
Resting State and Diffusion Neuroimaging Predictors of Clinical Improvements Following Constraint-Induced Movement Therapy in Children With Hemiplegic Cerebral Palsy.

Manning KY1, Fehlings D2, Mesterman R3, Gorter JW3, Switzer L2, Campbell C4, Menon RS5.

The aim was to identify neuroimaging predictors of clinical improvements following constraint-induced movement therapy. Resting state functional magnetic resonance and diffusion tensor imaging data was acquired in 7 children with hemiplegic cerebral palsy. Clinical and magnetic resonance imaging (MRI) data were acquired at baseline and 1 month later following a 3-week constraint therapy regimen. A more negative baseline laterality index characterizing an atypical unilateral sensorimotor resting state network significantly correlated with an improvement in the Canadian Occupational Performance Measure score (r = -0.81, P = .03). A more unilateral network with decreased activity in the affected hemisphere was associated with greater improvements in clinical scores. Higher mean diffusivity in the posterior limb of the internal capsule of the affect tract correlated significantly with improvements in the Jebsen-Taylor score (r = -0.83, P = .02). Children with more compromised networks and tracts improved the most following constraint therapy.

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Affected and Contralateral Hand Strength and Dexterity Measures in Children With Hemiplegic Cerebral Palsy.

Tomhave WA1, Van Heest AE2, Bagley A1, James MA1.

PURPOSE: To determine how the affected hemiplegic hand and contralateral dominant hand in children with hemiplegic cerebral palsy compare with age-matched norms for grip strength, pinch strength, and dexterity.

METHODS: We enrolled 37 children with hemiplegic cerebral palsy (26 boys; average age, 9.8 y). Grip and pinch strength and Box and Blocks Test for dexterity were measured in both hands. Affected and contralateral hands results were analyzed and compared with each other and with norms for age and sex. RESULTS: Affected hands had significantly less grip and pinch strength than the contralateral hands. Subjects transported significantly fewer blocks in one minute with the Box and Blocks Test (mean, 10.8 blocks) with the affected hand than the
contralateral hand. Compared with normative values, affected-side grip and pinch strengths were significantly less, whereas contralateral hand grip and pinch strengths were similar. Dexterity in both affected and contralateral hands was significantly less than normative values. Decreased dexterity in the contralateral hand was correlated with decreased nonverbal intelligence quotient. CONCLUSIONS: Dexterity of the contralateral hand is diminished in children with hemiplegia. Assessment of the contralateral hand may reveal opportunities for therapeutic intervention that improve fine motor function.

TYPE OF STUDY/LEVEL OF EVIDENCE: Therapeutic IV.

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The effect of simulated elbow contracture on temporal and distance gait parameters.

Trehan SK1, Wolff AL2, Gibbons M2, Hillstrom HJ2, Daluiski A3.

BACKGROUND: Elbow contractures can be functionally debilitating. Extensive research has been published on treatments to restore elbow motion, but few have discussed clinical implications beyond the affected extremity. Reciprocal arm swing in normal gait has been shown to increase stability and reduce energy expenditure. The importance of arm swing has been clinically demonstrated in patients with cerebral palsy, stroke and Parkinson's disease. We hypothesized that elbow contractures would result in an abnormal spatio-temporal gait parameters.

METHODS: Forty volunteer subjects walked on the Gaitmat II which provided real-time analysis of temporal and distance gait parameters. Five conditions were tested: no brace (control 1), elbow brace unlocked (control 2) and brace locked in 30°, 90° or 120° flexion (simulating fixed elbow contractures). Condition order was randomized for each subject. Each condition consisted of five walking trials. RESULTS: All three fixed elbow conditions (120°, 90° and 30°) demonstrated significantly decreased gait velocity (1.37, 1.39 and 1.39m/s) and stride length (1.45, 1.46 and 1.46m) compared to the control condition (1.42m/s and 1.48m, respectively). Single limb stance and double support times were decreased and increased, respectively, compared to control. There was no significant difference in cadence or limb asymmetry in the three fixed elbow conditions. CONCLUSIONS: Despite well-established functional limitations in elbow contracture patients and importance of arm swing in normal gait, the impact of elbow contractures on gait is unknown. This study demonstrates that simulated elbow contracture results in significant differences in spatio-temporal gait parameters suggesting that elbow contractures have a broader functional impact beyond the affected extremity.

LEVEL OF EVIDENCE: II.

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Estimation of the hip joint centre in human motion analysis: A systematic review.

Kainz H1, Carty CP2, Modenese L3, Boyd RN4, Lloyd DG3.

BACKGROUND: Inaccuracies in locating the three-dimensional position of the hip joint centre affect the calculated hip and knee kinematics, force- and moment-generating capacity of muscles and hip joint mechanics, which can lead to incorrect interpretations and recommendations in gait analysis. Several functional and predictive methods have been developed to estimate the hip joint centre location, and the International Society of Biomechanics recommends a functional approach for use with participants that have adequate range of motion at the hip, and predictive methods in those with insufficient range of motion. The purpose of the current systematic review was to substantiate the International Society of Biomechanics recommendations. This included identifying the most
accurate functional and predictive methods, and defining 'adequate' range of motion. METHODS: A systematic search with broad search terms was performed including five databases. FINDINGS: The systematic search yielded to 801 articles, of which 34 papers were included. Eleven different predictive and 13 different functional methods were identified. The results showed that the geometric sphere fit method and Harrington equations are the most accurate functional and predictive approaches respectively that have been evaluated in vivo. INTERPRETATION: In regard to the International Society of Biomechanics recommendations, the geometric sphere fit method should be used in people with sufficient active hip range of motion and the Harrington equations should be used in patients without sufficient hip range of motion. Multi-plane movement trials with at least 60° of flexion-extension and 30° of ab-adduction range of motion are suggested when using functional methods.

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Impaired gait function in adults with cerebral palsy is associated with reduced rapid force generation and increased passive stiffness.

Geertsen SS1, Kirk H2, Lorentzen J3, Jorsal M4, Johansson CB4, Nielsen JB5.

OBJECTIVE: It is still not clarified whether spasticity contributes to impairments of gait function. Here we compared biomechanical measures of muscle weakness and stiffness of ankle muscles to impairments of gait function in adults with cerebral palsy (CP). METHODS: Twenty-four adults with CP (mean age 34.3, range 18-57years) and fifteen healthy age-matched controls were biomechanically measured for passive and reflex-mediated stiffness of the ankle plantarflexors at rest, maximal voluntary plantarflexion and dorsiflexion effort (MVCpf,df) and rate of force development (RFDpf,df). Kinematic analysis of the ankle joint during treadmill walking was obtained by 3-D motion analysis. RESULTS: Passive stiffness was significantly increased in adults with CP compared to controls. Passive stiffness and RFDdf were correlated to reduced toe lift. RFDpf provided the best correlation to push-off velocity, range of movement in the ankle joint and gait speed. Reflex-mediated stiffness was not correlated to any parameters of impaired gait. CONCLUSIONS: Impaired gait function in adults with CP is associated with reduced RFD and increased passive stiffness of ankle muscles. SIGNIFICANCE: These findings suggest that reduced rapid force generation and increased passive stiffness of ankle muscles rather than increased reflex-mediated stiffness (spasticity) likely contributes to impaired gait function in adults with CP.

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The effect of treadmill exercise on gait efficiency during overground walking in adults with cerebral palsy.

Kim OY1, Shin YK2, Yoon YK3, Ko EJ1, Cho SR4.

OBJECTIVE: To investigate the effect of treadmill walking exercise as a treatment method to improve gait efficiency in adults with cerebral palsy (CP) and to determine gait efficiency during overground walking after the treadmill walking exercise. METHODS: Fourteen adults with CP were recruited in the experimental group of treadmill walking exercise. A control group of 7 adults with CP who attended conventional physical therapy were also recruited. The treadmill walking exercise protocol consisted of 3-5 training sessions per week for 1-2 months (total 20 sessions). Gait distance, velocity, VO2, VCO2, O2 rate (mL/kg·min), and O2 cost (mL/kg·m) were assessed at the beginning and at the end of the treadmill walking exercise. The parameters were measured by KB1-C oximeter. RESULTS: After the treadmill walking exercise, gait distance during overground walking up to 6 minutes significantly increased from 151.29±91.79 to 193.93±79.01 m, and gait velocity increased from 28.09±14.29 to 33.49±12.69 m/min (p<0.05). Energy efficiency evaluated by O2 cost during overground walking significantly improved from 0.56±0.36 to 0.41±0.18 mL/kg·m (p<0.05), whereas O2 rate did not improve significantly after the treadmill walking exercise.
On the other hand, gait velocity and O2 cost during overground walking were not significantly changed in the control group. CONCLUSION: Treadmill walking exercise improved the gait efficiency by decreased energy expenditure during overground walking in adults with CP. Therefore, treadmill walking exercise can be an important method for gait training in adults with CP who have higher energy expenditure.

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**Pamidronate Treatment to Prevent Reoccurring Fractures in Children With Cerebral Palsy.**

Sees JP1, Sitoula P, Dabney K, Holmes L Jr, Rogers KJ, Kecskemethy HH, Bachrach S, Miller F.

BACKGROUND: Some children with cerebral palsy (CP) have frequent fractures due to low bone mineral density and receive treatment with pamidronate, an intravenous bisphosphonate. Our review evaluates the outcome of pamidronate treatment in these children. METHODS: A retrospective chart review was performed, and 32 patients (14 girls and 18 boys) with CP Gross Motor Function Classification System level III (2 patients), IV (3 patients), and V (27 patients) treated with 5 courses of pamidronate for low mineral density were identified. Patients with a minimum of 2 years of follow-up were included in the study. Data collection was a review of the demographics and pretreatment, peritreatment, and posttreatment fracture history. RESULTS: The mean age at treatment was 11.6 years (range, 2.9 to 19.6 y). There were 102 fractures (mean duration 2.5 y) pretreatment and 28 fractures posttreatment. With an average follow-up of 6.4 years, posttreatment rate of fracture decreased to 0.10 fractures per year from the pretreatment rate of 2.4 fractures per year (P<0.001). The femur was the most common bone fractured both pretreatment (54%) and posttreatment (61%); the major site was the distal third of the femur. There were 11 fractures during the course of pamidronate treatment at a rate of 0.33 fractures per year. Only 11 patients (34%) sustained fracture posttreatment. No correlation with fracture pattern or occurrence was found with patient age, number of pretreatment fractures, or sex. Most fractures were caused by low-energy injuries, and most were managed nonoperatively. CONCLUSIONS: In patients with CP and disuse osteoporosis, the most common fracture sustained involved the distal femur via low-energy injury, and most fractures were treated nonoperatively. Although the fracture pattern and the treatment remained unchanged, reoccurring fractures in these children can be effectively treated medically to interrupt the fracturing tendency.

**LEVEL OF EVIDENCE:** Level IV.

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**Short-term effect of botulinum toxin a injection on spastic equinovarus foot in cerebral palsy patients: a study using the foot pressure measurement system.**

Son SM1, Park IS2, Yoo JS1.

OBJECTIVE: To evaluate the therapeutic effect of botulinum toxin A (BTX-A) injection on spastic gastrocnemius (GCM) and tibialis posterior muscles (TPo) by using the foot pressure measurement system (FPMS). METHODS: Eighteen ambulatory CP patients were recruited in this study. BTX-A was injected into the GCM at a dose of 6-12 units/kg and TPo at a dose of 4-9 units/kg according to the severity of equinus and varus deformity. Foot contact pattern, pressure time integral (PTI), coronal index using the FPMS and Modified Ashworth Scale (MAS), and visual inspection of gait pattern were used for evaluation of the therapeutic effect of BTX-A injection. Clinical and FPMS data were statistically analyzed according to the muscle group. RESULTS: A significant decrease in the MAS score of the GCM and TPo was observed, and spastic equinovarus pattern during gait showed improvement after injection. The GCM+TPo injection group showed a significant decrease in forefoot, lateral forefoot pad, and lateral column PTI, and a significant increase in hindfoot PTI and coronal index. In the GCM only injection group, forefoot PTI and lateral column PTI were significantly decreased and hindfoot PTI was significantly increased. The TPo only injection group showed a significant decrease in lateral column PTI and a significant increase in the coronal index. Change in PTI in the hindfoot showed a significant correlation with the change in MAS score of the GCM. Change in PTI of the lateral column and coronal index showed a significant correlation with the change in MAS score of the TPo.
CONCLUSION: The FPMS demonstrated the quantitative therapeutic effect of BTX-A on abnormal pressure distribution in equinovarus foot in detail. The FPMS can be a useful additional tool for evaluation of the effect of BTX-A injection.

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Are Gait Indices Sensitive Enough to Reflect the Effect of Ankle Foot Orthosis on Gait Impairment in Cerebral Palsy Diplegic Patients?


BACKGROUND: Neuromuscular impairments may compromise gait function in patients with cerebral palsy (CP). As such, ambulatory children with CP often use ankle foot orthosis (AFO) to facilitate and optimize their ability to walk. The aim of this study was to evaluate whether the different gait indices, the Gillette Gait Index (GGI), the Gait Deviation Index (GDI), and the Gait Profile Score (GPS), reflect the improved gait that was previously shown using AFO. METHODS: A retrospective analysis of 53 studies on children with spastic diplegic CP. All had undergone a comprehensive gait study and were analyzed while walking, both barefoot and with their braces, in the same session. Kinematic and temporal spatial data were determined and summarized by 3 methods: GPS, GDI, and GGI. RESULTS: Significant differences were found between the barefoot condition and the AFO conditions for temporal and kinematic parameters: changes in GGI, GDI, and GPS were not statistically significant, with an improvement of 9.33% in GGI (P=0.448) and no change in GDI and GPS. CONCLUSIONS: The use of AFO in diplegic CP children caused a statistically significant improvement in temporal and kinematic parameters. Interestingly, it was found that this improvement was not reflected by GGI, GDI, or GPS. These findings might suggest that gait indices, as outcome measures, may sometimes not reflect all the effects of specific interventions.

LEVEL OF EVIDENCE: Level III-retrospective study.

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Management of idiopathic and nonidiopathic flatfoot.

Frances JM1, Feldman DS.

Flatfoot in a child may be normal before development of the arch, but the prevalence decreases with age. Treatment is indicated only in the presence of pain and should begin with nonsurgical management options such as stretching of the Achilles tendon and the use of soft shoe orthotics. If pain persists, a modified Evans procedure, together with additional procedures to address forefoot supination, can be successful in correcting deformity and addressing pain. A thorough understanding of the pathology and correction desired will help minimize complications and recurrence. If neuromuscular pathology is present, treatment principles are altered and greatly depend on the severity of the deformity, the association of tibialis posterior spasticity, and ambulatory status. In mild to moderate pathology in walking patients with cerebral palsy, osteotomies can be successful. Various forms of arthrodesis can decrease recurrence when the deformity is severe in a nonambulatory patient with cerebral palsy and a symptomatic valgus foot deformity. In cases of collagen disorders, where soft-tissue laxity complicates management, deformity correction may be of higher importance. Overall alignment always should be evaluated and corrected when necessary to optimize the outcome in patients with valgus foot deformities. The successful treatment of flexible or rigid flatfoot deformity must take into account underlying pathology to optimize outcomes.

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Management of spasticity in children with cerebral palsy.


Cerebral palsy is the most common cause of spasticity and physical disability in children and spasticity is one of the commonest problems in those with neurological disease. The management of spasticity in children with cerebral palsy requires a multidisciplinary effort and should be started as early as possible. There are a number of treatments available for the management of spasticity. This article reviews the variety of options available for the clinical management of spasticity.

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Therapists’ perceptions of social media and video game technologies in upper limb rehabilitation.

Tatla SK1, Shirzad N, Lohse KR, Virji-Babul N, Hoens AM, Holsti L, Li LC, Miller KJ, Lam MY, Van der Loos HF.

BACKGROUND: The application of technologies, such as video gaming and social media for rehabilitation, is garnering interest in the medical field. However, little research has examined clinicians’ perspectives regarding technology adoption by their clients. OBJECTIVE: The objective of our study was to explore therapists’ perceptions of how young people and adults with hemiplegia use gaming and social media technologies in daily life and in rehabilitation, and to identify barriers to using these technologies in rehabilitation. METHODS: We conducted two focus groups comprised of ten occupational therapists/physiotherapists who provide neurorehabilitation to individuals with hemiplegia secondary to stroke or cerebral palsy. Data was analyzed using inductive thematic analysis. The diffusion of innovations theory provided a framework to interpret emerging themes. RESULTS: Therapists were using technology in a limited capacity. They identified barriers to using social media and gaming technology with their clients, including a lack of age appropriateness, privacy issues with social media, limited transfer of training, and a lack of accessibility of current systems. Therapists also questioned their role in the context of technology-based interventions. The opportunity for social interaction was perceived as a major benefit of integrated gaming and social media. CONCLUSIONS: This study reveals the complexities associated with adopting new technologies in clinical practice, including the need to consider both client and clinician factors. Despite reporting several challenges with applying gaming and social media technology with clinical populations, therapists identified opportunities for increased social interactions and were willing to help shape the development of an upper limb training system that could more readily meet the needs of clients with hemiplegia. By considering the needs of both therapists and clients, technology developers may increase the likelihood that clinicians will adopt innovative technologies.

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Adolescents with cerebral palsy and their contact with the GP and the habilitative services [Article in Norwegian]

Ramstad K1, Jahnsen RB1, Diseth TH2.

BACKGROUND Cerebral palsy (CP) often entails a need for health and social services throughout life. Upon scrutiny, it has been found that the transition from services for children and adolescents to services for adults is particularly challenging. The study investigates contact between adolescents with CP and their GPs/habilitative services up to and after the age of 18 years, and the percentage who have an individual habilitation plan (IHP). MATERIAL AND METHOD An attempt was made to identify all those with CP born in 1992 and 1993 and resident in southeast Norway. Seventy-four patients were included (time point I, interview and clinical examination). Forty-two (57 %) responded at the follow-up examination (time point II, questionnaire). RESULTS At time point I, 35 (47 %) of the adolescents had consulted their GP in the past year, 49 (66 %) had been in contact with the habilitative services, and 42 (57 %) had an IHP. Twenty-eight (38 %) used mobility aids. Use of mobility aids gave
lower odds of consultation with the GP. Longer distances from home to the habilitative services gave lower odds of contact with both the GP and the habilitative services. Five adolescents with mobility aids did not have an IHP. At time point II, the percentage who had consulted their GP had increased somewhat, the percentage who had been in contact with the habilitative services had reduced, and the percentage who had an IHP was unchanged. INTERPRETATION The findings reinforce the assumption that the health services provided to disabled adolescents are less locally based and less well coordinated than is supposed, and that there may be geographical differences in the service offered.


Brain State Before Error Making in Young Patients With Mild Spastic Cerebral Palsy.

Hakkarainen E1, Pirilä S2, Kaartinen J3, van der Meere JJ4.

In the present experiment, children with mild spastic cerebral palsy and a control group carried out a memory recognition task. The key question was if errors of the patient group are foreshadowed by attention lapses, by weak motor preparation, or by both. Reaction times together with event-related potentials associated with motor preparation (frontal late contingent negative variation), attention (parietal P300), and response evaluation (parietal error-preceding positivity) were investigated in instances where 3 subsequent correct trials preceded an error. The findings indicated that error responses of the patient group are foreshadowed by weak motor preparation in correct trials directly preceding an error.

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Prevention and Cure


Synthetic DNA approach to cytomegalovirus vaccine/immune therapy.

Wu SJ1, Villarreal DO, Shedlock DJ, Weiner DB.

There is no licensed vaccine or cure for human cytomegalovirus (CMV), a ubiquitous β-herpes virus that infects 60-95 % of adults worldwide. Infection is a major cause of congenital abnormalities in newborns, contributes to development of childhood cerebral palsy and medulloblastoma, can result in severe disease in immunocompromised patients, and is a major impediment during successful organ transplantation. While CMV has been increasingly associated with numerous inflammatory diseases and cancers, only recently has it been correlated with increased risk of heart disease in adults, the number-one killer in the USA. These data, among others, suggest that subclinical CMV infection, or microinfection, in healthy individuals may play more of a causative role than an epiphenomenon in development of CMV-associated pathologies. Due to the myriad of diseases and complications associated with CMV, an efficacious vaccine would be highly valuable in reducing human morbidity and mortality as well as saving billions of dollars in annual health-care costs and disability adjusted life years (DALY) in the developing world. Therefore, the development of a safe efficacious CMV vaccine or immune therapy is paramount to the public health. This review aims to provide a brief overview on aspects of CMV infection and disease and focuses on current vaccine strategies. The use of new synthetic DNA vaccines might offer one such approach to this difficult problem.

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Are sporadic fidgety movements as clinically relevant as is their absence?

Einspieler C1, Yang H2, Bartl-Pokorny KD3, Chi X4, Zang FF2, Marschik PB5, Guzzetta A6, Ferrari F7, Bos AF8, Cloni G6.

BACKGROUND: Infants with normal fidgety movements at 3 to 5 months after term are very likely to show neurologically normal development, while the absence of fidgety movements is an early marker for an adverse neurological outcome, mainly cerebral palsy (CP). The clinical significance of so-called sporadic fidgety movements (i.e., fidgety movements occur isolated in a few body parts and are of 1- to 3-second-duration) is not yet known. AIMS: Our objective was to determine whether infants who had developed CP and had sporadic fidgety movements have a better outcome than infants who did not have fidgety movements. STUDY DESIGN: Longitudinal study. Retrospective analysis of prospectively collected data. SUBJECTS: 61 infants who developed CP (46 male, 15 female; 29 infants born preterm; videoed for the assessment of movements and postures at 9 to 16 weeks post-term age). OUTCOME MEASURES: The Gross Motor Function Classification System (GMFCS) was applied at 3 to 5 years of age. RESULTS: There was no difference between children diagnosed with CP who had sporadic fidgety movements at 9 to 16 weeks post-term age (n=9) and those who never developed fidgety movements (n=50) with regard to their functional mobility and activity limitation at 3 to 5 years of age. One infant had normal FMs and developed unilateral CP, GMFCS Level I; the remaining infant had abnormal FMs and developed bilateral CP, GMFCS Level II. CONCLUSIONS: There is no evidence that the occurrence of occasional isolated fidgety bursts indicates a milder type of CP.

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Impact of risk factors other than prematurity on periventricular leukomalacia. A population-based matched case control study.

Herzog M1, Cerar LK1, Sršen TP1, Verdenik I1, Lučovnik M2.

OBJECTIVE: Periventricular leukomalacia (PVL) is a neonatal brain white matter injury associated with development of cerebral palsy, intellectual impairment, and visual disturbances. PVL is more common in premature neonates. Our objective was to examine the impact of several potential risk factors other than prematurity on the incidence of PVL. STUDY DESIGN: A case-control study based on the Slovenian National Perinatal Information System data for the period 2002-2011. All singleton and twin pregnancies delivered at ≥22 weeks' in Slovenia during the study period were included. Cases were pregnancies with PVL in at least one neonate. For each pregnancy in the case cohort, three pregnancies matched by gestational age and plurality were selected. Chi-square test was used to examine the associations between PVL and several potential risk factors: maternal age, pre-pregnancy body-mass-index, preexisting diabetes, gestational diabetes, pregnancy after in-vitro-fertilization, severe preeclampsia, vaginal delivery, no steroid therapy prior to delivery, small for gestational age, and fetal-inflammatory-response-syndrome. P<0.05 was considered statistically significant. RESULTS: One lakh ninety one thousand and eighty three singleton and 3377 twin pregnancies were matched in at least one neonate. For each pregnancy in the case cohort, three pregnancies matched by gestational age and plurality were selected. Chi-square test was used to examine the associations between PVL and several potential risk factors: maternal age, pre-pregnancy body-mass-index, preexisting diabetes, gestational diabetes, pregnancy after in-vitro-fertilization, severe preeclampsia, vaginal delivery, no steroid therapy prior to delivery, small for gestational age, and fetal-inflammatory-response-syndrome. P<0.05 was considered statistically significant. RESULTS: One lakh ninety one thousand and eighty three singleton and 3377 twin pregnancies delivered at ≥22 weeks' in Slovenia during the study period. PVL was diagnosed in 86 singletons (0.045%) and 25 twins (0.74%). In all twin pregnancy cases only one twin was diagnosed with PVL. 258 singleton and 75 twin controls were matched to the 86 singleton and 25 twin cases. Of all risk factors studied, only maternal obesity and chorioamnionitis were significantly associated with PVL. CONCLUSION: Maternal obesity and chorioamnionitis increase the risk of PVL beyond that expected solely from prematurity.

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Brain magnetic resonance imaging and outcome after hypoxic ischaemic encephalopathy.

Hayes BC1, Ryan S, McGarvey C, Mulvany J, Doherty E, Grehan A, Madigan C, Matthews T, King MD.

Objective: To correlate pattern of injury on neonatal brain magnetic resonance imaging (MRI) with outcome in infants ≥36 + 0 weeks gestation with hypoxic ischaemic encephalopathy. Methods: Prospective cohort study. Images were blindly reviewed. Children were assessed using a variety of standardised assessments. Results: MRI brain was performed on 88 infants. Follow up was available in 73 (83%) infants. Eight of 25 (32%) children with normal imaging had below normal assessment scores. Eight infants (12%) had isolated punctate white matter lesions and five of these had abnormal assessment scores. Death and cerebral palsy were seen only in children with imaging scores ≥3 on basal ganglia/thalami (BGT) score or ≥4 on watershed score. No developmental concerns were raised in 3/7 (43%) infants with isolated watershed injury. Ten of 13 (77%) infants with isolated BGT injury died or developed cerebral palsy. All 23 children with posterior limb of the internal capsule (PLIC) injury displayed developmental difficulties. Conclusions: Almost one-third of infants with a normal MRI brain may be at risk of developmental problems. Punctate foci of white matter injury are common and not always benign. PLIC involvement is usually associated with neurological sequelae including isolated cognitive deficits. Worst outcomes are associated with basal ganglia injury.

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2 year neurodevelopmental and intermediate perinatal outcomes in infants with very preterm fetal growth restriction (TRUFFLE): a randomised trial.

Lees CC1, Marlow N2, van Wassenaer- leemhuis A3, Arabin B4, Bilardo CM5, Brezinka C6, Calvert S7, Derks JB8, Diemert A9, Duvekot JJ10, Ferrazzi E11, Frusca T12, Ganzevoort W13, Hecher K9, Martinelli P14, Ostermayer E15, Papageorghiou AT7, Schlembach D16, Schneider KT15, Thilaganathan B7, Todros T17, Valcamonica A18, Visser GH8, Wolf H19; for the TRUFFLE study group.

BACKGROUND: No consensus exists for the best way to monitor and when to trigger delivery in mothers of babies with fetal growth restriction. We aimed to assess whether changes in the fetal ductus venosus Doppler waveform (DV) could be used as indications for delivery instead of cardiotocography short-term variation (STV). METHODS: In this prospective, European multicentre, unblinded, randomised study, we included women with singleton fetuses at 26-32 weeks of gestation who had very preterm fetal growth restriction (ie, low abdominal circumference [<10th percentile] and a high umbilical artery Doppler pulsatility index [>95th percentile]). We randomly allocated women 1:1:1, with randomly sized blocks and stratified by participating centre and gestational age (<29 weeks vs ≥29 weeks), to three timing of delivery plans, which differed according to antenatal monitoring strategies: reduced cardiotocograph fetal heart rate STV (CTG STV), early DV changes (pulsatility index >95th percentile; DV p95), or late DV changes (A wave [the deflection within the venous waveform signifying atrial contraction] at or below baseline; DV no A). The primary outcome was survival without cerebral palsy or neurosensory impairment, or a Bayley III developmental score of less than 85, at 2 years of age. We assessed outcomes in surviving infants with known outcomes at 2 years. We did an intention to treat study for all participants for whom we had data. Safety outcomes were deaths in utero and neonatal deaths and were assessed in all randomly allocated women. This study is registered with ISRCTN, number 56204499. FINDINGS: Between Jan 1, 2005 and Oct 1, 2010, 503 of 542 eligible women were randomly allocated to monitoring groups (166 to CTG STV, 167 to DV p95, and 170 to DV no A). The median gestational age at delivery was 30·7 weeks (IQR 26·1-34·6), and mean birthweight was 1019 g (SD 404). The proportion of infants surviving without neuroimpairment did not differ between the CTG STV (111 [77%] of 144 infants with known outcome), DV p95 (119 [84%] of 142), and DV no A (133 [85%] of 157) groups (ptrend=0·09). 12 fetuses (2%) died in utero and 27 (6%) neonatal deaths occurred. Of survivors, more infants where women were randomly assigned to delivery according to late ductus changes (133 [95%] of 144, 95%, 95% CI 90-98) were free of neuroimpairment when compared with those randomly assigned to CTG (111 [85%] of 131, 95% CI 78-90; p=0·005), but this was accompanied by a non-significant increase in perinatal and infant mortality. INTERPRETATION: Although the difference in the proportion of infants surviving without neuroimpairment was non-significant at the primary endpoint, timing of delivery based on the study protocol using late changes in the DV waveform might produce an improvement in developmental outcomes at 2 years of age. FUNDING: ZonMw, The

Long-term clinical efficacy of mild hypothermia therapy in neonates with hypoxic-ischemic encephalopathy: a Meta analysis [Article in Chinese]

Cao CQ, Li YN, Yang XM, Gong YG, Wang F, Li WG.

OBJECTIVE: To systematically evaluate the long-term clinical efficacy and safety of mild hypothermia therapy in neonates with hypoxic-ischemic encephalopathy (HIE). METHODS: All randomized controlled trials (RCTs) of mild hypothermia therapy for neonatal HIE from inception to March 2014 were retrieved from databases including Cochrane Library, PubMed, Embase, CBMDisc, and Wanfang Data. Meta analysis was performed using RevMan 5.1 Software. RESULTS: Eight RCTs met the search criteria. The results of Meta analysis showed that, compared with the control group, systemic hypothermia significantly reduced the mortality rate and the incidence of growth delay (RR=0.73, 95% CI: 0.61-0.89; RR=0.70, 95%CI: 0.54-0.93); selective head or systemic hypothermia therapy significantly reduced the incidence of cerebral palsy (RR=0.65, 95%CI: 0.46-0.94; RR=0.67, 95%CI: 0.52-0.86) up to 12-24 months of age. One study reported that hypothermia reduced the mortality rate and the rate of a composite end point of death or severe disability compared with the control group at 6 to 7 years of age. The incidence of adverse events including sinus bradycardia, thrombocytopenia and hypoglycemia was significantly higher in the hypothermia group than in the control group, whereas the incidence of cardiac arrhythmia, hypotension, thrombosis or bleeding, hypokalemia, sepsis, and liver dysfunction showed no significant differences between the two groups. CONCLUSIONS: Mild hypothermia therapy demonstrates a significant efficacy in children with HIE up to 12-24 months of age, but there is still a need for further research on childhood outcomes after mild hypothermia for neonatal HIE. This therapy has few adverse effects and a high clinical tolerability.

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Improving survival in cerebral palsy: where do we go from here?

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A Descriptive Study on the Neonatal Morbidity Profile of Autism Spectrum Disorders, Including a Comparison with Other Neurodevelopmental Disorders.

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The aim of this study was to describe the profile of specific neonatal morbidity in children later diagnosed with autism spectrum disorder (ASD), and to compare this profile with the profile of children with hyperkinetic disorder, cerebral palsy, epilepsy or intellectual disability. This is a Danish population based cohort study, including all children born in Denmark from 1994, through 2010, and surviving the first year of life. Children with ASD as a whole have significantly elevated rates of a range of neurologic, respiratory, inflammatory, and metabolic problems in the neonatal period compared to the general population, but there are few if any indicators of a distinctive neonatal morbidity profile in ASD compared to other neurodevelopmental outcomes.

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