Wang GB, Qiu YQ, Ying Y, Yu AP, Jiang S, Jia J, Jia X, Xu WD.


OBJECTIVE: Spastic arm paralysis after central neurological injury has a long-term effect on the patient's quality of life. Effective neurosurgical treatment for this dysfunction has been described in our previous studies. It is of great significance to determine a set of unified and concise clinical standards for motor function grading in the neurosurgical treatment and management. METHODS: We first conducted a retrospective study that included 51 hemiplegic patients from the Neurosurgery and Microsurgery outpatient database of Huashan Hospital. The neurosurgeons cooperated with rehabilitation experts to design and administer the new rating system (Hua-Shan Grading of Upper Extremity, H-S grading) after analyzing the scale scores and video records of these patients. We then randomly enrolled 64 patients with unilateral spastic arm paralysis after stroke or brain trauma. The Fugl-Meyer Assessment, the Ashworth scale and the new grading system were applied and analyzed to evaluate the participants' motor function. RESULTS: Based on rehabilitation medicine scales and long-term follow-up, a feasible and concise grading system was applied that was based on the patients' characteristics and the examination experiences of neurosurgeons and rehabilitation experts in clinical practice. This method could effectively grade upper extremity motor function, usually in 3-5 minutes. A significant correlation was found between H-S grading and the Fugl-Meyer score by the Spearman test (r = .937, P < .01). The mean difference between any two levels of the new grading system was significant (P < .05). And good test-retest reliability, the Cronbach's alpha coefficient and the validity indices were presented. In addition, it was more sensitive to motor function compared with the Ashworth scale. CONCLUSION: As a supplement to the classic scales, H-S grading was developed in the area of spastic hemiplegia treatment. It is standardized and simplified for patients in the chronic stage after central neurological injury.

PMID: 31129103

2. Reliability of Inclinometer-Derived Passive Range of Motion Measures in Youth with Cerebral Palsy.
Maltais DB, Ferland C, Perron M, Roy JS.


Aims: This study evaluated, for youth with cerebral palsy (CP), the reliability of passive range of motion (PROM) measures taken with an inclinometer, a device that may be simpler to use than a goniometer. Methods: The PROM for elbow and wrist extension, ankle dorsal flexion (knee flexed 90° and fully extended), and the knee popliteal angle of 30 youth with CP (18 boys, 12 girls, 7.0 ± 3.8 years old, classified in Gross Motor Function Classification levels I-V) was measured using an inclinometer. Two physical therapists took the measures during two different sessions, a maximum of 1 week apart. Results:
Good mean intra-rater inter-session, inter-rater intra-session, and inter-rater inter-session reliability (ICC = 0.75-0.89), was found for the elbow, ankle, and knee sites. Absolute reliability for these sites and conditions was 7.14° (90% confident) and 10.16° (95% confident). Reliability values for wrist extension were comparable, albeit slight lower. Conclusions: Similar to published values for goniometry, inclinometry yields reliable upper and lower limb PROM measures from ambulatory and non-ambulatory youth with CP whether measures are carried out by different evaluators within or across sessions or whether measures are performed by the same evaluator across sessions.

PMID: 31144588

3. Long-term results of tripolar constrained total hip arthroplasty in revision hip arthroplasty.
El-Husseiny M, Masri B, Duncan C, Garbuz DS.


AIMS: We investigated the long-term performance of the Tripolar Trident acetabular component used for recurrent dislocation in revision total hip arthroplasty. We assessed: 1) rate of re-dislocation; 2) incidence of complications requiring re-operation; and 3) Western Ontario and McMaster Universities osteoarthritis index (WOMAC) pain and functional scores. PATIENTS AND METHODS: We retrospectively identified 111 patients who had 113 revision tripolar constrained liners between 1994 and 2008. All patients had undergone revision hip arthroplasty before the constrained liner was used: 13 after the first revision, 17 after the second, 38 after the third, and 45 after more than three revisions. A total of 75 hips (73 patients) were treated with Tripolar liners due to recurrent instability with abductor deficiency. In addition, six patients had associated cerebral palsy, four had poliomyelitis, two had multiple sclerosis, two had spodyloepiphysial dysplasia, one had previous reversal of an arthrodesis, and 21 had proximal femoral replacements. The mean age of patients at time of Tripolar insertions was 72 years (53 to 89); there were 69 female patients (two bilateral) and 42 male patients. All patients were followed up for a mean of 15 years (10 to 24). Overall, 55 patients (57 hips) died between April 2011 and February 2018, at a mean of 167 months (122 to 217) following their tripolar liner implantation. We extracted demographics, implant data, rate of dislocations, and incidence of other complications. RESULTS: At ten years, the Kaplan-Meier survivorship for dislocation was 95.6% (95% confidence interval (CI) 90 to 98), with 101 patients at risk. At 20 years, the survivorship for dislocation was 90.6% (95% CI 81.0 to 95.5), with one patient at risk. Eight patients (7.2%) had a dislocation of their constrained liners. At ten years, the survival to any event was 89.4% (95% CI 82 to 93.8), with 96 patients at risk. At 20 years, the survival to any event was 82.5% (95% CI 71.9 to 89.3), with one patient at risk. Five hips (4.4%) had deep infection. Two patients (1.8%) developed dissociated constraining rings with pain but without dislocation, which required re-operation. Two patients (1.8%) had periprosthetic femoral fractures, without dislocation, that were treated by revision stems along with exchange of the well-functioning constrained liners. CONCLUSION: Constrained tripolar liners used at revision hip arthroplasty provided favourable results in the long term for treatment of recurrent dislocation and for patients at high risk of dislocation.

PMID: 31146561

Owen E.


PMID: 31140333

Zago M, Corsi C, Condoluci C, Galli M.


We evaluated the feasibility of a set of indexes based on ground reaction forces to discriminate between the degree of severity of spastic diplegia, identified via Gross Motor Function Classification System (GMFCS). A stepwise discriminant ordinal regression analysis performed on a sample of 58 children returned a subset of variables related to the ratio between braking and propulsive vertical forces and anteroposterior timings. Rather, parameters concerning bilateral symmetry were poorly
discriminating. The relative simplicity of the selected indexes allows for their easy implementation on existing gait analysis applications for screening purposes.

PMID: 31131627

6. The long-term outcome of pelvic asymmetry during gait in children with cerebral palsy following unilateral femoral derotation osteotomy.
Perotti L, Church C, Dina R Jr, Lennon N, Henley J, Sees J, Miller F.


In this retrospective study, children with cerebral palsy underwent a unilateral femoral derotation osteotomy and had a preoperative (PO), short-term postoperative (1-3 years), and a long-term postoperative (≥5 years) gait analysis. Patients were subdivided into groups by the PO pelvic presentation and Gross Motor Function Classification System level. In children with PO pelvic external rotation, femoral derotation osteotomy decreased the hip internal rotation and decreased the pelvic external rotation. These results could influence surgical planning to achieve long-term pelvic asymmetry.

PMID: 31136373

Li T, Chen X, Cao S, Zhang X, Chen X.


This paper aims to investigate human hands-and-knees crawling movement from the aspect of synchronous (SYN) and time-varying (TV) muscle synergy analysis. Nine healthy children and 11 children with cerebral palsy were recruited. During hands-and-knees crawling, surface electromyography (sEMG) signals from 12 main muscles of upper limbs and trunk were recorded, and muscle synergies were extracted based on TV synergy and SYN synergy theories. From the perspectives of repeatability, symmetry and similarity, the abilities of these two types of synergies to characterize crawling movement and to distinguish normal and abnormal crawling were explored. We found that: First, SYN synergy is better than TV synergy in depicting the body symmetry during crawling movement. However, TV synergy is more suitable than SYN synergy for distinguishing normal and abnormal crawling from the perspective of symmetry. Second, the abilities of SYN synergy and TV synergy in depicting the crawling repeatability are not comparable, and both have the potential to depict the crawling abnormality from the perspective of repeatability. Third, from the angle of inter-subject similarity, SYN synergy has the potential to describe the abnormal crawling pattern. However, the large individual differences suggest that TV synergy is a poor choice. This study provides a new way to analyze crawling movement from the perspective of neuromuscular control, and the research findings are meaningful for clinical assessment of abnormal crawling.

PMID: 31137224


BACKGROUND: A deterioration of crouch gait was found in a group of children with cerebral palsy (CP) after a short walking exercise. The increased knee flexion reported after a continuous walk could be related with muscle fatigue and muscle strength. AIM: Does muscle fatigue appears at the end of a walking exercise in children with CP who walk in a crouch gait? METHODS: Eleven children with cerebral palsy (GMFCS I to III) who walk in a crouch gait were included. Isometric muscle strength was assessed using a handheld dynamometer. Children were asked to walk for 6 min at comfortable speed. Spatio-temporal, kinematic and electromyographic (EMG) measurements were recorded at the first and the last minute of the 6-minute walking exercise. Muscle fatigue was evaluated using the shift of EMG signals median frequency. RESULTS: There was no significant difference in walking speed, cadence, and step length at the end of the 6mwe. Maximal and mean anterior pelvic tilt decreased and knee flexion increased (p < 0.05). Rectus femoris EMG median frequency decreased (p < 0.05). The median frequency in other muscles did not decrease significantly. Greater hip extensor strength was associated with lesser knee flexion.
at the end of the 6-minute walking exercise (p < 0.05). SIGNIFICANCE: The increase in knee flexion at the end of the 6-minute walking exercise can be explained by muscle fatigue found in rectus femoris. Hip extensor strength can limit the deterioration of crouch gait after a 6-minute walking exercise representative of daily activities.

PMID: 31132593

Snarski KE.


Purpose: The purpose of this case report is to describe the impact of family-centered, imbedded practice of stepping with postural support on the motor function of a pre-ambulatory child with cerebral palsy. Summary of Key Points: A child with a diagnosis of cerebral palsy completed 11 weeks of parent-directed, supported-stepping practice. Practice was imbedded into the family's daily routine as part of a family-centered early intervention program. The number of supported steps the client could take in two minutes as well as the percentage of steps requiring assistance was recorded during weekly physical therapy sessions. Outcomes: An increased number of supported steps taken, and a decrease in percentage of steps requiring assistance was documented. Improvement in the child's Gross Motor Function Measure score was also noted. Recommendations for Clinical Practice: There is preliminary support for the effectiveness of parent-directed, supported-stepping practice to improve gross motor function in children with cerebral palsy.

PMID: 31140888

Villalta Santos L, Benite Palma Lopes J, Almeida Carvalho Duarte N, Galli M, Collange Grecco LA, Santos Oliveira C.


PURPOSE: To compare the clinical and functional effects of treadmill training combined with anodic transcranial direct current stimulation (atDCS) on the primary motor cortex (Cz), specifically on the area of motor cortex representation of the lower limbs, and on the cerebellum (Cb) in children with spastic cerebral palsy (CP). METHODS: Thirty children and adolescents with spastic CP will be randomly allocated in 3 groups: (1) treadmill training and atDCS on Cz; (2) treadmill training and atDCS on Cb; (3) treadmill training and sham tDCS on Cz. Evaluations of gait spatial-temporal parameters, functional mobility, functional balance, gross motor function, and functional performance will be performed 1 week before intervention and 1 week, 1 month, and 3 months after intervention. Every 3 months the participants will cross over groups. DISCUSSION: This is a protocol for an intervention study comparing the clinical and functional effects of atDCS over Cz and Cb.

PMID: 31135599

11. An acoustic myography functional assessment of cerebral palsy subjects compared to healthy controls during physical exercise.
Pingel J, Andersen IT, Broholm R, Harder A, Bartels EM, Bülow J, Harrison A.


Individuals with cerebral palsy (CP) participate in reduced levels of physical activity and spend an increased amount of time in a sedentary state compared with healthy control subjects. Whether this in part can be explained by impaired muscle function is still unclear. The aim of the present study was to elucidate differences in muscle fibre recruitment during treadmill exercise between CP subjects and healthy age-, sex- and BMI-matched controls. This is a case-control study. Acoustic myography (AMG), a method recording fibre use and efficiency from contracting muscles, was applied during a period of treadmill exercise. The recorded AMG parameters revealed that the CP subjects had a significantly lower initial S-score (spatial summation) than the controls (P < 0.01). However, the T-score (temporal summation) and the E-score (efficiency) showed no significant differences between individuals with CP and the healthy control subjects. The present findings indicate that CP subjects use a higher degree of spatial summation (more fibres recruited) to keep up the same speed during treadmill exercise.
when compared to healthy matched control subjects. Our results suggest that individuals with CP have a tendency to recruit far more muscle fibres during bouts of exercise than healthy individuals. This may partly explain why CP subjects experience premature fatigue.

PMID: 31123956

12. Barriers to and facilitators of physical activity for children with cerebral palsy in special education.
   Cleary SL, Taylor NF, Dodd KJ, Shields N.


AIM: To explore the barriers to and facilitators of physical activity for young people with cerebral palsy in specialist schools. METHOD: Eleven focus groups involving 73 participants (10 young people with cerebral palsy, 13 parents of children with cerebral palsy, 27 teachers, 23 therapists) were held at two specialist schools. Focus groups were audio-recorded and transcribed verbatim. Transcripts were analysed using inductive thematic analysis by two researchers, independently. RESULTS: Four main themes emerged from the focus groups: school priorities; student factors; staffing and environment; and roles and relationships. Physical activity was promoted when academic work and physical activity were seen as equally important school priorities. Student factors that reduced physical activity included fluctuating health, school absences, and protracted rehabilitation after surgery. The staffing and environment unique to specialist schools played a pivotal role in assisting students to be active, as was the importance of collaborative, relationship-based care. INTERPRETATION: Physical activity programmes developed in specialist schools need to take into consideration complexities associated with the age, developmental stage, and academic requirements of young people with cerebral palsy. Particularly for adolescents, motivation was discussed as having a substantial influence on physical activity participation. These findings may assist school leadership teams, clinicians, and teachers in planning physical activity interventions. WHAT THIS PAPER ADDS: Specialist schools offer custom-built environments that promote physical activity and inclusion for students with physical impairments. Therapists and teaching staff work creatively and collaboratively to incorporate an 'all-day' approach to providing physical activity opportunities. Balancing time spent on physical activity versus academic work can cause tension.

PMID: 31131894


Purpose: Evidence is increasing for effective virtual reality therapy for motor rehabilitation for children with Cerebral Palsy. We assessed the feasibility of a virtual reality therapy mode of intervention, appropriateness of measures, and potential cost-effectiveness. Methods: A 12-week, 2-group, parallel-feasibility trial (ISRCTN 17624388) using Nintendo Wii FitTM at home. Children aged 5-16, with ambulatory Cerebral Palsy, who were able to follow simple instructions were randomised to two groups; one supported by physiotherapists (individualised activity programme), the other unsupported with children having free choice (control). Children were assessed in clinic at baseline, week 6, and week 12 by blinded assessors. Feasibility of the intervention was assessed via recruitment, adherence, and usefulness of measurement tools. Results: Forty-four children were eligible (out of 48 approached): 31 consented, 30 were randomised, 21 completed the study; 10 in the supported group and 11 in the unsupported group. Nine children discontinued from tiredness, after-school activities, homework, surgery, technical difficulties or negative system feedback. The supported group completed 19 of 36 (IQR 5-35) possible sessions; the unsupported group 24 of 36 sessions (IQR 8-36). Gross Motor Function Measure scores varied by Cerebral Palsy severity after the intervention. There were no adverse events. Conclusion: Virtual reality therapy offers potential as a therapeutic adjunct for children with Cerebral Palsy, warranting substantive confirmatory study. Gross Motor Function Measure, with modifications to improve sensitivity, appeared appropriate as a primary measure, with Timed up and Go test secondary. The intervention was inexpensive costing £20 per child. An explanatory trial to evaluate the clinical/cost-effectiveness of commercial system virtual reality therapy is feasible with minor methodological adaptation. Implications for rehabilitation Home-based interactive computer gaming was feasible, safe and cost effective as a therapy adjunct. Discontinue if additional pressures are present: imminent surgery, family resilience to technical difficulties, negative system feedback, after-school activities. Change in Gross Motor Function Measurement scores varied by severity of Cerebral Palsy.

PMID: 31131641
14. The Young Movers Project: A Case Series Describing Modified Toy Car Use as an Early Movement Option for Young Children With Mobility Limitations.
Pritchard-Wiart L, Bragg E, Thompson-Hodgetts S.


Modified toy cars for have gained popularity as a tool for early exposure to power mobility. Aims: to (1) determine modifications required, (2) describe frequency of home and community use, (3) describe assistance and encouragement provided, child's motivation and enjoyment of the car, and (4) explore therapist and parent experiences with the cars. Methods: This mixed-methods case series included children aged 13-58 months (n = 5) with cerebral palsy (n = 4) and arthrogryposis and hypotonia (n = 1). Four children received cars and follow-up visits from therapists in their homes. Quantitative data were collected using a family driving record. Qualitative interviews were conducted with parents (n = 5) and therapists (n = 2). The data management strategy described by Knafl (1988) facilitated qualitative data analysis. Results: One child could not be adequately supported; she did not receive a car. Driving frequency ranged from 1.3 to 2.9 days per week, 12-63 min in duration. Qualitative analysis resulted in four themes: (1) A gentle introduction to power mobility, (2) It's more than just mobility, (3) You just need to try it, and (4) Cars are simple tools. Conclusions: Modified toy cars are feasible for early exposure to power mobility with young children with physical disabilities who do not require extensive seating modifications.

PMID: 31144554

15. LEARN2MOVE 0-2 years, a randomized early intervention trial for infants at very high risk of cerebral palsy: family outcome and infant's functional outcome.
Hielkema T, Boxum AG, Hamer EG, La Bastide-Van Gemert S, Dirks T, Reinders-Messelink HA, Maathuis CGB, Verheijden J, Geertzen JHB, Hadders-Algra M.


Purpose: To compare family and functional outcome in infants at very high risk of cerebral palsy, after receiving the family centred programme "Coping with and Caring for infants with special needs (COPCA)" or typical infant physiotherapy. Materials and methods: Forty-three infants at very high risk were included before 9 months corrected age and randomly assigned to one year COPCA (n = 23) or typical infant physiotherapy (n = 20). Family and infant outcome were assessed before and during the intervention. Physiotherapy intervention sessions were assessed quantitatively for process analysis. Outcome was evaluated with non-parametric tests and linear mixed-effect models. Results: Between-group comparisons revealed no differences in family and infant outcomes. Within-group analysis showed that family's quality of life improved over time in the COPCA-group. Family empowerment was positively associated with intervention elements, including "caregiver coaching." Conclusions: One year of COPCA or typical infant physiotherapy resulted in similar family and functional outcomes. Yet, specific intervention elements, e.g., coaching, may increase empowerment of families of very high risk infants and may influence quality of life, which emphasizes the importance of family centred services. Implications for rehabilitation One year of the family centred programme "Coping with and a Caring for infants with special needs" compared with typical infant physiotherapy resulted in similar family outcome and similar functional outcome for the infants at very high risk for cerebral palsy. Specific contents of intervention, such as caregiver coaching, are associated with more family empowerment and increased quality of life. Emphasis on family needs is important in early intervention for infants at very high risk for cerebral palsy.

PMID: 31141410

Bennett S, Srirataratiwat W, Tanrangka N, Bennett MJ, Kanpittaya J.


The aim of this study was to compare diaphragmatic mobility (DM) and respiratory function between children with cerebral palsy (CP) and healthy controls (HC). CP was divided into non-ambulatory CP (NACP) and ambulatory CP (ACP). Eighteen children with NACP, 18 with ACP and 18 HC age between 8 and 18 years were recruited. Ultrasound was used to measure DM on both sides. Respiratory muscle strength (RMS), pulmonary function (PF) and chest expansion (CE) were also measured. The results showed that there was significantly lower right DM in CP than HC group. The NACP group had significantly lower DM than the ACP group. There were also significantly lower values of RMS, PF and CE in CP, compared to the HC group. There
are significant impairments of diaphragmatic and respiratory function in CP, relative to HC. Thus, appropriate interventions to improve diaphragmatic muscle strength are necessary for children with CP, especially in the NACP.

PMID: 31125702

17. Predictive Model for Gastrostomy Placement in Adolescents With Developmental Disabilities and Cerebral Palsy.
Bertoncelli CM, Altamura P, Vieira ER, Bertoncelli D, Latalski M, Berthet S, Solla F.


BACKGROUND: Factors associated with gastrostomy placement in adolescents with developmental disabilities (DDs) and cerebral palsy (CP) are poorly investigated. We aimed to develop and validate a machine learning (ML) model for gastrostomy placement in adolescents with DDs and CP. METHODS: We performed a multinational, double-blinded, case-control study including 130 adolescents with severe DD and CP (72 males, 58 females; mean age 16 ± 2 years). Data on etiology, diagnosis, spasticity, epilepsy, clinical history, and functional assessments such as the Eating and Drinking Ability Classification System, Manual Ability Classification System, and Gross Motor Function Classification System were collected between 2005 and 2015. Analysis included Fisher exact test, multiple logistic regressions, and a supervised ML model, named PredictMed, to identify factors associated with gastrostomy placement. "Transparent Reporting of a multivariable prediction model for Individual Prognosis or Diagnosis" guidelines were followed. RESULTS: Poor motor function (P < 0.001), trunk muscle tone disorder (P < 0.001), male gender (P < 0.01), epilepsy (P = 0.01), and severe neuromuscular scoliosis (P = 0.04) were factors linked with gastrostomy placement in univariate analysis. Epilepsy (P = 0.03), poor motor function (P = 0.04), and male gender (P = 0.04) were associated with gastrostomy placement in multivariate analysis with 95% accuracy. CONCLUSION: Epilepsy, poor motor function, trunk muscle tone disorder, and male gender were accurate, sensitive, and specific factors associated with gastrostomy need.

PMID: 31134674

18. [Neurosurgical treatment of dystonia].
Høck A, Jespersen B, Born AP, Løkkegaard A.

Ugeskr Laeger. 2019 May 13;181(20). pii: V06180404. [Article in Danish]

In this review, we present evidence of treatment effect with deep brain stimulation (DBS) in patients with isolated forms of dystonia with generalised-, segmental- and focal phenotypes as well as tardive dystonia and dyskinetic cerebral palsy. Dystonia is a heterogeneous movement disorder, which can be disabling and difficult to treat. Patients with dystonia, who do not experience relief with medication and botulinum toxin, may be candidates for DBS.

PMID: 31124449

19. Feasibility and effectiveness of a newly modified protocol-guided selective dorsal rhizotomy via single-level approach to treat spastic hemiplegia in pediatric cases with cerebral palsy.

Childs Nerv Syst. 2019 May 29. doi: 10.1007/s00381-019-04194-0. [Epub ahead of print]

PURPOSE: It still remains challenging to treat CP cases with spastic hemiplegia using SDR via a single-level approach when guided by the traditional EMG response grading system. Our aim was to assess the feasibility and effectiveness of a newly modified protocol-guided single-level laminectomy SDR to treat such pediatric patients. METHODS: A retrospective cohort review was conducted in the CP cases with spastic hemiplegia undergone our newly modified protocol-guided single-level approach SDR since May 2016 to October 2017, and followed by intensive rehabilitation program for at least 12 months in both Shanghai Children's Hospital and Shanghai Rehabilitation and Vocational Training Center for the Disabled. Inclusion and exclusion criteria were set for the selection of patients in the current study. Our study focused on the setup, EMG recording interpretation, and outcome measures for this newly modified rhizotomy scheme. RESULTS: Eleven cases were included in the current study. Based on our new rhizotomy protocol, a total of 34 rootlets over our 11 cases were cut (2 in 4, 3 in 4, 4 in 1, and 5 rootlets in 2 cases, respectively). After SDR and the following rehabilitation program at a mean duration of 19 months, muscle tone of those "target muscles" in affected lower extremities which identified during pre-op assessment decreased by a
mean of 1.4 degrees (Modified Ashworth Scale) in our cases. Strength of those target muscles and ROM of joints involved in their lower limbs were reported to have improved significantly as well. All cases showed major progress with regard to their motor function. A mean of about $10^{-7}$ point increase of GMFM-66 score was reported, and five of six cases who were with GMFCS level II preoperatively improved their GMFCS level at the last assessment. Kinematics of joints of hip, knee, and ankle on the affected side in our cases demonstrated a major correction, along with improvement of their foot pressure patterns to the ground during their gait cycles. Surgery-related complications, such as cerebral-spinal fluid leak/infection, long-term hypoesthesia, or urinary/bowel incontinence were not recorded in the current study. CONCLUSION: Single-level SDR when guided by our simplified rhizotomy protocol is feasible and effective to treat pediatric CP cases with spastic hemiplegia.

PMID: 31144022

20. Focus on risk factors for cardiometabolic disease in cerebral palsy: Towards a core set of outcome measurement instruments.
Benner JL, McPhee PG, Gorter JW, Hurvitz EA, Peterson MD, Obeid J, Wright M, Balemans ACJ, Verschuren O, Rita van den Berg-Emons HJG, van der Slot WMA, Roebroeck ME.


PMID: 31128113

Botkin ND, Turova VL, Kovtanyuk AE, Sidorenko IN, Lampe R.


Cerebral autoregulation is the ability to keep almost constant cerebral blood flow (CBF) for some range of changing the mean arterial pressure (MAP). In preterm infants, this range is usually very small, even absent, and a passive (linear) dependence of CBF on MAP is observed. Also, variations of the partial CO2 pressure and intracranial/venous pressure result in fluctuations of CBF. The absence of cerebral autoregulation may be a cause of intracranial hemorrhages due to instability of cerebral blood vessels, especially in the so-called germinal matrix which exists in a developing brain from 22 to 32 weeks of gestation. In the current paper, a mathematical model of impaired cerebral autoregulation is extended compared with previous works of the authors, and a heuristic feedback control that is able to keep deviations from a nominal CBF within a reasonable range is proposed. Viability theory is used to prove that this control can successfully work against a wide range of disturbances.

PMID: 31137216

22. Profile of children with cerebral palsy spectrum disorder and a normal MRI study.


OBJECTIVE: This study looks at what profile can be expected in children with cerebral palsy spectrum disorder (CP) and a normal MRI. METHODS: The data were excerpted from the Canadian Cerebral Palsy Registry database. Only patients who had undergone MRI were included in the analysis. Neuroimaging classification was ascertained by university-based pediatric neuroradiologists and split into 2 categories: normal and abnormal MRIs. Six factors were then compared between those 2 groups: prematurity, perinatal adversity, presence of more than 1 comorbidity, CP subtype, bimanual dexterity (Manual Ability Classification System [MACS]), and gross motor function (Gross Motor Function Classification System [GMFCS]). RESULTS: Participants with no perinatal adversity were 5.518 times more likely to have a normal MRI (p < 0.0001, 95% confidence interval [CI] 4.153-7.330). Furthermore, participants with dyskinetic, ataxic/hypotonic, and spastic diplegic forms of CP were 2.045 times more likely to have a normal MRI than those with hemiplegia, triplegia, and quadriplegia (p < 0.0001, 95% CI 1.506-2.778). No significant difference was found in prematurity, GMFCS levels, MACS levels, and the number of comorbidities. CONCLUSIONS: Normal MRIs were associated with lack of perinatal adversity as well as with the dyskinetic, ataxic/hypotonic, and spastic diplegic CP subtypes. As MRI normality is not strongly associated with the severity of CP, continuous follow-up in children with normal imaging appears warranted. Further advanced imaging modalities, as well as
strong consideration for metabolic and genetic testing, may provide additional insights into causal pathways in this population.

PMID: 31127072

Carlson HL, Sugden C, Brooks BL, Kirton A.


Successful language acquisition during development is imperative for lifelong function. Complex language networks develop throughout childhood. Perinatal stroke may cause significant language disabilities but function can also be remarkably normal. Studying such very early brain injury populations may inform developmental plasticity models of language networks. We examined functional connectivity (FC) of language networks in children with arterial and venous perinatal stroke and typically developing controls (TDC) in a population-based, controlled, cohort study. Resting state functional MRI was performed at 3 T (TR/TE = 2000/30 ms, 150 volumes, 3.6mm3 voxels). Seed-based analyses used bilateral inferior frontal and superior temporal gyri. A subset of stroke participants completed clinical language testing. Sixty-six children participated (median age: 12.85±3.8y, range 6-19; arterial N = 17; venous N = 15; TDC N = 34]. Children with left hemisphere strokes had comparable FC in their right hemispheres compared to TDC. Inter- and intra-hemispheric connectivity strengths were similar between TDC and PVI but lower for AIS. Reduced FC was associated with poorer language comprehension. Language networks can be estimated using resting-state fMRI in children with perinatal stroke. Altered connectivity may occur in both hemispheres, is more pronounced with arterial lesions, and is associated with clinical function. Our results have implications for therapeutic language interventions after early stroke.

PMID: 31141787

Srivastava R, Rajapakse T, Carlson HL, Keess J, Wei XC, Kirton A.


BACKGROUND: Neonatal arterial ischemic stroke is a leading cause of cerebral palsy and lifelong disability. Diffusion-weighted imaging has revolutionized diagnosis and facilitated outcome prognostication in acute neonatal arterial ischemic stroke. Diaschisis refers to changes in brain areas functionally connected but structurally remote from primary injury. We hypothesized that acute diffusion-weighted imaging can quantify cerebral diaschisis and is associated with outcome from neonatal arterial ischemic stroke. METHODS: Subjects were identified from a prospective, population-based research cohort (Alberta Perinatal Stroke Project). Inclusion criteria were unilateral middle cerebral artery neonatal arterial ischemic stroke, diffusion-weighted magnetic resonance imaging within 10 days of birth, and more than 12-months follow-up (pediatric stroke outcome measure). Diaschisis was characterized and quantified using a validated software method (ImageJ). Volumetric analysis assessed atrophy of affected structures. Diaschisis scores were corrected for infarct size and compared with outcomes (Mann-Whitney). RESULTS: From 20 eligible neonatal arterial ischemic strokes, two were excluded for poor image quality. Of 18 remaining (61% male, median age 3.2 days), 16 (89%) demonstrated diaschisis. Thalamus (88%) was the most common location in addition to corpus callosum (50%). Age at imaging was not associated with diaschisis. Affected structures demonstrated atrophy on imaging. Long-term outcomes available in 81% (median age 7.5 years) were not associated with diaschisis scores. CONCLUSIONS: Cerebral diaschisis occurs in neonatal arterial ischemic stroke and can be quantified with diffusion-weighted imaging. Occurrence is common and should not be mistaken for additional infarction. Determining clinical significance will require larger samples with well-characterized long-term outcomes.

PMID: 31147227

Nagai H, Tanaka T.


A stroke occurs when blood flow to the brain is critically reduced or blocked, potentially resulting in motor paralysis. One of
the most promising and effective neurorehabilitation methods for strokes is a closed-loop brain-computer interface (BCI) based on the motor imagery (MI). For the design of MI-based BCI, action observation (AO) during MI facilitates the detection of a user's motor intention. In this paper, we investigated whether or not the AO's targeted objects (the hand of a participant or another person) affects brain activity during MI. To investigate the differences in brain activity induced by the targeted objection, we recorded electroencephalography (EEG) data of 15 healthy right-handed males during three different conditions: (1) MI and AO of a participant's hand (MI+ownAO), (2) MI and AO of a non-participant's hand (MI+otherAO), and (3) MI only. Results showed that the event-related desynchronization (ERD) responses in the alpha frequency band (8-13 Hz) during MI+ownAO over the sensorimotor area (at the C3 and C4 channel locations) were stronger than those during the other two conditions. The results showed that the difference between participants' and non-participants' hands affected ERD responses during MI+ownAO and MI+otherAO.

PMID: 31144639

26. Placental abrasion and long-term neurological hospitalisations in the offspring.

BACKGROUND: Placental abrasion is a major determinant of maternal and perinatal morbidity and mortality, often related to asphyxia and preterm birth. However, the impact of abrasion on the long-term morbidity of the offspring is less investigated. METHODS: We designed a hospital-based cohort study, in which the incidence of long-term neurology-related hospitalisations of offspring to women with and without placental abrasion was assessed. All singleton deliveries between 1991 and 2014 were included in the study. Congenital anomalies, perinatal mortality, and multifetal pregnancies were excluded from the analyses. We compared cumulative morbidity incidence using Kaplan-Meier survival curves and estimated the risk for long-term neurological hospitalisations from Cox proportional hazards models after adjustment for putative including maternal age, parity, hypertensive disorders, pre-gestational and gestational diabetes, gender, ethnicity, and year of birth. RESULTS: Over the 22-year period, 2 202 269 person-years of follow-up, there were 217 910 deliveries of which 0.5% (n = 1003) were complicated with placental abrasion. The median (interquartile range) follow-up of children in the abrasion and non-aborption groups was 10.3 (4.6, 15.9) and 12.0 (6.3, 16.5) years, respectively. The cumulative incidence of total neurological hospitalisations was comparable between abrasion (3.32 per 1000 person-years) and non-aborption (3.16 per 1000 person-years). Abruption was associated with increased rates of cerebral palsy (hazard ratio [HR] 6.71, 95% CI 3.32, 13.58) and developmental disorders (HR 3.36, 95% CI 1.38, 8.13), but not for total neurology-related hospitalisations (HR 1.08, 95% CI 0.78, 1.49). CONCLUSION: Placental abrasion is associated with increased rate of cerebral palsy and developmental disorders in the offspring later in life. This study may define risk factors for childhood neuropsychiatric disorders, enabling early diagnosis and intervention in children with such disorders, and perhaps improving their prognosis.

PMID: 31131918

27. Cord Blood Haptoglobin, Cerebral Palsy and Death in Infants of Women at Risk for Preterm Birth: A Secondary Analysis of a Randomised Controlled Trial.

BACKGROUND: Antenatal exposure to intra-uterine inflammation results in precocious Haptoglobin (Hp) expression (switch-on status). We investigated the relationships between foetal Hp expression at birth with newborn and childhood outcomes. METHODS: We evaluated cord blood samples from 921 newborns of women at imminent risk for preterm delivery randomised to either placebo (n = 471, birth gestational age (GA) median [min-max]: 31 [24-41] weeks) or magnesium sulphate (n = 450, GA 31 [24-42] weeks). Primary outcome was infant death by 1 year and/or cerebral palsy (CP) ≥ 2 years of corrected age. Adjusted odd ratios (aOR) for neonatal and childhood outcomes were calculated controlling for GA, birth weight, sex, and magnesium exposure. FINDINGS: Primary outcome occurred in 2.8% of offspring. Newborns were classified in three pre-defined categorisation groups by cord blood Hp switch status and IL-6 levels: inflammation-noxposed (Category 1, n = 432, 47%), inflammation-exposed haptoglobinemic (Category 2, n = 449, 49%), and inflammation-exposed anhaptoglobinemic or hypohaptoglobinemic (Category 3, n = 40, 4%). Newborns, found anhaptoglobinemic or hypohaptoglobinemic (Category 3) had increased OR for intraventricular haemorrhage (IVH) and/or death (aOR: 7.0; 95% CI: 1.4-34.6, p = 0.02) and for CP and/or death (aOR: 6.27; 95% CI: 1.7-23.5, p = 0.006) compared with Category 2. Foetal ability to respond to inflammation by haptoglobinemia resulted in aOR similar to inflammation-noxposed newborns. Hp1-2 or Hp2-
2 phenotypes protected against retinopathy of prematurity (aOR = 0.66; 95% CI 0.48-0.91, p = 0.01). INTERPRETATION: Foetal ability to switch-on Hp expression in response to inflammation was associated with reduction of IVH and/or death, and CP and/or death. Foetal death increased such a response had an increased risk of adverse outcomes. Trial Registration: clinicaltrials.gov Identifier: NCT00014989.

PMID: 31143877

Levira F, Newton CR, Masanja H, Odermatt P.

Background: Neurological disorders (ND) have a profound consequence on human productivity, quality of life and survival. There are limited data on the burden of ND in Tanzania due to insufficient coverage of civil and vital registration systems. Objectives: This study was conducted to estimate mortality of ND in all ages in Tanzania using data from the Sample Vital Registration with Verbal Autopsy (SAVVY) study. Methods: Multistage random sampling was employed to select 23 districts, 1397 census enumeration areas and 154,603 households. During the baseline survey conducted between 2011 and 2014, deaths which occurred 12 months prior to the baseline survey were documented followed by verbal autopsy interviews. Causes of death were certified using International Classification of Diseases. Results: The baseline survey enrolled a total of 650,864 residents. A total of 6645 deaths were reported to have occurred 12 months before the date of survey. Death certification was available for 5225 (79%) deaths. The leading causes of death were cerebrovascular diseases with a cause-specific mortality fraction (CSMF) of 1.64% (95% CI: 1.30-1.99) and 3.82% (95% CI: 2.92-4.72) in all ages and adults older than 50 years, respectively. Stroke accounted for 92% of all cerebrovascular deaths. Mortality of epilepsy was estimated with a CSMF of 0.94% (95% CI: 0.68-1.20); meningitis with a CSMF of 0.80% (95% CI: 0.56-1.04); cerebral palsy and other paralytic syndromes with a CSMF of 0.46% (95% CI: 0.27-0.65); and intrauterine hypoxia in neonates with a CSMF of 2.06% (95% CI: 1.12-3.01). Overall, mortality of ND was estimated with a CSMF of 4.99% (95% CI: 4.40-5.58). Conclusions: The SAVVY survey provides estimates of mortality burden of ND in Tanzania. The study provides a basis for monitoring trends of ND and contributes to advancing knowledge of the burden of diseases. Integrating morbidity measures into the SAVVY design will provide comprehensive measures of burden of ND taking into account lifetime disabilities created by ND.

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Prevention and Cure

29. TRPV1 mediates astrocyte activation and interleukin-1β release induced by hypoxic ischemia (HI).
Yang XL, Wang X, Shao L, Jiang GT, Min JW, Mei XY, He XH, Liu WH, Huang WX, Peng BW.

BACKGROUND: Hypoxic-ischemic encephalopathy (HIE) is a serious birth complication with high incidence in both advanced and developing countries. Children surviving from HIE often have severe long-term sequelae including cerebral palsy, epilepsy, and cognitive disabilities. The severity of HIE in infants is tightly associated with increased IL-1β expression and astrocyte activation which was regulated by transient receptor potential vanilloid 1 (TRPV1), a non-selective cation channel in the TRP family. METHODS: Neonatal hypoxic ischemia (HI) and oxygen-glucose deprivation (OGD) were used to simulate HIE in vivo and in vitro. Primarily cultured astrocytes were used for investigating the expression of gliarial fibrillary acidic protein (GFAP), IL-1β, Janus kinase 2 (JAK2), signal transducer and activator of transcription 3 (STAT3), and activation of the NLRP3 inflammasome by using Western blot, q-PCR, and immunofluorescence. Brain atrophy, infarct size, and neurobehavioral disorders were evaluated by Nissl staining, 2,3,5-triphenyltetrazolium chloride monohydrate (TTC) staining and neurobehavioral tests (geotaxis reflex, cliff aversion reaction, and grip test) individually. RESULTS: Astrocytes were overactivated after neonatal HI and OGD challenge. The number of activated astrocytes, the expression level of IL-1β, brain atrophy, and shrinking infarct size were all downregulated in TRPV1 KO mice. TRPV1 deficiency in astrocytes attenuated the expression of GFAP and IL-1β by reducing phosphorylation of JAK2 and STAT3. Meanwhile, IL-1β release was significantly reduced in TRPV1 deficiency astrocytes by inhibiting activation of NLRP3 inflammasome. Additionally, neonatal HI-induced neurobehavioral disorders were significantly improved in the TRPV1 KO mice. CONCLUSIONS: TRPV1 promotes activation of astrocytes and release of astrocyte-derived IL-1β mainly via JAK2-STAT3 signaling and activation of the NLRP3 inflammasome. Our findings provide mechanistic insights into TRPV1-mediated brain damage and neurobehavioral disorders caused by neonatal HI and potentially identify astrocytic TRPV1 as a novel therapeutic target for treating HIE in the subacute stages (24 h).

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