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Cerebral palsy research news

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Interventions and Management

1. Team Approach: The Perioperative Management of Reconstructive Hip Surgery for the Non-Ambulatory Child with Cerebral Palsy and Spastic Hip Disease
Rachel L DiFazio, Laurie J Glader, Rachel Tombeno, Kathleen Lawler, Kristen Friel, Robert M Brustowicz, Benjamin J Shore

JBJS Rev. 2020 Jul;8(7):e1900185. doi: 10.2106/JBJS.RVW.19.00185.

PMID: 32678539

2. Association between pelvic obliquity and scoliosis, hip displacement and asymmetric hip abduction in children with cerebral palsy: a cross-sectional registry study
Gunnar Hägglund

BMC Musculoskelet Disord. 2020 Jul 14;21(1):464. doi: 10.1186/s12891-020-03484-y.

Background: Pelvic obliquity (PO) is common in individuals with cerebral palsy (CP). The prevalence of PO in a population of children with CP and its associations with scoliosis, hip displacement and asymmetric range of hip abduction were analysed. Methods: Over a 5-year period all pelvic radiographs from the Swedish surveillance programme for CP and the recorded data for scoliosis and hip abduction in children from southern Sweden at Gross Motor Function Classification System (GMFCS) levels II-V were analysed. PO and hip displacement calculated as migration percentage (MP) were measured on supine pelvic radiographs and compared with presence of scoliosis and side difference in hip abduction. Statistical analyses comprised chi-squared and binominal testing. Results: In total, 337 children were analysed, of whom 79 had a PO of ≥5°. The proportion of children with PO increased from 16% in GMFCS level II to 34% in level V. Scoliosis combined with PO was reported in 38 children, of whom 34 (89%, 95% confidence interval [CI] 80-99%) had the convexity opposite to the high side of the PO. Asymmetric abduction with PO was reported in 45 children, of whom 40 (89%, CI 79-99%) had reduced abduction on the high side of the PO. Asymmetric MP of ≥5% with PO was seen in 62 children, of whom 50 had higher MP on the high side of the PO (81%, CI 71-90%). Children in GMFCS levels II-IV more often had isolated infra-pelvic association with PO (47% versus 19% in GMFCS V, P = 0.025), while combined supra- and infrapelvic association was more common in GMFCS level V (65% versus 30% in GMFCS II-IV, P = 0.004). Isolated infrapelvic or no association was seen in 74% of children ≤10 years of age while 76% of children ≥11 years old had suprapelvic or combined supra- and infrapelvic association with PO (P < 0.001). Conclusions: There was a strong association between the high side of the PO and the side of scoliosis, highest MP, and lowest range of abduction when PO was measured in supine position. PO was more often associated with infrapelvic factors. PO was seen in young children indicating the need for early awareness of this complication.

PMID: 32664926

3. Locomotor patterns during obstacle avoidance in children with Cerebral Palsy
Germana Cappellini, Francesca Sylos-Labini, Michael James MacLellan, Carla Assenza, Laura Libernini, Daniela Morelli, Francesco Lacquaniti, Yury Ivanenko

J Neurophysiol. 2020 Jul 15. doi: 10.1152/jn.00163.2020. Online ahead of print.

We investigated how early injuries to developing brain affect the interaction of locomotor patterns with the voluntary action required by obstacle clearance. This task requires higher cognitive load and specific anticipatory sensorimotor integration than more automated steady-state gait. To this end, we compared the adaptive gait patterns during obstacle clearance in 40 children with cerebral palsy (CP) (24 diplegic, 16 hemiplegic, 2-12 years) and 22 typically developing (TD) children (2-12 years) by analyzing gait kinematics, joint moments during foot elevation, EMG activity of 11 pairs of bilateral muscles and muscle modules evaluated by factorization of the EMG signals. The results confirmed generally slower task performance, plus difficulty in motor planning and control in CP. Thus, about 30% of diplegic children failed to perform the task. Children with CP demonstrated higher foot lift, smaller range of motion of distal segments, difficulties in properly activating the hamstring muscles at lift-off and a modified hip strategy when elevating the trailing limb. Basic muscle modules were generally roughly similar to TD patterns, though they showed a limited adaptation. Thus, a distinct activation burst in the adaptable muscle module timed to the voluntary task (lift-off) was less evident in CP. Children with CP also showed prolonged EMG burst durations. Impaired obstacle task performance may reflect impaired or less adaptable supraspinal and spinal control of gait when a locomotor task is superimposed with the voluntary movement. Neurorehabilitation of gait in CP may thus be beneficial by adding voluntary tasks such as obstacle clearance during gait performance.

PMID: 32667246

4. [Modern opportunities and prognosis of physical rehabilitation of children with cerebral palsy] [Article in Russian]
V V Deineko, O B Krysyuk, L V Safonov, S N Shurygin

Zh Nevrol Psikhiatr Im S S Korsakova. 2020;120(6):88-91. doi: 10.17116/jnevro202012006188.

Objective: To evaluate the results of traditional and high-tech physical rehabilitation in cerebral palsy and in modeling of rehabilitation prognosis. Material and methods: One hundred and twenty-six patients with cerebral palsy (spastic diplegia); mean age 7.0±1.3 years, the duration of inpatient treatment 28 days, were studied. Forty patients received conventional treatment, 86 - a high-tech physical rehabilitation (robotic mechanic therapy with «Lokomat», «Armeo» and electric stimulation of the brain with «Brain-port» device). Results and conclusion: The advantage of more significant therapeutic effects of high-tech physical rehabilitation over traditional treatment is established. This effect consists in improving coordination and independent movement. On the basis of the regression analysis, mathematical models of the prognosis of the rehabilitation potential are constructed. High-tech physical rehabilitation has a significantly more pronounced therapeutic effect than traditional treatment.

PMID: 32678553

5. [Changes of the spasticity patterns in children with cerebral palsy GMFCS III at the age of 2 to 12 years] [Article in Russian]
A L Kurenkov, L M Kuzenkova, D A Fisenko, O A Klochkova, B I Bursagova, V V Chernikov

Zh Nevrol Psikhiatr Im S S Korsakova. 2020;120(6):36-44. doi: 10.17116/jnevro202012006136.

Spastic muscles in the pathological motor patterns may change at different ages that leads to the changes in anti-spastic treatment. Objective: To study the specific patterns of spasticity in CP patients with level III according to the Gross Motor Function Classification System (GMFCS) in different age periods. Material and methods: A retrospective analysis of injection protocols of Abobotulinum toxin A for 99 patients with bilateral spastic CP GMFCS III at the age of 2 to 12 years was performed. Spasticity patterns were evaluated according to the frequency of target muscle selection for the botulinum toxin A (Abobotulinum toxin A) injections. Results: The equinus foot deformity (89.7%, 95%CI 72.8-97.2) and its combination with internal hip rotation (79.3%, 95% CI 61.3-90.5) and/or hip adduction (65.5%, 95% CI 47.3-80.2) were the main lower

extremity spasticity pattern for the patients aged 2 to 4 years. Between 4 and 6 years, there was the decrease in injections to the gastrocnemius muscle (75%, 95% CI 52.8-89.2), and less to the m. gracilis (70%, 95% CI 47.9-85.7) and hip adductors (55% 95 CI 34.2-74.2). In the 6-12 year old patients, the predominant spasticity patterns were internal hip rotation (80%, 95% CI 66.8-88.9), adduction (54%, 95% CI 40.4-67.0) and knee flexion (66%, 95% CI 52.1-77.6). The leading upper extremity patterns at all observed ages were forearm pronation (70.7%, 95% CI 61.1-78.8) and elbow flexion (47.5%, 95% CI 37.9-57.2). The frequency of injections to these muscles slightly decreased in elder groups. Conclusions: CP GMFCS III patients demonstrate age-related changes of the spasticity patterns both in lower and upper extremities. These changes and typical spastic muscles should be taken into account during the rehabilitation and botulinum toxin treatment planning, as well as in the detection and prevention of the orthopaedic complications.

PMID: 32678546

6. Accurate measures of passive muscle-tendon stiffness in children with cerebral palsy are needed
Joanna Diong, Arkiev D'Souza

Eur J Appl Physiol. 2020 Jul 13. doi: 10.1007/s00421-020-04433-2. Online ahead of print.

PMID: 32661770

7. Screw Anterior Distal Femoral Hemiepiphysiodesis in Children With Cerebral Palsy and Knee Flexion Contractures: A Retrospective Case-Control Study
Jason T Long, Dominique Laron, Micah C Garcia, James J McCarthy

J Pediatr Orthop. 2020 Jul 7. doi: 10.1097/BPO.0000000000001634. Online ahead of print.

Background: In children with cerebral palsy who demonstrate hamstring tightness, increasing attention is being paid to less invasive methods of correcting knee flexion contractures. Guided growth principles represent one such approach, and in tandem with a serial extension casting protocol, may provide a less invasive method of addressing these contractures. To date, no evidence is available on this combination of procedures. The purpose of this study was to investigate the effectiveness of a combined lengthening/guided growth procedure (hamstring lengthening, percutaneous anterior screw hemiepiphysiodesis, and serial extension casting) in addressing knee flexion contracture, and to compare this approach to hamstring lengthening and serial extension casting alone. Methods: Measures from preoperative and postoperative gait analyses were reviewed retrospectively for 10 patients with cerebral palsy who underwent anterior screw hemiepiphysiodesis and hamstring lengthening followed by serial extension casting [anterior epiphysiodesis (AE) group]. These findings were compared with measures from 19 patients with cerebral palsy who underwent hamstring lengthening followed by serial extension casting [no anterior epiphysiodesis (NAE) group]. Postoperative changes in clinical, functional, and kinematic parameters were assessed. Radiographic parameters were also assessed for the AE group. Results: In the AE group, improvements were measured in knee contracture, popliteal angle, peak stance phase knee extension, knee range of motion, and Gait Deviation Index. Similar results were observed in the NAE group. In the AE group, the lateral distal femoral angle increased into extension by 20.9 degrees at an average of 26-month follow-up. Both groups showed an increase in pelvic tilt postoperatively. There were no surgical complications associated with the screw anterior hemiepiphysiodesis. Four patients did have complaints of knee pain, but the pain was attributable to the implants in only one patient. Discussion: The AE group demonstrated statistically greater postoperative improvement in popliteal angle, knee flexion contracture, and peak knee extension during stance than the NAE group. Both procedures led to improvements in clinical and functional measures, indicating the validity of this approach as a means of correcting flexion contracture that is less invasive and allows immediate weight bearing. Level of evidence: Level III-therapeutic study.

PMID: 32658158

8. Effect of an interval rehabilitation program with home-based, vibration-assisted training on the development of muscle and bone in children with cerebral palsy - an observational study
Ibrahim Duran, Kyriakos Martakis, Christina Stark, Leonie Schafmeyer, Mirko Rehberg, Eckhard Schoenau

J Pediatr Endocrinol Metab. 2020 Jul 13;/j/jpem.ahead-of-print/jpem-2020-0080/jpem-2020-0080.xml. doi: 10.1515/jpem-2020-0080. Online ahead of print.

Objectives In children with cerebral palsy (CP), the most common cause of physical impairment in childhood, less muscle and bone growth has been reported, when compared with typically developing children. The aim of this study was to evaluate the effect of an intensive rehabilitation program including physiotherapy in combination with 6 months of home-based, vibration-assisted training on muscle and bone growth in children with CP. Methods We included children with CP, who participated in a rehabilitation program utilizing whole-body vibration (WBV). Muscle mass was quantified by appendicular lean mass index (App-LMI) and bone mass by total-body-less-head bone mineral content (TBLH-BMC) assessed by Dual-energy X-ray absorptiometry (DXA) at the beginning of rehabilitation and one year later. To assess the functional muscle-bone unit, the relation of TBLH-BMC to TBLH lean body mass (TBLH-LBM) was used. Results The study population included 128 children (52 females, mean age 11.9 ± 2.7). App-LMI assessed in kg/m2 increased significantly after rehabilitation. The age-adjusted Z-score for App-LMI showed no significant change. TBLH-BMC assessed in gram increased significantly. The Z-scores for TBLH-BMC decreased lesser than expected by the evaluation of the cross-sectional data at the beginning of rehabilitation. The parameter T B L H - B M C T B L H - L B M $\frac{TBLH-BMC}{TBLH-LBM}$ did not change relevantly after 12 months. Conclusions Muscle growth and to a lesser extent bone growth could be increased in children with CP. The intensive rehabilitation program including WBV seemed to have no direct effect on the bone, but the observed anabolic effect on the bone, may only been mediated through the muscle.

PMID: 32653878

9. Evaluation and Management of Respiratory Illness in Children With Cerebral Palsy
Rachael Marpole, A Marie Blackmore, Noula Gibson, Monica S Cooper, Katherine Langdon, Andrew C Wilson

Review Front Pediatr. 2020 Jun 24;8:333. doi: 10.3389/fped.2020.00333. eCollection 2020.

Cerebral palsy (CP) is the most common cause of disability in childhood. Respiratory illness is the most common cause of mortality, morbidity, and poor quality of life in the most severely affected children. Respiratory illness is caused by multiple and combined factors. This review describes these factors and discusses assessments and treatments. Oropharyngeal dysphagia causes pulmonary aspiration of food, drink, and saliva. Speech pathology assessments evaluate safety and adequacy of nutritional intake. Management is holistic and may include dental care, and interventions to improve nutritional intake, and ease, and efficiency of feeding. Behavioral, medical, and surgical approaches to drooling aim to reduce salivary aspiration. Gastrointestinal dysfunction, leading to aspiration from reflux, should be assessed objectively, and may be managed by lifestyle changes, medications, or surgical interventions. The motor disorder that defines cerebral palsy may impair fitness, breathing mechanics, effective coughing, and cause scoliosis in individuals with severe impairments; therefore, interventions should maximize physical, musculoskeletal functions. Airway clearance techniques help to clear secretions. Upper airway obstruction may be treated with medications and/or surgery. Malnutrition leads to poor general health and susceptibility to infection, and improved nutritional intake may improve not only respiratory health but also constipation, gastroesophageal reflux, and participation in activities. There is some evidence that children with CP carry pathogenic bacteria. Prophylactic antibiotics may be considered for children with recurrent exacerbations. Uncontrolled seizures place children with CP at risk of respiratory illness by increasing their risk of salivary aspiration; therefore optimal control of epilepsy may reduce respiratory illness. Respiratory illnesses in children with CP are sometimes diagnosed as asthma; a short trial of asthma medications may be considered, but should be discontinued if ineffective. Overall, management of respiratory illness in children with CP is complex and needs well-coordinated multidisciplinary teams who communicate clearly with families. Regular immunizations, including annual influenza vaccination, should be encouraged, as well as good oral hygiene. Treatments should aim to improve quality of life for children and families and reduce burden of care for carers.

PMID: 32671000

10, Accelerating Telemedicine for Cerebral Palsy During the COVID-19 Pandemic and Beyond
Hilla Ben-Pazi, Liana Beni-Adani, Ron Lamdan

Review Front Neurol. 2020 Jun 26;11:746. doi: 10.3389/fneur.2020.00746. eCollection 2020.

The effects of COVID-19 extend beyond the pandemic and are expected to transform healthcare in various ways, many of

which remain unknown. With social distancing, telemedicine may become the preferred communication channel between caregivers and patients. Implications for cerebral palsy (CP) children are that this will pose a challenge within this transformation. CP, as a discreet entity, is not considered a risk factor. However, specific comorbidities in individuals with CP, such as chronic lung disease, are known as COVID-19 risk factors. The overall risk for the CP population is probably a factor of age and comorbidities. Staying at home for CP children is both a challenge and an opportunity. Escalation of behavioral conflicts or improved participation and equality within the household may emerge. Interestingly, restricted mobility for the general population narrows existing gaps of ambulation. Telemedicine is the primary way of providing services for chronic conditions during the pandemic and is expected to expand beyond pre-Coronavirus era use. The advantages of telemedicine vary, more so during pandemic times, according to severity, restrictions, and availably of telemedicine. A multidisciplinary therapeutic presence is more accessible with telemedicine, bringing together various specialties and approaches to the child's natural environment. Accessible, continuous care is expected to lower comorbidities, as demonstrated for other chronic conditions. Enhanced monitoring is crucial for younger children as devastating complications, such as hip dysplasia, could be minimized. Last but not least, we will discuss digital health care as an accelerator for participatory medicine, including networked patients and families, as responsible drivers of their health as full partners.

PMID: 32670193

11. Exploring sleep problems in young children with cerebral palsy - A population-based study
Kristina Löwing, Mirja Gyllensvärd, Kristina Tedroff

Eur J Paediatr Neurol. 2020 Jul 10;S1090-3798(20)30115-X. doi: 10.1016/j.ejpn.2020.06.006. Online ahead of print.

Objective: To describe and explore sleep problems in a population-based cohort of young children with cerebral palsy (CP) in Stockholm, Sweden. Methods: All children with CP, aged 5-10 years, and living in the Northern Karolinska University Hospital's catchment area were invited to participate in a cross-sectional study. Medical records obtained in the previous two-year period were reviewed, and a pre-planned parental telephone interview that included five structured questions and the Insomnia Severity Index (ISI) was conducted. Results: In total, 118 children, with a mean age of 7.4 years (SD 1.5), were included. Bilateral CP was present in 45%, unilateral in 37%, dyskinetic in 15%, and ataxic CP in 3%. Parents of 81% of the children participated in the interview. They reported sleep problems in 41% of their children, and in 80% of these children, night-time sleep was negatively affected by pain. Differences between the ISI total score in relation to CP subtypes ($p < 0.025$) and levels in GMFCS-E&R ($p < 0.001$) were detected, with increasing sleep problems for children with dyskinetic CP and children in GMFCS-E&R V. Sleep problems affected by pain were associated to the total score at ISI ($rs = 0.83$, $p < 0.001$, $n = 95$). Conclusion: The results identified that sleep problems were present in more than 40% of children with CP. Sleep problems were more frequently and extensively present in children with dyskinetic CP and children in GMFCS-E&R level V. Sleep problems were associated with the presence of pain and, in particular, in the most severely affected children.

PMID: 32669213

12. Think beyond movement & posture; mental disorders in cerebral palsy
Sarah McIntyre

Editorial Eur J Paediatr Neurol. 2020 Jul 2;S1090-3798(20)30120-3. doi: 10.1016/j.ejpn.2020.06.012. Online ahead of print.

PMID: 32660882

13. Recognizing chronic pain in cerebral palsy
Catherine E Ferland

Dev Med Child Neurol. 2020 Jul 12. doi: 10.1111/dmcn.14627. Online ahead of print.

PMID: 32654124

14, Challenges in pain assessment and management among individuals with intellectual and developmental disabilities
Chantel C Barney, Randi D Andersen, Ruth Defrin, Lara M Genik, Brian E McGuire, Frank J Symons

Pain Rep. 2020 Jun 16;5(4):e821. doi: 10.1097/PR9.0000000000000822. eCollection Jul-Aug 2020.

Introduction: Intellectual and developmental disabilities (IDD) include conditions associated with physical, learning, language, behavioural, and/or intellectual impairment. Pain is a common and debilitating secondary condition compromising functional abilities and quality of life. Objectives: This article addresses scientific and clinical challenges in pain assessment and management in individuals with severe IDD. Methods: This Clinical Update aligns with the 2019 IASP Global Year Against Pain in the Vulnerable and selectively reviews recurring issues as well as the best available evidence and practice. Results: The past decade of pain research has involved the development of standardized assessment tools appropriate for individuals with severe IDD; however, there is little empirical evidence that pain is being better assessed or managed clinically. There is limited evidence available to inform effective pain management practices; therefore, treatment approaches are largely empiric and highly variable. This is problematic because individuals with IDD are at risk of developing drug-related side effects, and treatment approaches effective for other populations may exacerbate pain in IDD populations. Scientifically, we are especially challenged by biases in self-reported and proxy-reported pain scores, identifying valid outcome measures for treatment trials, being able to adequately power studies due to small sample sizes, and our inability to easily explore the underlying pain mechanisms due to compromised ability to self-report. Conclusion: Despite the critical challenges, new developments in research and knowledge translation activities in pain and IDD continue to emerge, and there are ongoing international collaborations.

PMID: 32656458

15. Robotic assessment of rapid motor decision making in children with perinatal stroke
Rachel L Hawe, Andrea M Kuczynski, Adam Kirton, Sean P Dukelow

J Neuroeng Rehabil. 2020 Jul 14;17(1):94. doi: 10.1186/s12984-020-00714-1.

Background: Activities of daily living frequently require children to make rapid decisions and execute desired motor actions while inhibiting unwanted actions. Children with hemiparetic cerebral palsy due to perinatal stroke may have deficits in executive functioning in addition to motor impairments. The objective of this study was to use a robotic object hit and avoid task to assess the ability of children with hemiparetic cerebral palsy to make rapid motor decisions. Methods: Forty-five children with hemiparetic cerebral palsy due to perinatal stroke and 146 typically developing children (both groups ages 6-19 years) completed a robotic object hit and avoid task using the Kinarm Exoskeleton. Objects of different shapes fell from the top of the screen with increasing speed and frequency. Children were instructed to hit two specific target shapes with either hand, while avoiding six distractor shapes. The number of targets and distractors hit were compared between children with hemiparetic cerebral palsy and typically developing children, accounting for age effects. We also compared performance to a simpler object hit task where there were no distractors. Results: We found that children with hemiparetic cerebral palsy hit a greater proportion of total distractors compared to typically developing children, demonstrating impairments in inhibitory control. Performance for all children improved with age. Children with hemiparetic cerebral palsy hit a greater percentage of targets with each arm on the more complex object hit and avoid task compared to the simpler object hit task, which was not found in typically developing children. Conclusions: Children with hemiparetic cerebral palsy due to perinatal stroke demonstrated impairments in rapid motor decision making including inhibitory control, which can impede their ability to perform real-world tasks. Therapies that address both motor performance and executive functions are necessary to maximize function in children with hemiparetic cerebral palsy.

PMID: 32664980

16. Neurotransmission cognitive theory: A novel approach for non-invasive brain stimulation using mechanical vibrations for the rehabilitation of neurological patients
Aliya A Khan, Shahbaz K Ranjha, Muhammad U Akram, Sajid G Khawaja, Arslan Shaukat

Med Hypotheses. 2020 Jul 6;143:110078. doi: 10.1016/j.mehy.2020.110078. Online ahead of print.

Patients suffering from neurological disorders require not only the treatment but also the rehabilitation to have their productive role in society. With the advent of modern technology and neuroscience techniques, different treatments are proposed and tested clinically. We propose a therapeutic and interventional noninvasive brain stimulation method that applies mechanical vibrations to different nerve points of the body to activate the stimuli. These stimuli reach and activate dead parts of the brain which will eventually help in neurorehabilitation of such patients. We get the theoretical basis of the procedure from the concept of neurotransmission cognitive theory which is also presented in the paper. For the pilot results of the theory and its procedure, we have applied the theory/therapy to three of the patients, suffering from dysarthria and cerebral palsy and results are quite promising. More detailed clinical studies are still required to have a strong evidential basis for the procedure.

PMID: 32679423

17. A South African cerebral palsy registry is needed
T J Katangwe, R Van Toorn, R S Solomons, K Donald, S Steel, P E Springer, M Kruger

S Afr Med J. 2020 Apr 29;110(5):353-354. doi: 10.7196/SAMJ.2020.v110i5.14504.

PMID: 32657715

18. Movement Imitation Therapy for Preterm Babies (MIT-PB): a Novel Approach to Improve the Neurodevelopmental Outcome of Infants at High-Risk for Cerebral Palsy
Marina Soloveichick, Peter B Marschik, Ayala Gover, Michal Molad, Irena Kessel, Christa Einspieler

J Dev Phys Disabil. 2020;32(4):587-598. doi: 10.1007/s10882-019-09707-y. Epub 2019 Nov 18.

To improve the neurodevelopmental outcome in infants with high grade intraventricular haemorrhage and cramped-synchronised (CS) general movements (GMs). Four very preterm infants with intraventricular haemorrhage grade III (n = 3) or intraventricular haemorrhage with apparent periventricular haemorrhagic infarction (n = 1) were diagnosed with CS GMs at 33 to 35 weeks postmenstrual age. A few days later MIT-PB [Movement Imitation Therapy for Preterm Babies], an early intervention programme, was commenced: the instant an infant showed CS movements, the therapist intervened by gently guiding the infant's limbs so as to manoeuvre and smoothen the movements, thereby imitating normal GM sequences as closely as possible (at least for 10 min, 5 times a day, with increasing frequency over a period of 10 to 12 weeks). After a period of consistent CS GMs, the movements improved. At 14 weeks postterm age, the age specific GM pattern, fidgety movements, were normal in three infants, one infant had abnormal fidgety movements. At preschool age, all participants had a normal neurodevelopmental outcome. This report on four cases demonstrates that mimicking normal and variable GM sequences might have a positive cascading effect on neurodevelopment. The results need to be interpreted with caution and replication studies on larger samples are warranted. Nonetheless, this innovative approach may represent a first step into a new intervention strategy.

PMID: 32669775

19. A prospective observational study of developmental outcomes in survivors of neonatal hypoxic ischaemic encephalopathy in South Africa
D E Ballot, D Rakotsoane, P A Cooper, T D Ramdin, T Chirwa, M S Pepper

S Afr Med J. 2020 Mar 30;110(4):308-312. doi: 10.7196/SAMJ.2020.v110i4.14311.

Background: Neonatal hypoxic ischaemic encephalopathy (NHIE) is an important cause of long-term handicap in survivors. There is limited information on the burden of handicap from NHIE in sub-Saharan Africa. Objectives: To determine the developmental outcomes in survivors of NHIE in South Africa (SA). Methods: In this prospective observational study, the developmental outcomes in 84 infants who had survived hypoxic ischaemic encephalopathy (the NHIE group) were compared

with those in 64 unaffected infants (the control group). The Bayley Scales of Infant Development version III were used for assessment of developmental outcomes. Results: Significant differences were found between the developmental outcomes of the two groups, with a significantly lower composite language score and higher proportions with language, motor and cognitive developmental delays in the NHIE group than in the control group. Cerebral palsy (CP) was present in 13 of the infants with NHIE (15.5%) and none in the control group (p<0.001). CP was associated with developmental delay, and also with the severity of NHIE. Therapeutic hypothermia (TH) was administered in 58.3% of the study group, but although it was associated with lower rates of CP and developmental delay than in the group without TH, the only significant difference was for delay on the language subscale. Conclusions: Survivors of NHIE in SA are at risk of poor developmental outcomes.

PMID: 32657743

20. Optimizing High-risk Infant Follow-up in Nonresearch-based Paradigms: The New England Follow-up Network
Jonathan S Litt, Erika M Edwards, Shabnam Lainwala, Charles Mercier, Angela Montgomery, Deirdre O'Reilly, Lawrence Rhein, Melissa Woythaler, Tyler Hartman

Pediatr Qual Saf. 2020 May 5;5(3):e287. doi: 10.1097/pq9.0000000000000287. eCollection May-Jun 2020.

Objectives: To establish the first regional quality improvement collaborative solely dedicated to follow-through care of high-risk infants after Neonatal intensive care unit (NICU) discharge and to characterize extremely low birth weight (ELBW) follow-up in New England. Methods: Eleven of 14 follow-up programs in New England partnered with the Vermont Oxford Network (VON) ELBW project for an initial data collection project. We collected information about the health status and developmental outcomes of infants born ≤1,000 g or younger than 28 weeks 2014-2016 at the 18-24 months corrected for gestational age (CGA) follow-up visit. VON collected and compiled the data. Results: Of 993 eligible infants, 516 (52.0%) had follow-up visits. The rehospitalization rate was 33.9%, mostly respiratory illness. Ninety-six children (19.3%) had weight less than 10th percentile and 44 (8.9%) had weight less than third percentile at 18-24 months. Only 170 (61.4%) children had recommended hearing screening after NICU discharge. Forty-six (9.1%) had cerebral palsy; 81 of the 441 infants that completed all 3 sections of the Bayley Scales of Infant Development, third edition (18.4%) had any composite score less than 70. Over half of the social and demographic data were missing. Conclusion: Most quality initiatives in neonatology stop at NICU discharge. This first project by the New England Follow-up Network showed a low rate for clinical follow-up. It demonstrated many opportunities to improve postdischarge follow-through specific to NICU-based care. Future projects will aim to improve the quality of follow-through services through collaborative learning, data sharing, and comparative outcomes.

PMID: 32656462

21. Brain microstructure and morphology of very preterm-born infants at term equivalent age: associations with motor and cognitive outcomes at 1 and 2 years
Kerstin Pannek, Joanne M George, Roslyn N Boyd, Paul B Colditz, Stephen E Rose, Jurgen Fripp

Neuroimage. 2020 Jul 11;117163. doi: 10.1016/j.neuroimage.2020.117163. Online ahead of print.

Very preterm-born infants are at risk of adverse neurodevelopmental outcomes. Brain magnetic resonance imaging (MRI) at term equivalent age (TEA) can probe tissue microstructure and morphology, and demonstrates potential in the early prediction of outcomes. In this study, we use the recently introduced fixel-based analysis method for diffusion MRI to investigate the association between microstructure and morphology at TEA, and motor and cognitive development at 1 and 2 years corrected age (CA). Eighty infants born <31 weeks' gestation successfully underwent diffusion MRI (3T; 64 directions; b=2000s/mm2) at term equivalent age, and had neurodevelopmental follow-up using the Bayley-III motor and cognitive assessments at 1 year (n=78) and/or 2 years (n=76) CA. Diffusion MRI data were processed using constrained spherical deconvolution (CSD) and aligned to a study-specific fibre orientation distribution template, yielding measures of fibre density (FD), fibre-bundle cross-section (FC), and fibre density and bundle cross-section (FDC). The association between FD, FC, and FDC at TEA, and motor and cognitive composite scores at 1 and 2 years CA, and change in composite scores from 1 to 2 years, was assessed using whole-brain fixel-based analysis. Additionally, the association between diffusion tensor imaging (DTI) metrics (fractional anisotropy FA, mean diffusivity MD, axial diffusivity AD, radial diffusivity RD) and outcomes was investigated. Motor function at 1 and 2 years CA was associated with CSD-based measures of the bilateral corticospinal tracts and corpus callosum. Cognitive function was associated with CSD-based measures of the midbody (1-year outcomes only) and splenium of the corpus callosum, as well as the bilateral corticospinal tracts. The change in motor/cognitive outcomes from 1 to 2 years was associated with CSD-based measures of the splenium of the corpus callosum. Analysis of DTI-based measures showed overall

less extensive associations. Post-hoc analysis showed that associations were weaker for 2-year outcomes than they were for 1-year outcomes. Infants with better neurodevelopmental outcomes demonstrated higher FD, FC, and FDC at TEA, indicating better information transfer capacity which may be related to increased number of neurons, increased myelination, thicker bundles, and/or combinations thereof. The fibre bundles identified here may serve as the basis for future studies investigating the predictive ability of these metrics.

PMID: 32663645

22. Umbrella Review of School Age Health Outcomes of Preterm Birth Survivors
Michelle M Kelly, Patricia B Griffith

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Preterm birth affects approximately 10% of U.S. births, with survival rates close to 95%. All health care providers, regardless of population or setting, are treating preterm birth survivors. The purpose of this manuscript is to present an umbrella review of the health outcomes of 2- to 12-year-old children who were born preterm. The current umbrella review consisted of 29 reviews, 14 meta-analyses, eight systematic reviews, and seven described as both meta-analysis and systematic review. Studies were grouped into six health outcome categories: neurodevelopmental, motor and/or cerebral palsy, pulmonary, mental and/or behavioral health, quality of life and/or leisure, and eczema. The analysis supports a resounding recommendation to recognize preterm birth, at all gestations, as a risk factor to health and educational outcomes. Increased attention to developmental screenings is critical, specifically recognition that children who are on the lower ranges of normal may benefit from therapies or interventions that support the attainment of future skills.

PMID: 32660808

23. A web-based daily care training to improve the quality of life of mothers of children with cerebral palsy: A randomized controlled trial
Z Nobakht, M Rassafiani, S A Hosseini, S Hosseinzadeh

Res Dev Disabil. 2020 Jul 10;105:103731. doi: 10.1016/j.ridd.2020.103731. Online ahead of print.

Background: Mothers of moderately to severely affected children with cerebral palsy (CP) have to spend a long time to take care of their children. This time-consuming responsibility affects their physical and psychosocial health. Therefore, mothers as caregivers are required to receive special training to take care of their children. Aims: The aim of this study was to evaluate the effectiveness of a developed web-based intervention for daily care training of children with CP on their mothers' quality of life (QOL), anxiety, depression, stress, and their musculoskeletal pain. Methods and procedures: This study was a single blind randomized controlled trial. 91 mothers of children with CP with Gross Motor Function Classification System (GMFCS) levels III, IV, and V, who aged from 4 to 12 years were assigned to the intervention and control groups using block randomization. Mothers in the control group received their routine face to face occupational therapy intervention and mothers in the intervention group received 12 weeks web-based intervention. QOL, depression, anxiety, stress, and pain were measured before and after the intervention in both groups. Outcomes and results: The results of analysis of covariance showed that after controlling the mean score of pretest of pain, the mean score of post-tests in the intervention and control groups was significantly different ($P < 0.05$). The mean scores of physical health and total QOL scores of post-tests in the intervention group were significantly higher than the control group with controlling pretest scores. Conclusions and implications: Designed web-based intervention affects the caregivers' QOL and pain significantly. This intervention can be used to provide daily care training for mothers of children with CP.

PMID: 32659699

24. Cerebral Palsy: Etiology, Pathophysiology and Therapeutic Interventions
J Upadhyay, N Tiwari, M N Ansari

Review Clin Exp Pharmacol Physiol. 2020 Jul 13. doi: 10.1111/1440-1681.13379. Online ahead of print.

Cerebral palsy (CP) is the most common non-progressive neurodevelopmental disorder in which the impairment of motor and posture functions occurs. This condition may be present in many different clinical spectra. Various etiological and risk factors play a crucial role in the causation of CP. In various cases, the causes of CP may not be apparent.Interruption in the supply of oxygen to the fetus or brain asphyxia was considered to be the main causative factor explaining CP. Antenatal, perinatal, and postnatal factors could be involved in the origin of CP.Understanding its pathophysiology is also crucial for developing preventive and protective strategies. A major advancement in the brain stimulation techniques hasemerged as a promising status in diagnostic and interventional approaches. This review provides a brief explanation about the various etiological factors, pathophysiology, and recent therapeutic approaches in the treatment of cerebral palsy.

PMID: 32662125

25. Exploring the complexity of risk factors for cerebral palsy
Assimina Tsibidaki

Dev Med Child Neurol. 2020 Jul 16. doi: 10.1111/dmcn.14632. Online ahead of print.

PMID: 32672852

26. Pourfour du Petit (1664-1741)
J M S Pearce

Review Rev Neurol (Paris). 2020 Jul 9;S0035-3787(20)30604-4. doi: 10.1016/j.neurol.2020.04.023. Online ahead of print.

François Pourfour du Petit was a Parisian experimental neuro-anatomist, and ophthalmologist, who investigated his extensive wartime experiences of brain and spinal injuries and verified his conclusions by animal experiments. His results showed with great originality that brain injuries caused weakness or paralysis of the opposite limbs. He also clarified the anatomy of the spinal cord and decussation of the pyramidal tracts, and demonstrated the anatomy and clinical significance of the cervical sympathetic chain.

PMID: 32654778

27. DTI Tract-Based Quantitative Susceptibility Mapping: An Initial Feasibility Study to Investigate the Potential Role of Myelination in Brain Connectivity Change in Cerebral Palsy Patients During Autologous Cord Blood Cell Therapy Using a Rotationally-Invariant Quantitative Measure
Lijia Zhang, Susan Ellor, Jessica M Sun, Chunlei Liu, Joanne Kurtzburg, Allen W Song

J Magn Reson Imaging. 2020 Jul 16;e27286. doi: 10.1002/jmri.27286. Online ahead of print.

Background: Previous studies using diffusion tensor imaging (DTI)-based connectome analysis revealed improved connectivity in cerebral palsy (CP) patients who underwent autologous umbilical cord blood (UCB) stem-cell therapy. However, the potential mechanism for the connectivity increase remains unclear and needs to be further elucidated. Purpose: To develop a technique with improved accuracy for quantitative susceptibility mapping (QSM) with unique sensitivity to myelin, and demonstrate its use in elucidating the underlying mechanism of the observed motor function improvement and brain connectivity increase in CP patients who received autologous UCB stem-cell therapy. Study type: Prospective. Population: A cohort of eight pediatric CP patients (2.6 ± 0.6 years of age) with intact corticospinal tracts (CST) from a randomized, placebo-controlled trial of autologous UCB stem-cell therapy in CP children was included in this study. Field strength/sequence: DTI and 3D spoiled gradient recalled (SPGR) QSM at 3.0T. Assessment: Pre- and posttreatment magnetic susceptibility (χ) and the rotationally-invariant magnetic susceptibility anisotropy (MSA) along the CST were derived. Behavioral changes were assessed using the 66-item Gross Motor Function Measurement. Changes in χ and MSA were compared between patients with

and without substantial behavioral improvements. Statistical tests: Two-sample t-tests were performed to assess the differences in the changes of measurements of interest (Δχ, ΔMSA, and ΔFA) between patients who significantly improved and those who did not. Results: Patients who demonstrated posttreatment motor improvements exceeding expectations showed significantly more diamagnetic Δχ in the periventricular region along the CST (P = 0.003). Further analysis on the ΔMSA of this region was significantly increased (P = 0.006) for high responders, along with concurrent FA increase. Data conclusion: These initial findings suggest that the DTI tract-based QSM method has the potential to characterize white matter changes associated with behavioral improvements in CP children who underwent cord blood stem-cell therapy. Level of evidence: 2 TECHNICAL EFFICACY: Stage 2.

PMID: 32677156

Prevention and Cure

28. Molecular and behavioural abnormalities in the FUS-tg mice mimic frontotemporal lobar degeneration: Effects of old and new anti-inflammatory therapies

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Genetic mutations in FUS, a DNA/RNA-binding protein, are associated with inherited forms of frontotemporal lobar degeneration (FTLD) and amyotrophic lateral sclerosis (ALS). A novel transgenic FUS[1-359]-tg mouse line recapitulates core hallmarks of human ALS in the spinal cord, including neuroinflammation and neurodegeneration, ensuing muscle atrophy and paralysis, as well as brain pathomorphological signs of FTLD. However, a question whether FUS[1-359]-tg mouse displays behavioural and brain pro-inflammatory changes characteristic for the FTLD syndrome was not addressed. Here, we studied emotional, social and cognitive behaviours, brain markers of inflammation and plasticity of pre-symptomatic FUS[1-359]-tg male mice, a potential FTLD model. These animals displayed aberrant behaviours and altered brain expression of inflammatory markers and related pathways that are reminiscent to the FTLD-like syndrome. FTLD-related behavioural and molecular Journal of Cellular and Molecular Medicine features were studied in the pre-symptomatic FUS[1-359]-tg mice that received standard or new ALS treatments, which have been reported to counteract the ALS-like syndrome in the mutants. We used anti-ALS drug riluzole (8 mg/kg/d), or anti-inflammatory drug, a selective blocker of cyclooxygenase-2 (celecoxib, 30 mg/kg/d) for 3 weeks, or a single intracerebroventricular (i.c.v.) infusion of human stem cells (Neuro-Cells, 500 000-CD34+), which showed anti-inflammatory properties. Signs of elevated anxiety, depressive-like behaviour, cognitive deficits and abnormal social behaviour were less marked in FUS-tg-treated animals. Applied treatments have normalized protein expression of interleukin-1β (IL-1β) in the prefrontal cortex and the hippocampus, and of Iba-1 and GSK-3β in the hippocampus. Thus, the pre-symptomatic FUS[1-359]-tg mice demonstrate FTLD-like abnormalities that are attenuated by standard and new ALS treatments, including Neuro-Cell preparation.

PMID: 32667139