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Professor Nadia Badawi

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Interventions and Management

1. *J Neurosurg Pediatr.* 2013 Oct 11. [Epub ahead of print]

Reduction in upper-extremity tone after lumbar selective dorsal rhizotomy in children with spastic cerebral palsy.

Gigante P, McDowell MM, Bruce SS, Chirelstein G, Chiriboga CA, Dutkowsky J, Fontana E, Hyman J, Kim H, Morgan D, Pearson TS, Roye BD, Roye DP Jr, Ryan P, Vitale M, Anderson RC.

Department of Neurological Surgery, Columbia University.

Object: Randomized clinical trials have established that lumbar selective dorsal rhizotomy (SDR) reduces lower-extremity tone and improves functional outcome in children with spastic cerebral palsy. Significant data exist to support a secondary effect on upper-extremity function in patients with upper-extremity spasticity. The effects of SDR on upper-extremity tone, however, are not well characterized. In this report, the authors sought to assess changes in upper-extremity tone in individual muscle groups after SDR and tried to determine if these changes could be predicted preoperatively. Methods: The authors retrospectively reviewed 42 children who underwent SDR at Columbia University Medical Center/Morgan Stanley Children's Hospital of New York-Presbyterian between 2005 and 2011. Twenty-five had upper-extremity spasticity. All underwent pre- and postoperative examination for measuring tone (Modified Ashworth Scale) and assessing functional outcome. Follow-up examinations with therapists were performed at least once at a minimum of 2 months postoperatively (mean 15 months). Results: In the upper extremities, 23 (92%) of 25 patients had improvements of at least 1 Ashworth point in 2 or more independent motor groups on the Modified Ashworth Scale, and 12 (71%) of 17 families surveyed reported increases in motor control or spontaneous movement. The mean Modified Ashworth Scale scores for all upper-extremity muscle groups demonstrated an improvement from 1.34 to 1.22 ($p < 0.001$). Patients with a mean preoperative upper-extremity tone of 1.25-1.75 were most likely to benefit from reduction in tone ($p = 0.0019$). Proximal and pronator muscle groups were most likely to demonstrate reduced tone. Conclusions: In addition to improvements in lower-extremity tone and function, SDR has demonstrable effects on upper extremities. Greater than 90% of our patients with elevated upper-extremity tone demonstrated reduction in tone in at least 2 muscle groups postoperatively. Patients with a mean Modified Ashworth Scale upper-extremity score of 1.25-1.75 may encounter the greatest reduction in upper-extremity tone.

[PMID: 24116982](https://pubmed.ncbi.nlm.nih.gov/24116982/) [PubMed - as supplied by publisher]

2. Dev Med Child Neurol. 2013 Oct 15. doi: 10.1111/dmcn.12317. [Epub ahead of print]**Determinants of gross motor function of young children with cerebral palsy: a prospective cohort study.**

Bartlett DJ, Chiarello LA, McCoy SW, Palisano RJ, Jeffries L, Fiss AL, Rosenbaum P, Wilk P.

School of Physical Therapy, Western University, London, ON, Canada.

AIM: The aim of this study was to test a model of determinants of gross motor function of young children with cerebral palsy (CP). **METHOD:** Four hundred and twenty-nine children with CP (242 males, 187 females; mean age 3y 2mo, SD 11mo) representing all levels of the Gross Motor Function Classification System (GMFCS) participated. Children in levels I to II and III to V were classified as Groups 1 and 2 respectively. Distribution of CP was quadriplegia, 44%; hemiplegia, 24%; diplegia, 23%; triplegia, 6%; and monoplegia, 2% (data not available for 1%). Impairment and motor function data were collected by reliable assessors; parents completed questionnaires on health conditions and adaptive behavior. Seven months later, parents were interviewed about family life and services received. One year after the study onset, motor function was re-evaluated. Analysis involved structural equation modeling. **RESULTS:** The well-fitting model explained 58% and 75% of the variance in motor function at study completion for Groups 1 and 2 respectively. Primary impairments (spasticity, quality of movement, postural stability, and distribution of involvement; $\beta=0.52-0.68$) and secondary impairments (strength, range of motion limitations, and reduced endurance; $\beta=0.25-0.26$) explained the most variance. Adaptive behavior was a significant determinant only for Group 2 ($\beta=0.21$) and participation in community programs was significant only in Group 1 ($\beta=0.13$). **INTERPRETATION:** Motor function is supported by optimizing body structures and function for all children and enhancing adaptive behavior for children with greater motor challenges.

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3. J Neurosci. 2013 Jul 31;33(31):12898-907. doi: 10.1523/JNEUROSCI.1552-13.2013.**Selective effects of baclofen on use-dependent modulation of GABAB inhibition after tetraplegia.**

Barry MD, Bunday KL, Chen R, Perez MA.

University of Pittsburgh, Department of Physical Medicine and Rehabilitation, Center for the Neural Basis of Cognition, Systems Neuroscience Institute, Pittsburgh, Pennsylvania 15261, USA.

Baclofen is a GABAB receptor agonist commonly used to relief spasticity related to motor disorders. The effects of baclofen on voluntary motor output are limited and not yet understood. Using noninvasive transcranial magnetic and electrical stimulation techniques, we examined electrophysiological measures probably involving GABAB (long-interval intracortical inhibition and the cortical silent period) and GABAA (short-interval intracortical inhibition) receptors, which are inhibitory effects mediated by subcortical and cortical mechanisms. We demonstrate increased active long-interval intracortical inhibition and prolonged cortical silent period during voluntary activity of an intrinsic finger muscle in humans with chronic incomplete cervical spinal cord injury (SCI) compared with age-matched controls, whereas resting long-interval intracortical inhibition was unchanged. However, long-term (~6 years) use of baclofen decreased active long-interval intracortical inhibition to similar levels as controls but did not affect the duration of the cortical silent period. We found a correlation between signs of spasticity and long-interval intracortical inhibition in patients with SCI. Short-interval intracortical inhibition was decreased during voluntary contraction compared with rest but there was no effect of SCI or baclofen use. Together, these results demonstrate that baclofen selectively maintains use-dependent modulation of largely subcortical but not cortical GABAB neuronal pathways after human SCI. Thus, cortical GABA(B) circuits may be less sensitive to baclofen than spinal GABAB circuits. This may contribute to the limited effects of baclofen on voluntary motor output in subjects with motor disorders affected by spasticity.

[PMID: 23904624](#) [PubMed - indexed for MEDLINE] [PMCID: PMC3728695](#) [Available on 2014/1/31]

4. J Digit Imaging. 2013 Oct 16. [Epub ahead of print]**Design and Validation of Automated Femoral Bone Morphology Measurements in Cerebral Palsy.**

Park N, Lee J, Sung KH, Park MS, Koo S.

Department of Computer Science and Engineering, Seoul National University, Seoul, Republic of Korea.

Accurate quantification of bone morphology is important for monitoring the progress of bony deformation in patients with cerebral palsy. The purpose of the study was to develop an automatic bone morphology measurement method using one or two radiographs. The study focused on four morphologic measurements-neck-shaft angle, femoral anteversion, shaft bowing angle, and neck length. Fifty-four three-dimensional (3D) geometrical femur models were generated from the computed tomography (CT) of cerebral palsy patients. Principal component analysis was performed on the combined data of geometrical femur models and manual measurements of the four morphologic measurements to generate a statistical femur model. The 3D-2D registration of the statistical femur model for radiography computes four morphological measurements of the femur in the radiographs automatically. The prediction performance was tested here by means of leave-one-out cross-validation and was quantified by the intraclass correlation coefficient (ICC) and by measuring the absolute differences between automatic prediction from two radiographs and manual measurements using original CT images. For the neck-shaft angle, femoral anteversion, shaft bowing angle, and neck length, the ICCs were 0.812, 0.960, 0.834, and 0.750, respectively, and the mean absolute differences were 2.52°, 2.85°, 0.92°, and 1.88 mm, respectively. Four important dimensions of the femur could be predicted from two views with very good agreement with manual measurements from CT and hip radiographs. The proposed method can help young patients avoid instances of large radiation exposure from CT, and their femoral deformities can be quantified robustly and effectively from one or two radiograph(s).

[PMID: 24129653](#) [PubMed - as supplied by publisher]

5. Dev Med Child Neurol. 2013 Sep;55(9):779-80. doi: 10.1111/dmcn.12173. Epub 2013 Jun 29.**A population study of fractures: what we can learn and what we cannot learn.**

Henderson R.

Orthopaedics and Pediatrics, University of North Carolina, Chapel Hill, NC, USA.

Comment on

Fractures in children with cerebral palsy: a total population study. [Dev Med Child Neurol. 2013]

[PMID: 23808882](#) [PubMed - indexed for MEDLINE]

6. Front Neurol. 2013 Oct 14;4:138.**Virtual Sensory Feedback for Gait Improvement in Neurological Patients.**

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Computer Science Department, Technion - Israel Institute of Technology, Haifa, Israel.

We review a treatment modality for movement disorders by sensory feedback. The natural closed-loop sensory-motor feedback system is imitated by a wearable virtual reality apparatus, employing body-mounted inertial sensors and responding dynamically to the patient's own motion. Clinical trials have shown a significant gait improvement in patients with Parkinson's disease using the apparatus. In contrast to open-loop devices, which impose constant-velocity visual cues in a "treadmill" fashion, or rhythmic auditory cues in a "metronome" fashion, requiring constant vigilance and attention strategies, and, in some cases, instigating freezing in Parkinson's patients, the closed-loop device improved gait parameters and eliminated freezing in most patients, without side effects. Patients with multiple sclerosis, previous stroke, senile gait, and cerebral palsy using the device also improved their balance and gait substantially. Training with the device has produced a residual improvement, suggesting virtual sensory feedback for the treatment of neurological movement disorders.

[PMID: 24133478](#) [PubMed - as supplied by publisher] Free PMC Article

7. Dev Med Child Neurol. 2013 Sep;55(9):786-7. doi: 10.1111/dmcn.12230.

One side or two?

Sangeux M, Wolfe R, Graham HK.

Hugh Williamson Gait Analysis Laboratory, The Royal Children's Hospital, Parkville, Victoria, Australia.

[PMID: 23924082](#) [PubMed - indexed for MEDLINE]

8. Gait Posture. 2013 Sep 25. pii: S0966-6362(13)00604-8. doi: 10.1016/j.gaitpost.2013.09.009. [Epub ahead of print]

Motion of the center of mass in children with spastic hemiplegia: Balance, energy transfer, and work performed by the affected leg vs. the unaffected leg.

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Motion Analysis Lab, Shriners Hospitals for Children, Portland, OR, USA. Electronic address: jfeng@shrinenet.org.

Asymmetry between limbs in people with spastic hemiplegic cerebral palsy (HEMI) adversely affects limb coordination and energy generation and consumption. This study compared how the affected leg and the unaffected leg of children with HEMI would differ based on which leg trails. Full-body gait analysis data and force-plate data were analyzed for 31 children (11.9±3.8 years) with HEMI and 23 children (11.1±3.1 years) with typical development (TD). Results showed that peak posterior center of mass-center of pressure (COM-COP) inclination angles of HEMI were smaller than TD when the affected leg trailed but not when the unaffected leg trailed. HEMI showed greater peak medial COM-COP inclination angles and wider step width than TD, no matter which leg trailed. More importantly, when the affected leg of HEMI trailed, it did not perform enough positive work during double support to propel COM motion. Consequently, the unaffected leg had to perform additional positive work during the early portion of single support, which costs more energy. When the unaffected leg trailed, the affected leg performed more negative work during double support; therefore, more positive work was still needed during early single support, but energy efficiency was closer to that of TD. Energy recovery factor was lower when the affected leg trailed than when the unaffected leg trailed; both were lower than TD. These findings suggest that the trailing leg plays a significant role in propelling COM motion during double support, and the 'unaffected' side of HEMI may not be completely unaffected. It is important to strengthen both legs.

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9. Acta Chir Orthop Traumatol Cech. 2013;80(4):273-7.

Accuracy of Proximal Femur Correction Achieved with LCP Paediatric Hip Plates [Article in Czech]

Ročák K, Poul J, Urbášek K.

Oddělení ortopedie a traumatologie, o.z Nemocnice Přerov, Středomoravská nemocniční a.s, člen skupiny AGEL.

PURPOSE OF THE STUDY The aim of the study was to evaluate, in comparison with the pre-operative planning, the accuracy of proximal femur correction achieved with the use of locking compression paediatric hip plates (LCP) in children and adolescents and to assess pre- and post-operative complications. **MATERIAL AND METHODS** A group of 52 patients in whom proximal femoral osteotomy using the LCP was performed on a total of 55 hips between September 2009 and February 2013 were retrospectively evaluated. The following diagnoses were treated: unstable hip in cerebral palsy, 18 operations; Legg-Calvé-Perthes disease, 10 operations; coxa vara of

aetiology other than coxa vara adolescentium (CVA), eight operations; true CVA, six operations; femoral shortening by the Wagner method, six procedures; proximal femoral derotation osteotomy, four procedures; and post-traumatic pseudoarthrosis of the proximal femur, three operations. **RESULTS** Compared with the pre-operative plan, the average deviation of the colodiaphyseal angle was 5.2° (1° to 11°) in 18 unstable hips; 4.7° (1° to 10°) in 10 cases of Legg-Calvé-Perthes disease; 4.5° (3° to 6°) in eight hips with coxa vara of aetiology other than CVA; 6.5° (2° to 13°) in six CVA hips; 4.5° (1° to 10°) in six cases of femoral shortening; 3.5° (1° to 5°) in four derotation osteotomies; and 3.7° (0° to 6°) in three corrections of pseudoarthrosis. In one patient, osteosynthesis failed due to screws being pulled out from the proximal fragment; re-osteosynthesis was carried out using a conventional angled blade plate. **DISCUSSION** As in other international studies, our results confirmed a high accuracy of proximal femur correction with use of the LCP instrumentation. The reported higher time requirement for this technique seems to be related to the learning curve and, with more frequent use, will probably be comparable to the time needed for application of conventional hip angled plates. **CONCLUSIONS** The up-to-date LCP fixation system using the principle of angular stability for correction of the proximal femur in children is a clear advancement and its higher costs are certain to be outweighed by its higher accuracy and thus better results. **Key words:** locking compression plate, paediatric hip. *Práce.*

[PMID: 24119475](#) [PubMed - in process]

10. IEEE Trans Neural Syst Rehabil Eng. 2013 Oct 7. [Epub ahead of print]

Interactive Rehabilitation System for Improvement of Balance Therapies in People With Cerebral Palsy.

Jaume-I-Capo A, Martinez-Bueso P, Moya-Alcover B, Varona J.

The present study covers a new experimental system, designed to improve the balance and postural control of adults with cerebral palsy. This system is based on a serious game for balance rehabilitation therapy, designed using the prototype development paradigm and features for rehabilitation with serious games: feedback, adaptability, motivational elements and monitoring. In addition, the employed interaction technology is based on computer vision because motor rehabilitation consists of body movements that can be recorded, and because vision capture technology is noninvasive and can be used for clients who have difficulties in holding physical devices. Previous research has indicated that serious games help to motivate clients in therapy sessions; however, there remains a paucity of clinical evidence involving functionality. We rigorously evaluated the effects of physiotherapy treatment on balance and gait function of adult subjects with cerebral palsy undergoing our experimental system. A 24-week physiotherapy intervention program was conducted with 9 adults from a cerebral palsy center who exercised weekly in 20-minute sessions. Findings demonstrated a significant increase in balance and gait function scores resulting in indicators of greater independence for our participating adults. Scores improved from 16 to 21 points in a scale of 28, according to the Tinetti Scale for risk of falls, moving from High Fall Risk to Moderate Fall Risk. Our promising results indicate that our experimental system is feasible for balance rehabilitation therapy.

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11. J Rehabil Med. 2013 Oct 15. doi: 10.2340/16501977-1233. [Epub ahead of print]

Postural alignments in children with bilateral spastic cerebral palsy using a bimanual interface for powered wheelchair control.

Liu WY, Chen FJ, Lin YH, Kuo CH, Lien HY, Yu YJ.

Graduate Institute of Rehabilitation Science, Chang Gung University, Taoyuan, Taiwan.

Objective: To examine postural alignment in children with bilateral spastic cerebral palsy while driving a powered wheelchair using both a unilateral joystick and an innovative bimanual interface. **Design:** Cross-sectional study. **Subjects:** A total of 20 children with bilateral spastic cerebral palsy (mean age 9.0 years (standard deviation 2.1); 11 with diplegia, 9 with quadriplegia) and 14 typically developing children (mean age 7.7 years (standard deviation 2.9)). **Methods:** All children drove the powered wheelchair in both the unilateral and bimanual conditions. The Seated Postural Control Measure quantified the postural alignment of subjects while driving the powered wheelchair. Statistical analysis was carried out using repeated measures analysis of variance and Spearman's rank

correlation coefficient. Results: As expected, typically developing children had better postural alignment in both driving conditions than children with cerebral palsy. Children with cerebral palsy demonstrated more symmetrical postural alignment while using the bimanual interface than when using the unilateral joystick. In addition, the severity of cerebral palsy correlated moderately with postural symmetry in both conditions. Conclusion: The results suggest that this innovative bimanual interface might be beneficial for promoting symmetrical postural alignment in some children with bilateral spastic cerebral palsy.

[PMID: 24129561](#) [PubMed - as supplied by publisher]

12. Ann Phys Rehabil Med. 2013 Sep 27. pii: S1877-0657(13)01286-4. doi: 10.1016/j.rehab.2013.08.002. [Epub ahead of print]

Rehabilitation of 190 non-ambulatory children with cerebral palsy in structures of care or in liberal sector.

Poirot I, Laudy V, Rabilloud M, Roche S, Ginhoux T, Joubrel I, Porsmoguer E, Grimont E, Vuillerot C, Kassaï B.

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AIMS: To describe the rehabilitation of non-ambulatory children with cerebral palsy and to explore adjustability on their individual needs. MATERIAL AND METHOD: Data described are extracted from an on-going national cohort study, following during 10years 385 children with cerebral palsy, aged from 4 to 10, Gross Motor Function Classification System IV and V. We analysed data from the first 190 patients (mean age 6years 10months (SD 2.0), 111 boys), focusing on physiotherapy, ergotherapy, psychomotility and speech therapy in medico-social and liberal sectors. RESULTS: In medico-social sector, duration of paramedical care is significantly more important than in liberal sector (structure of care: median=4.25h/week, liberal sector: median=2.00h/week) ($P<0.0001$). More than 4 different types of care per week are given in medico-social sector, while in liberal sector children benefit from only 2 different types of care a week. In investigators opinion, rehabilitation in structures of care is 71.65% adapted as opposed to 18.75% in the liberal sector ($P<0.001$). Children level V have less time of rehabilitation than the others ($P=0.0424$). INTERPRETATION: Rehabilitation of children with cerebral palsy who are not able to walk, with an objective to improve quality of life, is truly multidisciplinary and suitable in medico-social sector.

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13. Curr Opin Neurol. 2013 Oct 16. [Epub ahead of print]

Bioengineering solutions for neural repair and recovery in stroke.

Modo M, Ambrosio F, Friedlander RM, Badylak SF, Wechsler LR.

a McGowan Institute for Regenerative Medicine b Department of Radiology cDepartment of Bioengineering d Department of Physical Medicine & Rehabilitation e Department of Neurological Surgery f Department of Surgery g Department of Neurology, University of Pittsburgh, Pittsburgh, Pennsylvania, USA.

PURPOSE OF REVIEW: This review discusses emerging bioengineering opportunities for the treatment of stroke and their potential to build on current rehabilitation protocols. RECENT FINDINGS: Bioengineering is a vast field that ranges from biomaterials to brain-computer interfaces. Biomaterials find application in the delivery of pharmacotherapies, as well as the emerging field of tissue engineering. For the treatment of stroke, these approaches have to be seen in the context of physical therapy in order to maximize functional outcomes. There is also an emergence of rehabilitation that engages engineering solutions, such as robot-assisted training, as well as brain-computer interfaces that can potentially assist in the case of paralysis. SUMMARY: Stroke remains the main cause of adult disability with rehabilitation therapy being the focus for chronic impairments. Bioengineering is offering new opportunities to both support and synergize with currently available treatment options, and also promises to potentially dramatically improve available approaches.

VIDEO ABSTRACT AVAILABLE: See the Video Supplementary Digital Content 1 (<http://links.lww.com/CONR/A21>).

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14. Dev Med Child Neurol. 2013 Oct 15. doi: 10.1111/dmcn.12313. [Epub ahead of print]

A systematic review of ordinal scales used to classify the eating and drinking abilities of individuals with cerebral palsy.

Sellers D, Pennington L, Mandy A, Morris C.

Chailey Heritage Clinical Services, Sussex Community NHS Trust, Brighton, UK.

AIM: The aim of this review was to examine systematically the scope, validity, and reliability of ordinal scales used to classify the eating and drinking ability of people with cerebral palsy (CP). **METHOD:** Six electronic databases were searched to identify measures used to classify eating and drinking ability; in addition, two databases were used to track citations of key texts. The constructs assessed by each measure were examined in relation to the World Health Organization International Classification of Functioning, Disability and Health. Evidence of validity and reliability of the identified scales was appraised from peer-reviewed studies using standard criteria. **RESULTS:** Fifteen scales were identified in 23 papers. Clinician or researcher assessment was required for 13 scales; nine scales made use of information from parents and carers through interviews or questionnaires. Eight scales used the terms mild, moderate, and severe (with varying definitions) to describe different aspects of eating and drinking impairment. There was an assessment of either content validity and/or reliability for five scales; however, none met the recommended psychometric quality standards. **INTERPRETATION:** Currently, there is a lack of evidence of the validity and reliability of ordinal scales of functional eating and drinking abilities of people with CP.

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15. Dev Med Child Neurol. 2013 Sep;55(9):776. doi: 10.1111/dmcn.12240.

Developing cohesive and strategic communication research.

Pennington L.

[PMID: 23924079](#) [PubMed - indexed for MEDLINE]

16. Dev Med Child Neurol. 2013 Oct 15. doi: 10.1111/dmcn.12314. [Epub ahead of print]

Visual disorders in children with cerebral palsy: is the picture still 'blurred'?

Guzzetta A.

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[PMID: 24127758](#) [PubMed - as supplied by publisher]

17. J Clin Nurs. 2013 Oct 17. doi: 10.1111/jocn.12218. [Epub ahead of print]

The MM-CGI Cerebral Palsy: modification and pretesting of an instrument to measure anticipatory grief in parents whose child has cerebral palsy.

Al-Gamal E, Long T.

Community Health Nursing Department, Faculty of Nursing, The University of Jordan, Amman, Jordan.

AIMS AND OBJECTIVES: To establish the potential of a modified version of the MM-CGI Childhood Cancer to assess anticipatory grief in parents of children with cerebral palsy, to amend the existing scale for use with the specific patient group, to test the psychometric properties of the modified version (MM-CGI Cerebral Palsy) and to review the clinical potential of the new scale. **BACKGROUND:** Parents of children with cerebral palsy may experience reactions similar to parents of children with other enduring or life-limiting conditions, and anticipatory grief may be one such psychological reaction. While the burden of caring is sometimes balanced by positive perceptions of the child, which enhance coping ability, for many parents the outcome is damage to their physical and mental health and impaired family functioning. **DESIGN:** A cross-sectional, descriptive, correlational design. **METHODS:** The MM-CGI Cerebral Palsy was administered in structured interviews with 204 parents. Standardised measures of caregivers' depression, stress and perceived social support were also administered. Mothers and fathers were recruited from healthcare centres and schools for special education. Cronbach's alpha was used to assess internal consistency, and Pearson's product-moment correlation was used to assess construct validity. **RESULTS:** The subscales were each found to measure a single dimension of anticipatory grief, and significant correlations were established with existing instruments. The instrument demonstrated excellent internal consistency reliability and good construct validity. **CONCLUSIONS:** The MM-CGI Cerebral Palsy could be useful for diagnosing anticipatory grief among parents of children with cerebral palsy. This preliminary work moves the programme on to testing in intervention studies. **RELEVANCE TO CLINICAL PRACTICE:** In the absence of an existing measure for the assessment of anticipatory grief, specifically in parents of children with cerebral palsy, the MM-CGI Cerebral Palsy could prove to be an effective assessment tool for clinicians and researchers.

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Prevention and Cure

18. Dev Med Child Neurol. 2013 Oct 5. doi: 10.1111/dmcn.12281. [Epub ahead of print]

Monitoring the prevalence of severe intellectual disability in children across Europe: feasibility of a common database.

van Bakel M, Einarsson I, Arnaud C, Craig S, Michelsen SI, Pildava S, Uldall P, Cans C.

Register for Severely Disabled Children and Perinatal Observatory (RHEOP), Grenoble, France.

AIM: Our aim was to study the feasibility of creating a framework for monitoring and undertaking collaborative research on intellectual disability at the European level, based on existing databases of children with such disability. **METHOD:** The characteristics of five existing European intellectual disability databases from four countries (Iceland, Latvia, Ireland, and two in France), were discussed on the basis of ideal criteria set by a working group on childhood intellectual disability as part of the Surveillance of Cerebral Palsy in Europe Network (SCPE-NET). Mean prevalence values for severe intellectual disability for the birth years 1990 till 2002 were compared across databases. **RESULTS:** Methods of case recruitment and diagnosis differed across databases, but classification of intellectual disability and completeness were similar. Severe intellectual disability (IQ<50) prevalence estimates were significantly ($p<0.001$) different across databases (south-east France: 3.3 out of 1000; south-west France: 3.0 out of 1000; Latvia: 3.9 out of 1000; Ireland: 5.0 out of 1000; and Iceland 5.1 out of 1000). **INTERPRETATION:** In spite of differences in diagnosis and case inclusion across databases, the construction of a common database for severe intellectual disability was deemed feasible through harmonization of certain criteria, such as age, and through restriction to those with severe intellectual disability.

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19. Dev Med Child Neurol. 2013 Oct 5. doi: 10.1111/dmcn.12293. [Epub ahead of print]**Risk of cerebral palsy in term-born singletons according to growth status at birth.**

Dahlseng MO, Andersen GL, Irgens LM, Skranes J, Vik T.

Department of Laboratory Medicine, Children's and Women's Health, Faculty of Medicine, Norwegian University of Science and Technology, Trondheim, Norway.

AIMS: An excess risk of cerebral palsy (CP) has been reported in children of both low and high birthweight. However, the risk associated with deviations from the mean of other anthropometric measurements has been less well studied. The aim of our study therefore was to determine the association between size measurements at birth and incidence of CP in singletons born at term. **METHOD:** Standard deviation z-scores for weight, length, head circumference, and ponderal index at birth of term-born singletons born between 1996 and 2006 were calculated using data from the Medical Birth Registry of Norway. The measurements of 398 children with CP recorded in the Cerebral Palsy Registry of Norway were compared with those of 490 022 typically developing infants. **RESULTS:** Children with low birthweight ($p < 0.001$; <10th centile) as well as low and high z-scores for length ($p < 0.001$ and $p < 0.001$) and head circumference ($p < 0.001$ and $p < 0.003$; <90th centile) had an excess risk of CP, in particular of spastic bilateral CP. Spastic unilateral CP was associated only with low z-scores, whereas children with the greatest body length and largest head circumference, but with low ponderal index, had an excess risk of spastic quadriplegic and dyskinetic CP. **INTERPRETATION:** Our results are consistent with the notion that most subtypes of CP are due to antenatal factors leading to poor intrauterine growth, whereas CP in children who were large at birth is more likely to be due to intrapartum factors.

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20. Dev Med Child Neurol. 2013 Oct 1. doi: 10.1111/dmcn.12268. [Epub ahead of print]**Prevalence of cerebral palsy, co-occurring autism spectrum disorders, and motor functioning - Autism and Developmental Disabilities Monitoring Network, USA, 2008.**

Christensen D, Van Naarden Braun K, Doernberg NS, Maenner MJ, Arneson CL, Durkin MS, Benedict RE, Kirby RS, Wingate MS, Fitzgerald R, Yeargin-Allsopp M.

Division of Birth Defects and Developmental Disabilities, National Center on Birth Defects and Developmental Disabilities, Centers for Disease Control and Prevention, Atlanta, GA, USA.

AIM: The aim of this study was to report the prevalence and characteristics of children with cerebral palsy (CP). **METHOD:** Children with CP ($n=451$) were ascertained by the Autism and Developmental Disabilities Monitoring (ADDM) Network, a population-based, record-review surveillance system monitoring CP in four areas of the USA. Prevalence was calculated as the number of children with CP among all 8-year-old children residing in these areas in 2008. Motor function was categorized by Gross Motor Function Classification System level and walking ability. Co-occurring autism spectrum disorders (ASD) and epilepsy were ascertained using ADDM Network surveillance methodology. **RESULTS:** The period prevalence of CP for 2008 was 3.1 per 1000 8-year-old children (95% confidence interval 2.8-3.4). Approximately 58% of children walked independently. Co-occurring ASD frequency was 6.9% and was higher (18.4%) among children with non-spastic CP, particularly hypotonic CP. Co-occurring epilepsy frequency was 41% overall, did not differ by ASD status or CP subtype, and was highest (67%) among children with limited or no walking ability. **INTERPRETATION:** The prevalence of CP in childhood from US surveillance data has remained relatively constant, in the range of 3.1 to 3.6 per 1000, since 1996. The higher frequency of ASD in non-spastic than in spastic subtypes of CP calls for closer examination.

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21. Dev Med Child Neurol. 2013 Oct 9. doi: 10.1111/dmcn.12274. [Epub ahead of print]

The intriguing relationship between cerebral palsy and autism.

Zwaigenbaum L.

Department of Pediatrics, Glenrose Rehabilitation Hospital, University of Alberta, Edmonton, AB, Canada.

[PMID: 24116659](#) [PubMed - as supplied by publisher]

22. Free Radic Biol Med. 2013 Oct 12. pii: S0891-5849(13)00629-1. doi: 10.1016/j.freeradbiomed.2013.09.026. [Epub ahead of print]

Caffeine protects neuronal cells against injury caused by hyperoxia in the immature brain.

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Caffeine administered to preterm infants has been shown to reduce rates of cerebral palsy and cognitive delay, as compared to placebo. We investigated the neuroprotective potential of caffeine for the developing brain in a neonatal rat model featuring transient systemic hyperoxia. Using 6 day-old rat pups, we found that after 24h and 48h of 80% oxygen exposure, apoptotic (TUNEL+) cell numbers increased in the cortex, hippocampus, and central grey matter, but not in the hippocampus or DG. In the dentate gyrus, high oxygen exposure led to a decrease in the number of proliferating (Ki67+) cells and the number of Ki67+ cells double staining for nestin (immature neurons), doublecortin (progenitors), and NeuN (mature neurons). Absolute numbers of nestin+, doublecortin+, and NeuN+ cells also decreased after hyperoxia. This was mirrored in a decline of transcription factors expressed in immature neurons (Pax6, Sox2), progenitors (Tbr2), and mature neurons (Prox1, Tbr1). Administration of a single dose of caffeine (10mg/kg) prior to high oxygen exposure almost completely prevented these effects. Our findings suggest that caffeine exerts protection for neonatal neurons exposed to high oxygen, possibly via its antioxidant capacity.

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23. Paediatr Perinat Epidemiol. 2013 Nov;27(6):542-52. doi: 10.1111/ppe.12082. Epub 2013 Oct 10.

Maternal Infections during Pregnancy and Cerebral Palsy: A Population-based Cohort Study.

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BACKGROUND: Cerebral palsy (CP) is a common motor disability in childhood. We examined the association between maternal infections during pregnancy and the risk of congenital CP in the child. **METHODS:** Liveborn singletons in Denmark between 1997 and 2003 were identified from the Danish National Birth Registry and followed from 1 year of life until 2008. Redemption of antibiotics from the National Register of Medicinal Product Statistics and maternal infections reported by the National Hospital Register were used as markers of maternal infection during pregnancy. CP diagnoses were obtained from the Danish Cerebral Palsy Registry. Adjusted hazard ratio (HR) and 95% confidence interval (CI) were estimated by Cox proportional hazard models. **RESULTS:** Of the 440 564 singletons with follow-up data, 840 were diagnosed with congenital CP. Maternal genito-urinary tract infections (HR 2.1, 95% CI 1.4, 3.2) were associated with CP in all births, in term births (HR 1.9, 95% CI 1.1, 3.2), in children with spastic CP (HR 2.1, 95% CI 1.4, 3.3), and among first-born children (HR 1.9, 95% CI 1.4, 3.3). Overall, we found associations between redeemed nitrofurantoin (HR 1.7, 95% CI 1.1, 2.8) and CP. Among trimester-specific exposures, CP risk was associated with prescriptions redeemed in the first trimester for any antibacterials, beta-lactam antibacterials, and nitrofurantoin, an antibiotic commonly used to treat lower urinary tract infection, and

genito-urinary tract infections in the third trimester. **CONCLUSION:** Genito-urinary tract infections and antibiotic use during pregnancy were associated with increased risks of CP, indicating that some maternal infections or causes of maternal infections present in prenatal life may be part of a causal pathway leading to CP.

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24. JAMA Pediatr. 2013 Oct 14. doi: 10.1001/jamapediatrics.2013.2764. [Epub ahead of print]

Multiple Courses of Antenatal Corticosteroids for Preterm Birth Study: Outcomes in Children at 5 Years of Age (MACS-5).

Asztalos EV, Murphy KE, Willan AR, Matthews SG, Ohlsson A, Saigal S, Armson BA, Kelly EN, Delisle MF, Gafni A, Lee SK, Sananes R, Rovet J, Guselle P, Amankwah K, Saleem M, Sanchez J; for the MACS-5 Collaborative Group.

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IMPORTANCE A single course of antenatal corticosteroid therapy is recommended for pregnant women at risk of preterm birth between 24 and 33 weeks' gestational age. However, 50% of women remain pregnant 7 to 14 days later, leading to the question of whether additional courses should be given to women remaining at risk for preterm birth. The Multiple Courses of Antenatal Corticosteroids for Preterm Birth Study (MACS) was an international randomized clinical trial that compared multiple courses of antenatal corticosteroids with a single course in women at risk of preterm birth. **OBJECTIVE** To determine the effects of single vs multiple courses of antenatal corticosteroid therapy on death or neurodevelopmental disability (neuromotor, neurosensory, or neurocognitive/neurobehavioral function) at 5 years of age in children whose mothers participated in MACS. Our secondary aims were to determine the effect on height, weight, head circumference, blood pressure, intelligence, and specific cognitive (visual, spatial, and language) skills. **DESIGN, SETTING, AND PARTICIPANTS** Cohort follow-up study of children seen between June 2006 and May 2012 at 55 centers. In total, 1724 women (2141 children) were eligible for the study, of whom 1728 children (80.7% of the 2141 eligible children) participated and 1719 children contributed to the primary outcome. **INTERVENTION** Single and multiple courses of antenatal corticosteroid therapy. **MAIN OUTCOMES AND MEASURES** The primary outcome was death or survival with a neurodevelopmental disability in 1 of the following domains: neuromotor (nonambulatory cerebral palsy), neurosensory (blindness, deafness, or need for visual/hearing aids), or neurocognitive/neurobehavioral function (abnormal attention, memory, or behavior). **RESULTS** There was no significant difference between the groups in the risk of death or neurodevelopmental disability: 217 of 871 children (24.9%) in the multiple-courses group vs 210 of 848 children (24.8%) in the single-course group (odds ratio, 1.02 [95% CI, 0.81 to 1.29]; P = .84). **CONCLUSIONS AND RELEVANCE** Multiple courses, compared with a single course, of antenatal corticosteroid therapy did not increase or decrease the risk of death or disability at 5 years of age. Because of a lack of strong conclusive evidence of short-term or long-term benefits, it remains our opinion that multiple courses not be recommended in women with ongoing risk of preterm birth. **TRIAL REGISTRATION** clinicaltrials.gov Identifier: NCT00187382 and International Standard Randomized Controlled Trial Number Register identifier ISRCTN2654148.

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25. Mol Pharm. 2013 Oct 11. [Epub ahead of print]

Biodistribution of Fluorescently-labeled PAMAM Dendrimers in Neonatal Rabbits: Effect of Neuroinflammation.

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Dendrimers are being explored in many pre-clinical studies as drug, gene, and imaging agent delivery systems. Understanding their detailed organ, tissue, cellular uptake, and retention can provide valuable insights into their effectiveness as delivery vehicles, and the associated toxicity. This work explores a fluorescence-quantification

based assay that enables simultaneous quantitative biodistribution and imaging of dendrimers with a single agent. We have labeled an ethylenediamine-core generation-4 hydroxyl-terminated poly(amidoamine) (PAMAM) dendrimer using the fluorescent, photostable, near-IR cyanine dye (Cy5) and performed quantitative and qualitative biodistribution of the dendrimer-Cy5 conjugates (D-Cy5) in healthy neonatal rabbits, and neonatal rabbits with cerebral palsy (CP). The biodistribution of D-Cy5 and free Cy5 dye was evaluated in newborn rabbits, based on developed quantification methods using fluorescence spectroscopy, HPLC and SEC, and supported by microscopic imaging. The uptake was assessed in the brain, heart, liver, lungs, kidneys, blood serum and urine. Results obtained based on these three independent methods are in good agreement, and indicate the fast renal clearance of D-Cy5 and free Cy5 with relatively higher organs accumulation of the D-Cy5 conjugate. Following systemic administration, the D-Cy5 mainly accumulated in kidneys and bladder at 24 hrs. The quantitative biodistribution is in good agreement with previous studies based on radiolabeling. These methods for dendrimers quantification are easier and more practical, provide excellent sensitivity (reaching 0.1 ng per gram of tissue), and allow for quantification of dendrimers in different organs over longer time periods without concerns for radioactive decay, while also enabling tissue and cellular imaging in the same animal. In kits with fetal-neuroinflammation induced CP, there was a significantly higher uptake of D-Cy5 in the brain, while biodistribution in other organs was similar to that of healthy kits.

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26. Neuron. 2013 Jul 24;79(2):241-53. doi: 10.1016/j.neuron.2013.05.022.

Optogenetic inhibition of synaptic release with chromophore-assisted light inactivation (CALI).

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Optogenetic techniques provide effective ways of manipulating the functions of selected neurons with light. In the current study, we engineered an optogenetic technique that directly inhibits neurotransmitter release. We used a genetically encoded singlet oxygen generator, miniSOG, to conduct chromophore assisted light inactivation (CALI) of synaptic proteins. Fusions of miniSOG to VAMP2 and synaptophysin enabled disruption of presynaptic vesicular release upon illumination with blue light. In cultured neurons and hippocampal organotypic slices, synaptic release was reduced up to 100%. Such inhibition lasted >1 hr and had minimal effects on membrane electrical properties. When miniSOG-VAMP2 was expressed panneuronally in *Caenorhabditis elegans*, movement of the worms was reduced after illumination, and paralysis was often observed. The movement of the worms recovered overnight. We name this technique Inhibition of Synapses with CALI (InSynC). InSynC is a powerful way to silence genetically specified synapses with light in a spatially and temporally precise manner.

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Bringing optogenetics to the synapse. [Neuron. 2013]

Techniques: Optogenetics takes more control. [Nat Rev Neurosci. 2013]

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27. Neuropediatrics. 2013 Oct 13. [Epub ahead of print]

Reliability of Fractional Anisotropy Measurement for Children with Cerebral Palsy.

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Objective: Periventricular leukomalacia (PVL) is the leading cause of disability in children with cerebral palsy (CP). Diffusion tensor imaging (DTI) is a magnetic resonance imaging technique for detecting microstructural lesions of

white matter. Fractional anisotropy (FA) is a widely used DTI index with clinical significance in children with CP. This study aims to estimate the reliability of FA for children with CP. Design: Four observers measured FA values in 78 children with spastic CP from PVL. Region of interests (ROIs) were placed in three anatomical loci at each side: medial and lateral portions of posterior limb of internal capsule and ascending sensory tract. Intra- and interobserver reliability indices including intraclass correlation coefficient (ICC), standard error of measurement, smallest real difference percentage (SRD%), and limit of agreement using Bland-Altman analysis were examined. Results: Intraobserver ICCs were 0.85 or greater in all ROIs, and SRD% ranged from 3.59 to 12.33%. Interobserver ICCs exceeded 0.90 in all ROIs, and the SRD% were less than 10%. The Bland-Altman analysis showed good intra- and interobserver agreements. The reliability was not affected by severity of impairment. Conclusions: Reliability of DTI-derived FA value using ROIs was satisfactory in children with PVL.

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