (MRIs) by expert clinicians. Automated analysis systems can support these assessments by providing quantitative measures of brain injury. However, the assessment of deep gray matter structures, which are critical to motor and executive function, remains difficult as a result of large anatomical injuries commonly observed in children with Cerebral Palsy (CP). Hence, this article proposes a robust surrogate marker of the extent of deep gray matter injury based on impingement due to local ventricular enlargement on surrounding anatomy. Local enlargement was computed using a statistical shape model of the lateral ventricles constructed from 44 healthy subjects. Measures of injury on 95 age-matched CP patients were used to train a regression model to predict six clinical measures of function. The robustness of identifying ventricular enlargement was demonstrated by an area under the curve of 0.91 when tested against a dichotomised expert clinical assessment. The measures also showed strong and significant relationships for multiple clinical scores, including: motor function ($r^2 = 0.62$, $P < 0.005$), executive function ($r^2 = 0.55$, $P < 0.005$), and communication ($r^2 = 0.50$, $P < 0.005$), especially compared to using volumes obtained from standard anatomical segmentation approaches. The lack of reliance on accurate anatomical segmentations and its resulting robustness to large anatomical variations is a key feature of the proposed automated approach. This coupled with its strong correlation with clinically meaningful scores, signifies the potential utility to repeatedly assess MRIs for clinicians diagnosing children with CP. *Hum Brain Mapp*, 2016. © 2016 Wiley Periodicals, Inc.

[PMID: 27257958](#)

16. *IEEE/ACM Trans Comput Biol Bioinform*. 2016 May 9. [Epub ahead of print]

Brain Modulyzer: Interactive Visual Analysis of Functional Brain Connectivity.

Murugesan S, Bouchard K, Brown JA, Hamann B, Seeley WW, Trujillo A, Weber GH.

We present Brain Modulyzer, an interactive visual exploration tool for functional magnetic resonance imaging (fMRI) brain scans, aimed at analyzing the correlation between different brain regions when resting or when performing mental tasks. Brain Modulyzer combines multiple coordinated views—such as heat maps, node link diagrams and anatomical views—using brushing and linking to provide an anatomical context for brain connectivity data. Integrating methods from graph theory and analysis, e.g., community detection and derived graph measures, makes it possible to explore the modular and hierarchical organization of functional brain networks. Providing immediate feedback by displaying analysis results instantaneously while changing parameters gives neuroscientists a powerful means to comprehend complex brain structure more effectively and efficiently and supports forming hypotheses that can then be validated via statistical analysis. To demonstrate the utility of our tool, we present two case studies—exploring progressive supranuclear palsy, as well as memory encoding and retrieval.

[PMID: 27244747](#)

17. Indian Pediatr. 2016 May 8;53(5):391-3.

Neurodevelopmental Outcome of Extremely Low Birth Weight Children at Corrected Age of Two Years.

Mukhopadhyay K, Mahajan R, Malhi P, Kumar A.

OBJECTIVE: To assess the neurodevelopmental, cognitive and behavioral function of extremely low birth weight babies (ELBW) till corrected age of two years. **METHODS:** 79 ELBW babies were enrolled and followed at 1 year (n=50), 18 months (n=47) and 2 years (n=36). Adverse composite outcome was defined as death or moderate-to-severe neurodevelopmental impairment (defined as either cerebral palsy or DQ score <70 or deafness or blindness). **RESULTS:** At 1 year, 24% were neurologically abnormal. At 18 months, average score (>85) was seen in 25 (54%) children in motor and 8 (17%) in mental development. Abnormal behavioral score (?12) was seen in 89% children. Adverse composite outcome was present in 28 (35.4%) babies. **CONCLUSIONS:** ELBW neonates are at a high risk of neurodevelopmental and behavioral impairment.

[PMID: 27254046](#)

18. Iran J Child Neurol. 2016 Spring;10(2):1-9.

The Role of Information Systems to Manage Cerebral Palsy.

Ajami S, Maghsoudlorad AA.

Objective In healthcare system, it is necessary to have exact and accurate information in order to address health care needs and requirements of society members as well as expectations of policy makers, planners and decision makers. The aim of this narrative review article was to explain the role of information systems in cerebral palsy management and identify the advantages and barriers to the development of cerebral palsy registry system. Data were collected using databases such as of Science Direct, PubMed, Proquest, Springer, and SID (Scientific Information Database). Overall, 65 sources were selected. One of the biggest challenges for children with physical and motor disabilities in rehabilitation center is access to a system, which provides a comprehensive data set reflecting all information on a patient's care. Thus, data and information management in children with physical and motor disability such as cerebral palsy facilitates access to data and cerebral palsy data comparison as well as the monitoring incidence rate of cerebral palsy, enhancing health care quality; however, there are always numerous barriers to establish the system. One of the ways to overcome these problems is the establishment of a standard framework of minimum data sets and exact definition of its data components. Reliable standards in the use of applications as well as user-friendly software will ensure patients' data extraction and registration.

[PMID: 27247578](#)

19. J Child Neurol. 2016 May 27. pii: 0883073816650038. [Epub ahead of print]

Clinical Trial of Erythropoietin in Young Children With Cerebral Palsy.

Cho KH, Min K, Lee SH, Lee S, An SA, Kim M.

This study was conducted to assess the safety and efficacy of recombinant human erythropoietin in young children with cerebral palsy aged between 6 months and 3 years. All participants received subcutaneous recombinant human erythropoietin and 8 weeks of rehabilitation therapy. Adverse events, changes of vital signs, and hematologic tests were monitored up to 8 weeks postinjection. Functional measures of development at 4 and 8 weeks postinjection were compared with baseline values, and improvements were compared with those of an age-matched historical control group. Nine participants completed the trial from June 2012 to February 2015. No adverse events were related to recombinant human erythropoietin. Erythropoiesis was noted, although within normal range. Functional improvements were observed in all participants ($P < .05$) and increases in motor function were higher in recombinant human erythropoietin group than the control group. Accordingly, recombinant human erythropoietin administration was safe without any significant adverse events and improved the functional outcomes in young children with cerebral palsy.

[PMID: 27233796](#)

20. Pediatrics. 2016 May;137(5). pii: e20153482. doi: 10.1542/peds.2015-3482. Epub 2016 Apr 7.

Birth Spacing and Risk of Autism and Other Neurodevelopmental Disabilities: A Systematic Review.

Conde-Agudelo A, Rosas-Bermudez A, Norton MH.

CONTEXT: Both short and long interpregnancy intervals (IPIs) have recently been associated with increased risk of autism spectrum disorder (ASD). However, this association has not been systematically evaluated. OBJECTIVE: To examine the relationship between birth spacing and the risk of ASD and other neurodevelopmental disabilities. DATA SOURCES: Electronic databases from their inception to December 2015, bibliographies, and conference proceedings. STUDY SELECTION: Observational studies with results adjusted for potential confounding factors that reported on the association between IPIs or birth intervals and neurodevelopmental disabilities. DATA EXTRACTION: Two reviewers independently extracted data on study characteristics, IPIs/birth intervals, and outcome measures. RESULTS: Seven studies (1 140 210 children) reported an association between short IPIs and increased risk of ASD, mainly the former subtype autistic disorder. Compared with children born to women with IPIs of ≥ 36 months, children born to women with IPIs of < 12 months had a significantly increased risk of any ASD (pooled adjusted odds ratio [OR] 1.90, 95% confidence interval [CI] 1.16-3.09). This association was stronger for autistic disorder (pooled adjusted OR 2.62, 95% CI 1.53-4.50). Three of these studies also reported a significant association between long IPIs and increased risk of ASD. Short intervals were associated with a significantly increased risk of developmental delay (3 studies; 174 940 children) and cerebral palsy (2 studies; 19 419 children). LIMITATIONS: Substantial heterogeneity, and few studies assessing neurodevelopmental disabilities other than ASD. CONCLUSIONS: Short IPIs are associated with a significantly increased risk of ASD. Long IPIs also appear to increase the risk of ASD.

[PMID: 27244802](#)**21. Pediatrics. 2016 Jun;137(6). pii: e20153334. doi: 10.1542/peds.2015-3334.**

Asphyxia, Neurologic Morbidity, and Perinatal Mortality in Early-Term and Postterm Birth.

Seikku L, Gissler M, Andersson S, Rahkonen P, Stefanovic V, Tikkanen M, Paavonen J, Rahkonen L.

BACKGROUND AND OBJECTIVES: Neonatal outcomes vary by gestational age. We evaluated the association of early-term, full-term, and postterm birth with asphyxia, neurologic morbidity, and perinatal mortality. METHODS: Our register-based study used retrospective data on 214 465 early-term (37(+0)-38(+6) gestational weeks), 859 827 full-term (39(+0)-41(+6)), and 55 189 postterm ($\geq 42(+0)$) live-born singletons during 1989-2008 in Finland. Asphyxia parameters were umbilical cord pH and Apgar score at 1 and 5 minutes. Neurologic morbidity outcome measures were cerebral palsy (CP), epilepsy, intellectual disability, and sensorineural defects diagnosed by the age of 4 years. Newborns with major congenital anomalies were excluded from perinatal deaths. RESULTS: Multivariate analysis showed that, compared with full-term pregnancies, early-term birth increased the risk for low Apgar score (< 4) at 1 and 5 minutes (odds ratio 1.03, 95% confidence interval 1.03-1.04 and 1.24, 1.04-1.49, respectively), CP (1.40, 1.27-1.55), epilepsy (1.14, 1.06-1.23), intellectual disability (1.39, 1.27-1.53), sensorineural defects (1.24, 1.17-1.31), and perinatal mortality (2.40, 2.14-2.69), but risk for low umbilical artery pH ≤ 7.10 was decreased (0.83, 0.79-0.87). Postterm birth increased the risk for low Apgar score (< 4) at 1 minute (1.26, 1.26-1.26) and 5 minutes (1.80, 1.43-2.34), low umbilical artery pH ≤ 7.10 (1.26, 1.19-1.34), and intellectual disability (1.19, 1.00-1.43), whereas risks for CP (1.03, 0.84-1.26), epilepsy (1.00, 0.87-1.15), sensorineural defects (0.96, 0.86-1.07), and perinatal mortality (0.91, 0.69-1.22) were not increased. CONCLUSIONS: Early-term birth was associated with low Apgar score, increased neurologic morbidity, and perinatal mortality. Asphyxia and intellectual disability were more common among postterm births, but general neurologic morbidity and perinatal mortality were not increased.

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Neurodevelopmental Outcomes Following Bevacizumab Injections for Retinopathy of Prematurity.

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BACKGROUND AND OBJECTIVE: Bevacizumab intravitreal injection, a vascular endothelial growth factor inhibitor, is used to treat retinopathy of prematurity (ROP). However, concerns have been raised regarding its systemic absorption and ef-

fect on developing tissues including brain. This study compared neurodevelopment at 18 months' corrected age in preterm infants of <29 weeks' gestation treated with bevacizumab versus laser ablation. **METHODS:** Data from the Canadian Neonatal Network and the Canadian Neonatal Follow-Up Network databases were retrospectively reviewed. Infants born at <29 weeks' in 2010-2011 with treated ROP were studied. Neurodevelopmental outcome at 18 months was assessed by using neurologic examination and the Bayley Scales of Infant and Toddler Development Third Edition. Regression analyses were performed. **RESULTS:** Of 125 treated infants, 27 received bevacizumab and 98 laser. The bevacizumab group, compared with laser, obtained a median Bayley Scales of Infant and Toddler Development Third Edition motor composite score of 81 (interquartile range, 70-91) versus 88 (79-97), a language composite score of 79 (65-97) versus 89 (74-97), and a cognitive score of 90 (80-100) versus 90 (85-100). Difference was detected on the motor score only ($P = .02$). Odds of severe neurodevelopmental disabilities (Bayley scores <70, severe cerebral palsy, hearing aids, or bilateral blindness) was 3.1 times higher (95% confidence interval: 1.2-8.4) in infants treated with bevacizumab versus laser after adjusting for gestational age, gender, maternal education, Score for Neonatal Acute Physiology-II score, bronchopulmonary dysplasia, sepsis, and severe brain injury. **CONCLUSIONS:** Preterm infants treated with bevacizumab versus laser had higher odds of severe neurodevelopmental disabilities. Further investigation on the long-term safety of antivascular endothelial growth factor treatment of ROP is needed.

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