

Cerebral palsy research news

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Interventions and Management

1. Corpus Callosum Integrity Relates to Improvement of Upper-Extremity Function Following Intensive Rehabilitation in Children With Unilateral Spastic Cerebral Palsy Maxime T Robert, Jennifer Gutterman, Claudio L Ferre, Karen Chin, Marina B Brandao, Andrew M Gordon, Kathleen Friel

Neurorehabil Neural Repair. 2021 May 6;15459683211011220. doi: 10.1177/15459683211011220. Online ahead of print.

Background: The corpus callosum (CC) plays an important role in upper extremity (UE) function. The impact on UE function in children with unilateral spastic cerebral palsy (USCP) and improvements following intensive interventions remain unknown. Objectives: To examine the (1) relationship between UE function and CC integrity and (2) relationship between CC integrity and changes in UE function following intensive interventions. Methods: We retrospectively analyzed clinical and neuroimaging data from a sample of convenience of 44 participants (age 9.40 ± 3.10 years) from 2 larger trials. Participants received 90 hours of Hand-Arm Bimanual Intensive Therapy (HABIT) or Constraint-Induced Movement Therapy (CIMT). Unimanual dexterity (Jebsen-Taylor Test of Hand Function [JTTHF]) and bimanual performance (Assisting Hand Assessment [AHA]) were assessed preintervention and postintervention. CC tractography was reconstructed with diffusion tensor imaging (DTI) and segmented into 3 regions (genu, midbody, splenium). Pearson correlations and regression were used to assess the relationship between outcomes and DTI parameters (ie, fractional anisotropy [FA], number of streamlines, and mean, radial, and axial diffusivity). Results: Both groups improved in bimanual performance (P < .01). The CIMT group improved in unimanual dexterity (P < .01). Baseline unimanual dexterity and bimanual performance correlated with FA and number of streamlines for most CC regions ($P \le .05$). Following CIMT, pre-post changes in JTTHF were negatively correlated with axial and radial diffusivity of the CC, and AHA with splenium and number of streamlines for the CC, midbody, and splenium (all P < .05). Following HABIT, midbody FA was positively correlated with pre-post AHA changes (r = 0.417; P = .042). Conclusions: CC integrity is important for UE function in children with USCP.

PMID: <u>33955304</u>

2. [Simultaneous Bilateral Femoral Osteotomies in Neurogenic Hip Instability: a Feasibility Study] [Article in Czech] J Poul, M Malá, K Urbášek, P Zoufalý, K Ročák

Acta Chir Orthop Traumatol Cech. 2021;88(2):95-100.

PURPOSE OF THE STUDY The study aimed to evaluate the intraoperative and early postoperative response to simultaneous bilateral femoral osteotomy usually accompanied by soft tissue release of hip joints, or open reduction, capsuloplasty, pelvic osteotomy or extraarticular shelf procedure. MATERIAL AND METHODS A bilateral surgery was performed in 16 children. Twelve children suffered from (spastic) cerebral palsy and there was one case of paralytic dislocation in a patient with myelomeningocele, while the remaining patients suffered from chromosome I aberrations, Dandy-Walker syndrome and

merosin-deficient muscular dystrophy. GMFCS Level IV and V prevailed. The patients with femoral head deformity or severe adduction contracture were removed from the study group. In all cases the LCP Pediatric Hip Plate 3.5 or 5.0 (Synthes) was used for osteosynthesis. The postoperative fixation by a hip spica cast was applied for 6 weeks, after which in most cases SWASH orthosis was used at night. The age of the patient, the hip joint finding, the GMFCS level and the type of procedure were recorded. RESULTS The evaluation took into account the use of general anaesthesia only or a combination of general and epidural anaesthesia, most often through caudal block, duration of surgery, time when blood transfusion was necessary and the volumes of blood needed, duration of stay in the Anaesthesiology and Resuscitation Unit, or Intensive Care Unit. As a response to surgery, the changes in haemoglobin levels in g/l and VAS pain score were studied. In four patients only the operative time exceeded 3 hours. Blood transfusion was necessary in 13 patients, with one blood unit being always sufficient. Two patients were admitted to the Anaesthesiology and Resuscitation Unit, the remaining patients spent 1-3 days after surgery in the ICU. The average length of hospital stay did not exceed a week. The postoperative decrease in haemoglobin levels quickly improved. The pain intensity was regularly recorded postoperatively and on day 3-4 it was evaluated as moderate, with patients responding well to common analgesics (VAS 4-7). DISCUSSION The evaluation of duration of simultaneous bilateral procedure, postoperative recovery based on the need for blood transfusion, changes in blood count and VAS scores indicated that the procedure performed on both hip joints simultaneously does not significantly exceed the reasonable limits in terms of the patient's burden. In literature, we found only a single article on a topic of this sort, the conclusions of which are very similar. CONCLUSIONS The simultaneous bilateral femoral osteotomy can be considered a fairly safe procedure. Key words: hip joint instability, simultaneous femoral osteotomy, cerebral palsy.

PMID: 33960921

3. The Relationship of One Leg Standing Duration to GMFM Scores and to Stance Phase of Walking in Children with Hemiplegic Cerebral Palsy

Gamze Ertürk, Nazif Ekin Akalan, Halenur Evrendilek, Gülşah Karaca, Fuat Bilgili

Physiother Theory Pract. 2021 May 7;1-5. doi: 10.1080/09593985.2021.1920078. Online ahead of print.

Background: Lack of stability during stance negatively impacts gait and motor function for children with unilateral cerebral palsy. Improving stability and balance are the focus for gait rehabilitation). The One-Leg-Standing-Test may give valuable information about motor function and stability of stance for patients with unilateral cerebral palsy. Objective: This study aimed to investigate the relationship between the One-Leg-Standing-Test and the gross-motor-function-measurement and single-limb support time. Methods: The study included 18 patients with unilateral cerebral palsy (age 11.08 [SD 2.84] years old). The One-Leg-Standing-Test and pedobarographic evaluation were performed. Sections D and E of the gross-motor-function-measurement were assessed, and in pedobarographic evaluation, the single-limb support time (the total duration of mid-stance and terminal-stance during walking) was calculated to describe stability during stance. Results: For patients, the One-Leg-Standing-Test scores and single-limb support time values were lower on the affected side than on the unaffected side. The One-Leg-Standing-Test was also correlated to total stance phase and section D. Conclusion: The One-Leg-Standing-Test gives valuable information about gross-motor-function but cannot be substituted for motor function tests. The single-limb support time value may be used to describe stability in stance during walking.

PMID: 33957844

4. Long-term functional outcomes after an external femoral derotation osteotomy in individuals with cerebral palsy Elizabeth R Boyer, Elizabeth A Duffy, Kathryn Walt, Antonio Muñoz Hamen, Michael T Healy, Michael H Schwartz, Tom F Novacheck

Gait Posture. 2021 Apr 22;87:184-191. doi: 10.1016/j.gaitpost.2021.04.029. Online ahead of print.

Background: It is unknown how a femoral derotation osteotomy (FDO) during childhood affects functional outcomes in adulthood among individuals with bilateral cerebral palsy (CP). Research questions: How do long-term functional outcomes after an FDO compare to matched individuals who did not have an FDO? How do outcomes change over time? Methods: We queried the gait laboratory database for individuals who underwent an external FDO in childhood and were currently \geq 25 years old. Participants returned for a long-term analysis (gait, physical examination, functional tests, imaging, questionnaires). The matched non-FDO group included only individuals in Gross Motor Function Classification System levels I-II, yielding three groups (non-FDO I-II, FDO I-II, FDO III-IV). Results: Sixty-one adults (11 non-FDO, 34 FDO I-II, 16 FDO III-IV) returned

13-25 years after baseline (non-FDO) or surgery (FDO). The non-FDO and FDO I-II groups were matched at baseline on most variables, except the FDO group had weaker hip abductors. At long-term, groups were similar on gait variables (median long-term hip rotation [primary outcome], non-FDO: -4°, FDO I-II: -4°, FDO III-IV: -5°), hip abduction test, fear of falling, and most pain measures despite anteversion being 29° greater in the non-FDO group. The FDO I-II group reported more falls than the non-FDO group. All groups improved on hip rotation, foot progression, and hip abductor strength. Speed and step length decreased/tended to decrease for all three groups. Hip abduction moment and gait deviation index did not change. Improvements in the FDO groups were maintained from short- to long-term. Significance: These results challenge the notion that an FDO is necessary to correct mean stance hip rotation for higher functioning individuals since nearly identical results were achieved by adulthood in the non-FDO I-II group. However, an FDO provides improvement earlier and maintenance from short- to long-term. This should factor into the shared decision-making process.

PMID: 33945965

5. The importance of a consistent workflow to estimate muscle-tendon lengths based on joint angles from the conventional gait model

Hans Kainz, Michael H Schwartz

Gait Posture. 2021 Apr 27;88:1-9. doi: 10.1016/j.gaitpost.2021.04.039. Online ahead of print.

Background: Musculoskeletal models enable us to estimate muscle-tendon length, which has been shown to improve clinical decision-making and outcomes in children with cerebral palsy. Most clinical gait analysis services, however, do not include muscle-tendon length estimation in their clinical routine. This is due, in part, to a lack of knowledge and trust in the musculoskeletal models, and to the complexity involved in the workflow to obtain the muscle-tendon length. Research question: Can the joint angles obtained with the conventional gait model (CGM) be used to generate accurate muscle-tendon length estimates? Methods: Three-dimensional motion capture data of 15 children with cerebral palsy and 15 typically developing children were retrospectively analyzed and used to estimate muscle-tendon length with the following four modelling frameworks: (1) 2392-OSM-IK-angles: standard OpenSim workflow including scaling, inverse kinematics and muscle analysis; (2) 2392-OSM-CGM-angle: generic 2392-OpenSim model driven with joint angles from the CGM; (3) modif-OSM-IK-angles: standard OpenSim workflow including inverse kinematics and a modified model with segment coordinate systems and joint degrees-of-freedom similar to the CGM; (4) modif-OSM-CGM-angles: modified model driven with joint angles from the CGM. Joint kinematics and muscle-tendon length were compared between the different modelling frameworks. Results: Large differences in hip joint kinematics were observed between the CGM and the 2392-OpenSim model. The modif-OSM showed similar kinematics as the CGM. Muscle-tendon length obtained with modif-OSM-IK-angles and modif-OSM-CGM-angles were similar, whereas large differences in some muscle-tendon length were observed between 2392-OSM-IKangles and 2392-OSM-CGM-angles. Significance: The modif-OSM-CGM-angles framework enabled us to estimate muscletendon lengths without the need for scaling a musculoskeletal model and running inverse kinematics. Hence, muscle-tendon length estimates can be obtained simply, without the need for the complexity, knowledge and time required for musculoskeletal modeling and associated software. An instruction showing how the framework can be used in a clinical setting is provided on https://github.com/HansUniVie/MuscleLength.

PMID: 33933913

6. Spastic Hips in Cerebral Palsy - Retrospective Study of Salvage with the McHale Procedure Helder Henzo Yamada, Dante Galvanese Amato Neto, Juliano Mangini Dias Malpaga, Patricia Maria de Moraes Barros Fucs

Rev Bras Ortop (Sao Paulo). 2021 Apr;56(2):244-250. doi: 10.1055/s-0040-1713391. Epub 2020 Sep 22.

Objective To perform a retrospective and cross-sectional assessment to determine the pain and positional improvement of all patients with spastic cerebral palsy (CP) and severe hip deformity who underwent a McHale procedure in our center. A second objective was to analyze the potential complications from the procedure. Methods All consecutive patients treated between 1995 and 2017 were analyzed. Clinically, the patients should present pain on hip mobilization, difficulty in positioning for sitting and hygiene care, and medical records with complete data; functionally was assessed through the Gross Motor Function Classification System (GMFCS). In the preoperative radiographs, we analyzed the migration percentage (MP), the type of deformity according to the Melbourne Cerebral Palsy Hip Classification Scale (MCPHCS), and the type of deformity of the femoral head. After the surgery, we assessed the proximal migration of the proximal femoral fragment, implant changes and/or

failure, and potential heterotopic ossification. The outcomes were reported as successful (D1) in patients presenting remission of pain, painless mobility, and improved positioning, or unsuccessful (D2) in those presenting procedural failure that required a new surgery. Results In total, 47 patients (53 hips) were treated. Functionally, 43 patients were classified as GMFCS V (91%), 3 as GMFCS IV patients (6%), and 1 as GMFCS III (2%). The mean age was 13 years and 2 months. The follow-up ranged from 1 year to 15 years and 4 months, with an average of 4 years and 8 months. A total of 36 patients (41 hips) presented successful (D1) outcomes after the McHale procedure, corresponding to 77% of our cases, whereas 11 (23%) cases had unsuccessful (D2) outcomes. Conclusion The McHale procedure is a treatment option for GMFCS IV and V, but we must be aware of the potential complications.

PMID: <u>33935321</u>

7. Quantification and Monitoring of the Effect of Botulinum Toxin A on Paretic Calf Muscles of Children With Cerebral Palsy With MRI: A Preliminary Study

Claudia Weidensteiner, Philipp Madoerin, Xeni Deligianni, Tanja Haas, Oliver Bieri, Tugba Akinci D'Antonoli, Katrin Bracht-Schweizer, Jacqueline Romkes, Enrico De Pieri, Francesco Santini, Erich Rutz, Reinald Brunner, Meritxell Garcia

Front Neurol. 2021 Apr 16;12:630435. doi: 10.3389/fneur.2021.630435. eCollection 2021.

Background: Muscles from patients with cerebral palsy (CP) are often spastic and form contractures that limit the range of motion. Injections of botulinum toxin A (BTX) into the calf muscles are an important treatment for functional equinus; however, improvement in gait function is not always achieved. BTX is also used to test muscle weakening for risk evaluation of muscle lengthening surgery. Our aim was to assess the effect of BTX over time on calf muscle properties in pediatric CP patients with MRI. Material and Methods: Six toe-walking CP patients (mean age 11.6 years) with indication for lengthening surgery were prospectively enrolled and received BTX injections into the gastrocnemius and soleus muscles. MRI scans at 3T of the lower legs and clinical examinations were performed pre-BTX, 6 weeks (6w), and 12 weeks (12w) post-BTX. A fatsuppressed 2D multi-spin-echo sequence was used to acquire T2 maps and for segmentation. Fat fraction maps were calculated from 3D multi-echo Dixon images. Diffusion tensor imaging (DTI) with a 2D echo-planar imaging (EPI) sequence yielded maps of the mean apparent diffusion coefficient (ADC) and of the fractional anisotropy (FA). Hyperintense regions of interest (ROIs) on the T2-weighted (T2w) images at 6w were segmented in treated muscles. Mean values of T2, fat fraction, ADC, and FA were calculated in hyperintense ROIs and in reference ROIs in non-treated muscles. Results: Hyperintensity on T2w scans and increased T2 (group mean \pm standard deviation: 35 ± 1 ms pre-BTX, 45 ± 2 ms at 6w, and 44 ± 2 ms at 12w) were observed in all patients at the injection sites. The T2 increase was spatially limited to parts of the injected muscles. FA increased $(0.30 \pm 0.03 \text{ pre-BTX}, 0.34 \pm 0.02 \text{ at 6w, and } 0.36 \pm 0.03 \text{ at 12w})$ while ADC did not change in hyperintense ROIs, indicating a BTX-induced increase in extracellular space and a simultaneous decrease of muscle fiber diameter. Fat fraction showed a trend for increase at 12w. Mean values in reference ROIs remained unchanged. Conclusion: MRI showed limited spatial distribution of the BTX-induced effects in pediatric CP patients. It could be a promising non-invasive tool for future studies to test BTX treatment protocols.

PMID: 33935939

8. Radiographic and plantar pressure assessment of pes planovalgus severity in children with cerebral palsy Nicole Look, Patrick Autruong, Zhaoxing Pan, Frank M Chang, James J Carollo

Clin Biomech (Bristol, Avon). 2021 Apr 27;85:105364. doi: 10.1016/j.clinbiomech.2021.105364. Online ahead of print.

Background: Pes planovalgus is common in children with cerebral palsy. Although severity influences treatment, there still lacks standard clinical measurements to objectively quantify pes planovalgus in this population. The comparison of pedobarographic data and radiographic measurements to clinical evaluation has not been reported in this population. Methods: 395 feet were identified from a population of ambulatory pediatric patients with cerebral palsy. Each patient initially underwent clinical evaluation by an experienced physical therapist who classified feet as: 136 controls, 116 mild, 100 moderate, and 43 severe pes planovalgus. Quantitative measurements were then calculated from antero-posterior and lateral radiographs of the foot. Pedobarographic analysis included the arch index, center of pressure index, and a newly defined medial index. Findings: A multivariate analysis was performed on the radiographic and pedobarographic measurements collected. It identified seven variables that improved objective classification of pes planovalgus severity when utilized together. These include the foot progression angle, initial contact force, arch index, medial index, antero-posterior talonavicular coverage, lateral calcaneal pitch and lateral Meary's angle. While the lateral calcaneal pitch angle statistically differed amongst all severity classes, no

pedobarographic value statistically differed between all severity classes. Interpretation: Overall, the combination of radiographic and pedobarographic measurements provides valuable information for objectively classifying severity of pes planovalgus in children with cerebral palsy by utilizing these values together rather than independently. In a clinical setting, radiographs and pedobarographic data may be obtained to enhance assessment of severity and guide treatment.

PMID: 33940478

9. Effect of oral sensorimotor stimulation on oropharyngeal dysphagia in children with spastic cerebral palsy: a randomized controlled trial

Amira M Abd-Elmonem, Sara S Saad-Eldien, Walaa A El-Nabie

Eur J Phys Rehabil Med. 2021 May 7. doi: 10.23736/S1973-9087.21.06802-7. Online ahead of print.

Background: Children with cerebral palsy show various degrees of dysphagia causing late development of oral motor skills. Aim: To investigate effect of oral sensorimotor stimulation on oropharyngeal dysphagia in children with spastic quadriplegia. Design: This was a double-masked, randomized controlled clinical trial. Setting: Out-patient Clinics of Faculty of Physical Therapy, Cairo University and Modern University of Technology and information. Population: A convenient sample of 71 children age ranged from 12 to 48 months diagnosed with spastic quadriplegia, were randomly assigned into two groups. Methods: Children in the control group received 90 minutes conventional physical therapy training five times/week for 4 successive months while those in the experimental group received 20 minutes of oral sensorimotor stimulation before the same program as in control group for 60 minutes. Oral motor function, body weight, segmental trunk control and gross motor function were assessed at base-line and after completing treatment. Results: In total, 64 (experimental n=32, control n=32) children completed treatment and data collection. The baseline assessment showed non-significant difference regarding all measured variables while with-in group comparison showed significant improvement in the two groups. The post-treatment comparisons revealed significant difference the oral motor function and physical growth in favor of the experimental group (p < 0.05). Finally, there was non-significant difference regarding segmental trunk control and gross motor function (p > 0.05). Conclusions: Oral sensorimotor stimulation has the capability to improve feeding in children with spastic cerebral palsy diagnosed with oropharyngeal dysphagia. Clinical rehabilitation impact: OSMS has effect on some of the essential oral motor skills that contribute toward the improvement of feeding performance in children with spastic CP. The results of our study offer remarkable clinical importance for the children and their families.

PMID: 33960181

10. Salivary Biomarker Levels and Oral Health Status of Children with Cerebral Palsy and Their Healthy Siblings: A Comparative Study

Palanichamy Anjugam, Veerabadhran Mahesh Mathian, Murugesan Gawthaman, Selvaraj Vinod, Easwaramurthy Yamuna Devi

Rambam Maimonides Med J. 2021 Apr 29;12(2):e0015. doi: 10.5041/RMMJ.10437.

Background: The dental needs of cerebral palsy children are an area of study much in need of attention. The neglect of this aspect should be rectified, and simpler diagnostic methodologies should be established and used to serve this purpose. Aim: This study aimed to determine oral health status and salivary biomarkers (salivary flow rate, pH, buffering capacity) among children with cerebral palsy (CP), to compare their data with that of their healthy siblings, and to evaluate the relationship between salivary biomarkers and dental caries. Methods: A total of 30 CP children (study group) and 30 normal healthy siblings (controls) were selected between the ages of 5 and 12 years. Salivary biomarkers were assessed, and oral health status was examined. Statistical analysis: Chi-square test was used for comparison of oral health status. Unpaired t test was used to compare caries indexes (decay/filled teeth-primary dentition [dft] and decay/missing/filled teeth-permanent dentition [DMFT]) and salivary biomarkers between the groups. Pearson correlation was used to find the correlation between salivary biomarkers and caries. Results: The dft scores were significantly higher in the study group (P<0.05). The pH values and salivary flow rates were significantly lower in the study group (P<0.05). Conclusion: Low pH and low salivary flow rate might be risk factors for dental caries in CP populations; moreover, the significant correlation between DMFT score and salivary flow rate suggests that salivary flow rate could be used as a screening tool for assessing at-risk subjects in such populations.

PMID: 33938802

11. Diet quality in adults with cerebral palsy: a modifiable risk factor for cardiovascular disease prevention Meagan C Brown, Christina M Marciniak, Ariane M Garrett, Deborah J Gaebler-Spira

Dev Med Child Neurol. 2021 May 6. doi: 10.1111/dmcn.14913. Online ahead of print.

Aim: To assess diet quality and its relationship with cardiovascular health measures for adults with cerebral palsy (CP). Method: A convenience sample of 45 adults with CP (26 females, 19 males; mean age 35y 10mo [SD 14y 9mo]). were recruited for this cross-sectional study. Demographic, medical, and Gross Motor Function Classification System (GMFCS) information were obtained through in-person visits. Participants completed two 24-hour dietary recalls using the Automated Self-Administered 24-hour Dietary Assessment Tool. Specific macronutrient intake was compared to 2015 to 2020 US Department of Agriculture (USDA) guidelines. Other data included body mass index (BMI), waist-to-hip ratio (WHR), blood pressure, and hemoglobin A1c (HgA1c;n=43). Results: Adults across GMFCS levels I to V were enrolled, 20 participants were in GMFCS levels IV or V. Mean calorie intake was 1777.91/day (SD 610.54), while sodium intake was 3261.75mg/day (SD 1484.92). Five participants met USDA vegetable and seven fruit guidelines. None met whole grain targets. Sixteen were overweight/obese by BMI. Sixteen participants without hypertension diagnoses had elevated blood pressure and nine had abnormal HgA1c without prediabetes/diabetes history. Percent calories from saturated fat was inversely associated with WHR in unadjusted models (p=0.002 and p=0.003 respectively); all other dietary recommendations assessed (total calories, sodium, and sugar) were non-significant. Post hoc analyses were unchanged using 2020 to 2025 USDA guidelines. Interpretation: Assessment of nutrient intake and diet quality is feasible and warrants further study in adults with CP, as USDA guidelines.

PMID: 33959958

12. Musculoskeletal diagnoses, comorbidities, and physical and occupational therapy use among older adults with and without cerebral palsy

Deborah Thorpe, Mary Gannotti, Mark D Peterson, Chin-Hua Wang, Janet Freburger

Disabil Health J. 2021 Apr 15;101109. doi: 10.1016/j.dhjo.2021.101109. Online ahead of print.

Background: Musculoskeletal (MSK) disorder in adults with cerebral palsy (CP) is higher than in the general population. Evidence lacks about physical therapy (PT) and occupational therapy (OT) service utilization among older adults (65> years) living with CP. Objective: We compared the presence of comorbidities and patterns of PT and OT use among older adults with and without CP seeking care for MSK disorders. Methods: A 20% national sample of Medicare claims data (2011-2014) identified community-living older adults with (n = 8796) and without CP (n = 5,613,384) with one or more ambulatory claims for MSK diagnoses. The sample matched one CP case to two non-CP cases per year on MSK diagnoses, age, sex, race, dual eligibility, and census region. Exposure variable was the presence/absence of a CP diagnosis. Outcomes were use of PT and OT services identified via CPT and revenue center codes, and the presence/absence of Elixhauser comorbidities. Results: In older adults with MSK diagnoses, less than a third regularly utilized PT and/or OT services, and adults with CP utilized significantly less PT than adults without CP, and for some MSK diagnoses had fewer visits than their matched peers. Older adults with CP were at greater risk for secondary conditions that influence morbidity, mortality, and quality of life compared to their agematched peers without CP. Conclusions: Older adults with CP and MSK diagnoses had a greater prevalence of numerous comorbidities and lower use of PT services relative to their non-CP peers.

PMID: 33933399

13. The design of Lil'Flo, a socially assistive robot for upper extremity motor assessment and rehabilitation in the community via telepresence

Michael J Sobrepera, Vera G Lee, Michelle J Johnson

J Rehabil Assist Technol Eng. 2021 Apr 19;8:20556683211001805. doi: 10.1177/20556683211001805. eCollection Jan-Dec 2021.

Introduction: We present Lil'Flo, a socially assistive robotic telerehabilitation system for deployment in the community. As shortages in rehabilitation professionals increase, especially in rural areas, there is a growing need to deliver care in the communities where patients live, work, learn, and play. Traditional telepresence, while useful, fails to deliver the rich interactions and data needed for motor rehabilitation and assessment. Methods: We designed Lil'Flo, targeted towards pediatric patients with cerebral palsy and brachial plexus injuries using results from prior usability studies. The system combines traditional telepresence and computer vision with a humanoid, who can play games with patients and guide them in a present and engaging way under the supervision of a remote clinician. We surveyed 13 rehabilitation clinicians in a virtual usability test to evaluate the system. Results: The system is more portable, extensible, and cheaper than our prior iteration, with an expressive humanoid. The virtual usability testing shows that clinicians believe Lil'Flo could be deployed in rural and elder care facilities and is more capable of remote stretching, strength building, and motor assessments than traditional video only telepresence. Conclusions: Lil'Flo represents a novel approach to delivering rehabilitation care in the community while maintaining the clinician-patient connection.

PMID: 33953938

14. Sample size estimation in locomotion kinematics and electromyography for statistical parametric mapping Francesco Luciano, Luca Ruggiero, Gaspare Pavei

J Biomech. 2021 Apr 24;122:110481. doi: 10.1016/j.jbiomech.2021.110481. Online ahead of print.

In biomechanics, kinematic and electromyographic data can be represented as one-dimensional (1D) waveforms and compared by using 1D hypothesis tests. These statistical techniques are increasingly applied in the study of locomotion. However, although widely agreed as a key step to obtain reliable and replicable findings, no a priori sample size estimation is usually conducted. This can also be done in 1D tests by calculating the statistical power - i.e., the probability of rejecting the null hypothesis when it is false - by using statistical parametric mapping. With the present study we characterised the parameters needed to estimate sample size in locomotion, and how they impact on statistical power in 1D tests. First, noise and signal in kinematics and electromyography were defined using experimental data on locomotion in physiological and pathological participants. Then, 1D power analysis was performed in representative conditions, and a dataset of tabulated sample sizes was generated. Kinematic and electromyographic data showed a smooth Gaussian noise, with amplitude and full-width-at-half-maximum depending on the physiological or pathological condition, and the considered joint or muscle. Given a certain noise, statistical power increased i) with greater signal amplitude and signal full-width-at-half-maximum, ii) when setting a region of interest and iii) when using a paired (vs. unpaired) study design. The present work provides initial benchmarks for appropriate sampling in 1D hypothesis testing, meant to evaluate statistical power in 1D tests and assists sample size estimation in studies on locomotion.

PMID: 33933861

15. Rehabilitation status of children with cerebral palsy in Bangladesh: Findings from the Bangladesh Cerebral Palsy Register

Mahmudul Hassan Al Imam, Israt Jahan, Manik Chandra Das, Mohammad Muhit, Hayley Smithers-Sheedy, Sarah McIntyre, Nadia Badawi, Gulam Khandaker

PLoS One. 2021 May 3;16(5):e0250640. doi: 10.1371/journal.pone.0250640. eCollection 2021.

Objective: The objective of this study was to assess the rehabilitation status and factors associated with rehabilitation service utilisation among children with cerebral palsy (CP) in Bangladesh. Materials and methods: This is a population-based surveillance study conducted among children with CP registered in the Bangladesh CP Register (BCPR), the first population-based register of children with CP aged <18 years (y) in Bangladesh. Children with CP were identified from the community using the key informant method and underwent a detailed neurodevelopmental assessment. Socio-demographic, clinical and rehabilitation status were documented. Unadjusted and adjusted analyses with a 95% confidence interval (CI) were used to identify potential predictors of rehabilitation service uptake. Results: Between January 2015 and December 2019, 2852 children with CP were registered in the BCPR (mean (standard deviation, SD) age: 7 y 8 months (mo) (4 y 7 mo), 38.5% female). Of these, 50.2% had received rehabilitation services; physiotherapy was the most common type of service (90.0%). The mean (SD) age at commencement of rehabilitation services was 3 y 10 mo (3 y 1 mo). The odds of not receiving

rehabilitation was significantly higher among female children (adjusted odds ratio (aOR) 1.3 [95% CI: 1.0-1.7], children whose mothers were illiterate and primary level completed (aOR 2.1 [95% CI: 1.4-3.1] and aOR 1.5 [95% CI: 1.1-2.1], respectively), fathers were illiterate (aOR 1.9 [95% CI: 1.3-2.8]), had a monthly family income ~US\$ 59-118 (aOR: 1.8 [95% CI: 1.2-2.6]), had hearing impairment (aOR: 2.3 [95% CI: 1.5-3.5]) and motor severity (i.e. Gross Motor Function Classification System level III (aOR: 0.6 [95% CI: 0.3-0.9]) and level V (aOR: 0.4 [95% CI: 0.2-0.7])). Conclusions: Rehabilitation status was poor among the majority of the children with CP in the BCPR cohort, limiting their opportunities for functional improvement. A community-based rehabilitation model focusing on socio-demographic and clinical characteristics should be a public health priority in Bangladesh.

PMID: <u>33939721</u>

16. Increasing prevalence of cerebral palsy among children and adolescents in China 1988-2020: A systematic review and meta-analysis

Shengyi Yang, Jiayue Xia, Jing Gao, Lina Wang

J Rehabil Med. 2021 May 7. doi: 10.2340/16501977-2841. Online ahead of print.

To investigate the pooled prevalence of cerebral palsy in China, analyse the differences between different subgroups, and explore the trend over the 32-year period from 1988 to 2020. All potential studies related to the prevalence of cerebral palsy among children and adoles-cents in China were identified from 3 English- language databases and 4 Chinese-language databases. Pooled prevalence was calculated to estimate the prevalence of cerebral palsy among 0-18 years old and different geographical regions in China, using a random-effects meta-analysis model. Continuous fractional polynomial regression modelling was used to estimate the trend in prevalence of cerebral palsy over time. Subgroup analysis and meta-regression were conducted to investigate heterogeneity. Funnel plots and Egger's test were used to explore potential publication bias. The pooled prevalence of cerebral palsy over the study period among 0-18 years old and different geographical regions in China was 2.07% (95% confidence interval (95% CI) 1.66-2.47%), and the prevalence of cerebral palsy was higher in males compared with females (2.25% vs 1.59%), and in rural residents compared with urban residents (2.54% vs 1.9%), respectively. The prevalence of cerebral palsy varied significantly between different geographical regions. In subjects with birthweights < 2.5 and > 4 kg the prevalence of cerebral palsy was significantly higher than in subjects with birthweights between 2.5 and 4kg. The trend in pooled prevalence of cerebral palsy increased continuously over the period studied, and could be divided into 3 stages; the mean annual increase in prevalence from 1988 to 1996 and from 2008 to 2019 was more rapid. Multivariate metaregression found that the year of study was one of the sources of heterogeneity among overall prevalence. (p=0.006). The pooled prevalence of cerebral palsy over the 32-year period from 1988 to 2020 was 2.07%. There was an increasing trend in prevalence of cerebral palsy among children and adolescents in China over this period.

PMID: 33961057

17. The effects of COVID-19 pandemic countermeasures on patients receiving botulinum toxin therapy and on their caregivers: a study from an Italian cohort

Domiziano Tarantino, Rossana Gnasso, Federico Migliore, Irene Iommazzo, Felice Sirico, Bruno Corrado

Neurol Sci. 2021 May 6;1-7. doi: 10.1007/s10072-021-05282-3. Online ahead of print.

COVID-19 outbreak had a huge worldwide impact, and several countermeasures to contain its spread have been adopted, such as the interruption of nonurgent outpatient clinics. We wanted to describe the effects of the national lockdown on the wellbeing of a cohort of Italian patients with cerebral palsy (CP) receiving botulinum toxin (BT) therapy and of their caregivers. Twenty-five patients receiving BT therapy were surveyed using the structuralized questionnaire by Dressler and Adib Saberi, while the caregivers were assessed using the Caregiver Burden Scale. The lockdown delayed BT therapy by 9 ± 2.8 months. Around 44% of the selected patients noticed increased muscle cramps, 24% increased muscle pain, and 32% both of them. Due to the lockdown, the patient's quality of life was reduced by $68.4 \pm 21.1\%$. After the lockdown, 100% of patients perceived BT therapy as more important than before. Around 76% of the patients perceived the lockdown as inadequate and felt that their rights were not respected. The overall score of the Caregivers Burden Scale, as regarded before the lockdown, was 29.12 ± 11.63 , while the overall score as regarded after the lockdown was 37.44 ± 14.85 . The overall score increased, from before the lockdown to after the lockdown, for 92% of caregivers. The BT outpatient clinic's interruption was seen to significantly worsen the psychophysical condition of subjects with CP and the care burden of their caregivers, exposing them to greater stress than before. Therefore, any kind of BT treatment suspension or delay should be avoided.

18. Neurological diseases and COVID-19: prospective analyses using the UK Biobank

Nicola Veronese, Lee Smith, Mario Barbagallo, Gianluigi Giannelli, Maria Gabriella Caruso, Anna Maria Cisternino, Maria Notarnicola, Chao Cao, Thomas Waldhoer, Lin Yang

Acta Neurol Belg. 2021 May 5;1-9. doi: 10.1007/s13760-021-01693-3. Online ahead of print.

COVID-19 (Coronavirus disease-19) may present with neurological signs, but whether people already affected by neurological conditions are at a higher risk of contracting COVID-19 is still not known. We, therefore, aimed to investigate the association of previously diagnosed neurological conditions with COVID-19. 502,536 community-dwelling UK Biobank participants (54.4% male, mean age 56.6 ± 10.3 years) were included. Among these, 57,463 participants had a diagnosis of neurological conditions (11.43%) and a total of 1326 COVID-19-positive cases were identified (0.26%). Neurological conditions were identified through medical history and linkage to data on hospital admissions (ICD-10 code G00-G99). COVID-19 presence was diagnosed using the data provided by Public Health England. The association of previous diagnosis of neurological conditions with COVID-19 was evaluated through logistic regressions, adjusted for potential confounders, reported as odds ratios (ORs) with their 95% confidence intervals (CIs). Nerve, nerve root and plexus disorders (G50-G59) were the most common conditions identified. The presence of COVID-19 was almost doubled in neurological conditions compared to the general population (0.45 vs. 0.24%, p < 0.0001). Previously diagnosed neurological conditions were associated with 60% higher odds of COVID-19 positive in the multivariable-adjusted model (OR = 1.6, 95% CI 1.4-1.8). Other degenerative diseases of the nervous system, extrapyramidal and movement disorders, polyneuropathies and other disorders of the peripheral nervous system, cerebral palsy and other paralytic syndromes were significantly associated with a higher odds of COVID-19. The presence of neurological conditions was associated with a significantly higher likelihood of COVID-19 compared to the general population.

PMID: 33954931

19. Cerebral Palsy and Criteria Implicating Intrapartum Hypoxia in Neonatal Encephalopathy - An Obstetric Perspective for the South African Setting

I Bhorat, E Buchmann, P Soma-Pillay, E Nicolaou, L Pistorius, I Smuts

S Afr Med J. 2021 Mar 31;111(3b):280-288. doi: 10.7196/SAMJ.2021.v111i3b.15399.

The science surrounding cerebral palsy indicates that it is a complex medical condition with multiple contributing variables and factors, and causal pathways are often extremely difficult to delineate. The pathophysiological processes are often juxtaposed on antenatal factors, genetics, toxins, fetal priming, failure of neuroscientific autoregulatory mechanisms, abnormal biochemistry and abnormal metabolic pathways. Placing this primed compromised compensated brain through the stresses of an intrapartum process could be the final straw in the pathway to brain injury and later CP. It is thus simplistic to base causation of cerebral palsy on only an intrapartum perspective with radiological 'confirmation', as is often the practice in medicolegal cases in South African courts. The present modalities (MRI and CTG when available) that retrospectively attempt to determine causation in courts are inadequate when used in isolation. Unless a holistic scientific review of the case including all contributing clinical factors (antepartum, intrapartum and neonatal), fetal heart rate monitoring, neonatal MRI if possible (and preferred) or late MRI, and histology (placental histology if performed) are taken into account, success for plaintiff or defendant currently in a court of law will depend on eloquent legal argument rather than true scientific causality. The 10 criteria set out in this document to implicate acute intrapartum hypoxia in hypoxic ischaemic encephalopathy/neonatal encephalopathy serve as a guideline in the medicolegal setting.

PMID: 33944711

20. Reliability and minimal detectable change of the Challenge, an advanced motor skills test for children with cerebral palsy, Danish version

Kirsten Nordbye-Nielsen, Thomas Maribo, F Virginia Wright, Ole Rahbek, Bjarne Møller-Madsen

Disabil Rehabil. 2021 May 6;1-8. doi: 10.1080/09638288.2021.1906332. Online ahead of print.

Purpose: To translate and cross-culturally adapt the Challenge, and investigate the reliability and minimal detectable change (MDC) of the Danish Challenge in children with cerebral palsy (CP). Materials and methods: A Danish version of the Challenge was created through a standardized translation process. Four physiotherapists evaluated face validity. Independently ambulatory children with CP were tested. Live performance rating was conducted by assessors independently scoring the Challenge. Video-rating was undertaken for a subset of assessments. Same day assessment test-retest reliability was estimated. The Challenge's Best Score Total was of primary interest. Results: Forty-five children (5-18 years: mean 10 years 9 months; 19 girls) in Gross Motor Function Classification System levels I and II were tested. Inter-rater reliability was excellent for live assessments (n = 45) ICC = 0.998 (95% CI 0.998-0.999) and video assessments (n = 15) ICC = 0.991 (95% CI 0.963-0.997) and intra-rater reliability was excellent for live versus video-recorded assessments (n = 10) ICC = 0.977 (95% CI 0.895-0.994). Test-retest reliability (n = 22) was excellent with ICC = 0.991 (95% CI 0.979-0.996) and minimal detectable change (MDC90) of 4.7 points. Conclusions: The Danish Challenge showed excellent reliability in this testing context when physiotherapists scored from live- or video-recorded assessments. The Challenge's ability to detect 4.7 points change seems a clinically realistic target for progress. Clinical trial registration: This trial has been approved by the Data Protection Agency, Central Region Denmark, Ref nr.: 615216, Case nr.: 1-16-02-46-16. Registration date: 01-01-2016. Implications for rehabilitation. The Challenge remained reliable and maintained a promising minimal detectable change of less than five points after translation and cultural adaptation. The Danish version of the Challenge 20-item version can be used to measure advanced motor skill performance in children with cerebral palsy, GMFCS level I and GMFCS level II. Challenge live scoring is as reliable as the more time-consuming video-recorded scoring, meaning that physiotherapists can choose the method that fits best with their clinical context and preference.

PMID: 33955308

21. Towards Automated Emotion Classification of Atypically and Typically Developing Infants Sofiya Lysenko, Nidhi Seethapathi, Laura Prosser, Konrad Kording, Michelle J Johnson

Proc IEEE RAS EMBS Int Conf Biomed Robot Biomechatron. Nov-Dec 2020;2020:503-508. doi: 10.1109/ BioRob49111.2020.9224271. Epub 2020 Oct 15.

The World Health Organization estimates that 15 million infants are born preterm every year [1]. This is of concern because these infants have a significant chance of having neuromotor or cognitive developmental delays due to cerebral palsy or other developmental issues [2]. Our long-term goal is to determine the roles emotion and movement play in the diagnosis of atypical infants. In this paper, we examine how automated emotion assessment may have potential to classify typically and atypically developing infants. We compare a custom supervised machine learning algorithm that utilizes individual and grouped facial features for infant emotion classification with a state-of-the-art neural network. Our results show that only three concavity features are needed for the concavity algorithm, and the custom algorithm performed with relatively similar performance to the neural network. Automatic sentiment labels used in tandem with infant movement kinematics would be further investigated to determine if emotion and movement are interdependent and predictive of an infant's neurodevelopmental delay in disorders such as cerebral palsy.

PMID: 33959406

22. A Spatio-temporal Attention-based Model for Infant Movement Assessment from Videos Binh Nguyen-Thai, Vuong Le, Catherine Morgan, Nadia Badawi, Truyen Tran, Svetha Venkatesh

IEEE J Biomed Health Inform. 2021 May 6; PP. doi: 10.1109/JBHI.2021.3077957. Online ahead of print.

The absence or abnormality of fidgety movements of joints or limbs is strongly indicative of cerebral palsy in infants. Developing computer-based methods for assessing infant movements in videos is pivotal for improved cerebral palsy screening. Most existing methods use appearance-based features and are thus sensitive to strong but irrelevant signals caused by background clutter or a moving camera. Moreover, these features are computed over the whole frame, thus they measure gross whole body movements rather than specific joint/limb motion. Addressing these challenges, we develop and validate a new method for fidgety movement assessment from consumer-grade videos using human pose extracted from short clips. Human pose capture only relevant motion profiles of joints and limbs and are thus free from irrelevant appearance artifacts. The dynamics and coordination between joints are modeled using spatio-temporal graph convolutional networks. Frames and body parts that contain discriminative information about fidgety movements are selected through a spatio-temporal attention mechanism. We validate the proposed model on the cerebral palsy screening task using a real-life consumer-grade video dataset collected at an Australian hospital through the Cerebral Palsy Alliance, Australia. Our experiments show that the proposed method achieves the ROC-AUC score of 81.84%, significantly outperforming existing competing methods with better interpretability.

PMID: 33956636

23. Effects of a powered mobility summer camp as perceived by school staff: a qualitative study Lori Rosenberg, Ruth Cohen, Adina Maeir, Yafit Gilboa

Disabil Rehabil Assist Technol. 2021 May 7;1-8. doi: 10.1080/17483107.2021.1923840. Online ahead of print.

Purpose: Powered mobility has a positive effect on social skills, self-esteem and overall development of children with motor impairments, but almost all previous studies were conducted with pre-school children. The aim of this study was to explore change beyond mobility following a therapeutic powered mobility summer camp for school-aged children and adolescents with severe cerebral palsy, as perceived by school staff. Materials and methods: The participants in the therapeutic camp, which ran for 3 weeks, 5 days a week, three times over the summers 2018-2019, were children ages 7-19 (median age 11) with severe cerebral palsy who needed assistance in mobility and had limited hand function. Following the intervention, 19 semi-structured audio-recorded interviews were conducted with school staff, then transcribed and thematically analyzed using an inductive qualitative descriptive design with a phenomenological theoretical framework. Results: Four overarching themes were identified: (1) "Every step you take: mastering new, sometimes unexpected, skills", (2) "Break on through to the other side: changes in behaviour", (3) "Make new friends (but keep the old): Boosting social behaviour" and (4) "I'm a believer: The journey through self-efficacy to empowerment". Conclusions: The interviews showed the immediate positive influence of powered mobility for children who previously did not have independent mobility, following an intensive intervention. Changes in initiative, empowerment, social relationships and behaviour highlight the importance of self-generated mobility, regardless of whether independence was achieved. School-aged children with severe cerebral palsy seem to benefit from an intensive powered mobility intervention in areas other than mobility skills themselves. IMPLICATIONS FOR REHABILITATION Powered mobility intervention seems to encourage activity and initiation among children and youth with severe CP. This research adds to the understanding of the effect powered mobility can have on social interaction and communication. Powered mobility might be a means to allow development, in addition to being an important end.

PMID: 33961532

24. Hippotherapy in neurodevelopmental disorders: a narrative review focusing on cognitive and behavioral outcomes Giuseppa Maresca, Simona Portaro, Antonino Naro, Ramona Crisafulli, Antonio Raffa, Ileana Scarcella, Barbara Aliberti, Gaetano Gemelli, Rocco Salvatore Calabrò

Appl Neuropsychol Child. 2020 Dec 1;1-8. doi: 10.1080/21622965.2020.1852084. Online ahead of print.

Hippotherapy (HT) is a rehabilitative tool inducing psychological and motor improvements using human-horse interaction. HT provides sensory stimulation to the rider through the rhythmic and repetitive movements of the horse, facilitating communication between patients and healthcare professionals, favoring the establishment of a therapeutic alliance. The purpose of this review is to evaluate the effects of HT treatment on cognitive-behavioral processes in neurodevelopmental disorders. We screened studies published between 2002 and 2020 on PubMed, Scopus, Cochrane, and Web of Sciences databases. The search combined the following terms: "hippotherapy"; "horseback riding"; "equine-assisted therapy"; "developmental disorder", "autism spectrum disorder"; "dyspraxia"; "infantile cerebral palsy"; and "attention-deficit/hyperactivity disorder". This review shows that HT can be a valuable tool for the treatment of developmental disorders. The psychological, cognitive and relational areas could benefit from the animal-child interaction to promote child autonomy, self-esteem, self-efficacy and openness to others. Physical, motor and psychosocial benefits were found in adolescents with anxiety and/or depression disorders, in autism spectrum disorders, dyspraxia, as well as in infantile cerebral palsy and attention deficit hyperactivity disorder. HT could be considered an alternative therapeutic tool thanks to the relationship between patient-horse-instructor and to the sensory-motor and cognitive stimulation that enforce learning processes.

PMID: <u>33949903</u>

25. Adverse childhood experiences and developmental disabilities: risks, resiliency, and policy Kiley Morgart, Joyce Nolan Harrison, Alexander H Hoon Jr, Anna Maria Wilms Floet

Review Dev Med Child Neurol. 2021 May 3. doi: 10.1111/dmcn.14911. Online ahead of print.

Thanks to the seminal work of Robert Anda and Vincent Felitti, it is now widely accepted that adverse childhood experiences (ACEs) can have lifelong effects on physical, behavioral, and mental health and that many adult diseases can be considered developmental disorders that began early in life. Genomics has advanced the neurobiological understanding that underpins ACEs, wellness, and disease, which are modulated through stress pathways and epigenetic modifications. While data are currently limited, children with developmental disabilities have an increased ACE risk compared to typically developing peers. This recognition has important ramifications for health and policy interventions that address the root causes of ACEs, especially in this vulnerable population. With increased societal recognition, advances in policy will lead to medical, financial, and public benefits in years to come, hopefully changing healthcare models from 'sick care' to 'well care'.

PMID: <u>33938573</u>

26. Considerable mortality and morbidity in neonates born below 500 gram

Katharina Goeral, Renate Fuiko, Julia Binder, Claudia Lindtner, Raphaela Jernej, Judith Rittenschober-Boehm, Katrin Klebermass-Schrehof, Angelika Berger, Agnes Grill

Acta Paediatr. 2021 May 6. doi: 10.1111/apa.15885. Online ahead of print.

Aim: Data evaluating mortality and morbidity in infants born \leq 500g is scarce and shows wide variability. To support counselling and decision-making, we analysed neurodevelopmental outcome in all neonates \leq 500g birth weight. Methods: Retrospective analysis including preterm infants with a birth weight \leq 500g and a gestational age >22 weeks born at a single tertiary perinatal centre between 2010 and 2017. Results: Of 59 live births 88% received standard care. Birth weight ranged from 318 and 500g and gestational age from 23 and 29 weeks. 56% of neonates were born \leq 3rd percentile and 42% of treated infants survived. Neurodevelopmental outcome was available in 91% of patients and was evaluated using Bayley Scales of Infant Development at two years. 50% showed a favourable mental development (normal or mild impairment), 75% a favourable motor development and 45% a favourable outcome in both outcome subcategories. When additionally considering visual and hearing disability and, or, cerebral palsy level \geq 2 according to the Gross Motor Function Classification System 35% had a good neurodevelopmental outcome. Conclusion: Survival rate was 37% for all live births and 42% for infants with standard care. More than one-third of survivors showed no significant neurodevelopmental impairment at two years.

PMID: <u>33955057</u>

27. A Decision-Tree Approach to Assist in Forecasting the Outcomes of the Neonatal Brain Injury Bogdan Mihai Neamțu, Gabriela Visa, Ionela Maniu, Maria Livia Ognean, Rubén Pérez-Elvira, Andrei Dragomir, Maria Agudo, Ciprian Radu Șofariu, Mihaela Gheonea, Antoniu Pitic, Remus Brad, Claudiu Matei, Minodora Teodoru, Ciprian Băcilă

Int J Environ Res Public Health. 2021 Apr 30;18(9):4807. doi: 10.3390/ijerph18094807.

Neonatal brain injury or neonatal encephalopathy (NE) is a significant morbidity and mortality factor in preterm and full-term newborns. NE has an incidence in the range of 2.5 to 3.5 per 1000 live births carrying a considerable burden for neurological outcomes such as epilepsy, cerebral palsy, cognitive impairments, and hydrocephaly. Many scoring systems based on different risk factor combinations in regression models have been proposed to predict abnormal outcomes. Birthweight, gestational age, Apgar scores, pH, ultrasound and MRI biomarkers, seizures onset, EEG pattern, and seizure duration were the most referred

predictors in the literature. Our study proposes a decision-tree approach based on clinical risk factors for abnormal outcomes in newborns with the neurological syndrome to assist in neonatal encephalopathy prognosis as a complementary tool to the acknowledged scoring systems. We retrospectively studied 188 newborns with associated encephalopathy and seizures in the perinatal period. Etiology and abnormal outcomes were assessed through correlations with the risk factors. We computed mean, median, odds ratios values for birth weight, gestational age, 1-min Apgar Score, 5-min Apgar score, seizures onset, and seizures duration monitoring, applying standard statistical methods first. Subsequently, CART (classification and regression trees) and cluster analysis were employed, further adjusting the medians. Out of 188 cases, 84 were associated to abnormal outcomes. The hierarchy on etiology frequencies was dominated by cerebrovascular impairments, metabolic anomalies, and infections. Both preterms and full-terms at risk were bundled in specific categories defined as high-risk 75-100%, intermediate risk 52.9%, and low risk 0-25% after CART algorithm implementation. Cluster analysis illustrated the median values, profiling at a glance the preterm model in high-risk groups and a full-term model in the inter-mediate-risk category. Our study illustrates that, in addition to standard statistics methodologies, decision-tree approaches could provide a first-step tool for the prognosis of the abnormal outcome in newborns with encephalopathy.

PMID: 33946326

28. The visibility of the periventricular crossroads of pathways in preterm infants as a predictor of neurological outcome and occurrence of neonatal epileptic seizures

Branka Bunoza, Barišić Nina, Petra Grdan Števanović, Ana Bogdanić, Vesna Benjak, Ruža Grizelj, Daniel Turudić, Danko Milošević, Marko Radoš

Croat Med J. 2021 Apr 30;62(2):165-172.

Aim: To evaluate the relationship between the neurological outcome, neonatal epileptic seizures, and signal-intensity visibility of the frontal and parietal periventricular crossroads of pathways on brain magnetic resonance imaging (MRI) in preterm infants at term-equivalent age. Methods: The study enrolled 48 preterm infants born between 2012 and 2016. The signal-intensity characteristics of the frontal and parietal periventricular crossroads were evaluated and classified into four grades. A non-favorable outcome was defined as a motor and functional disorder with developmental delay and/or cerebral palsy. Results: Neonatal seizures, epilepsy, pathological EEG and brain ultrasound finding, and brain MRI abnormalities were mostly found in neonates with non-favorable outcomes. Visible frontal and parietal periventricular crossroads were associated with a normal neurologic outcome (P=0.0004; P=0.0009, respectively). Not-visible or slightly visible periventricular crossroads were associated with a normal neurologic outcomes in the case of frontal crossroads (P=0.036) and not-visible periventricular crossroads in the case of both frontal and parietal crossroads (P=0.001, P=0.015, respectively). The visibility of the frontal and parietal periventricular crossroads were more frequently slightly visible, while the parietal periventricular crossroads were more frequently visible. Conclusion: Poor visibility of the frontal and parietal crossroads of pathways on MRI is associated with neonatal epileptic seizures and poor neurological outcomes in preterm infants at term-equivalent age.

PMID: 33938656

29. Focal Ischemic Injury to the Early Neonatal Rat Brain Models Cognitive and Motor Deficits with Associated Histopathological Outcomes Relevant to Human Neonatal Brain Injury Brett J Kagan, Charlotte M Ermine, Stefano Frausin, Clare L Parish, Jess Nithianantharajah, Lachlan H Thompson

Int J Mol Sci. 2021 Apr 29;22(9):4740. doi: 10.3390/ijms22094740.

Neonatal arterial ischemic stroke is one of the more severe birth complications. The injury can result in extensive neurological damage and is robustly associated with later diagnoses of cerebral palsy (CP). An important part of efforts to develop new therapies include the on-going refinement and understanding of animal models that capture relevant clinical features of neonatal brain injury leading to CP. The potent vasoconstrictor peptide, Endothelin-1 (ET-1), has previously been utilised in animal models to reduce local blood flow to levels that mimic ischemic stroke. Our previous work in this area has shown that it is an effective and technically simple approach for modelling ischemic injury at very early neonatal ages, resulting in stable deficits in motor function. Here, we aimed to extend this model to also examine the impact on cognitive function. We show that focal delivery of ET-1 to the cortex of Sprague Dawley rats on postnatal day 0 (P0) resulted in impaired learning in a touchscreen-based test of visual discrimination and correlated with important clinical features of CP including damage to large white matter structures.

PMID: 33947043

30. Tertiary cystic white matter injury as a potential phenomenon after hypoxia-ischaemia in preterm f sheep Benjamin A Lear, Christopher A Lear, Joanne O Davidson, Jialin Sae-Jiw, Johanna M Lloyd, Alistair J Gunn, Laura Bennet

Brain Commun. 2021 Mar 9;3(2):fcab024. doi: 10.1093/braincomms/fcab024. eCollection 2021.

White matter injury, including both diffuse and cystic elements, remains highly associated with neurodevelopmental disability and cerebral palsy in preterm infants, yet its pathogenesis and evolution are still poorly understood and there is no established treatment. We examined the long-term evolution of white matter injury in chronically instrumented preterm fetal sheep (0.7 gestation) after 25 min of complete umbilical cord occlusion or sham occlusion. Fetal brains were processed for histology after $\overline{3}$ days (n = 9, sham n = 9), 7 days (n = 8, sham n = 8), 14 days (n = 9, sham n = 8) and 21 days (n = 9, sham n = 9) of recovery. At 3 and 7 days recovery, umbilical cord occlusion was associated with diffuse white matter injury, with loss of total and mature oligodendrocytes and reduced myelination in both the parietal and temporal lobes. At 14 days after umbilical cord occlusion, extensive microglial and astrocytic activation were observed in the temporal lobe. At 21 days recovery a spectrum of severe white matter degeneration was observed, including white matter atrophy, ventriculomegaly and overt cystic white matter lesions. The most severe injury was observed in the temporal lobe after 21 days recovery, including the majority of cystic lesions, persistent oligodendrocyte maturational arrest and impaired myelination. The spatial distribution of delayed white matter degeneration at 21 days recovery was closely related to the location of dense microglial aggregates at earlier timepoints, implicating a role for exuberant inflammation originating from microglial aggregates in the pathogenesis of cystic white matter injury. The delayed appearance of cystic injury is consistent with continuing tertiary evolution of necrotic cell death. This slow evolution raises the tantalizing possibility that there may a relatively long therapeutic window to mitigate the development of cystic white matter injury. Delayed anti-inflammatory treatments may therefore represent a promising strategy to reduce neurodevelopmental disability in the preterm infants.

PMID: 33937767

31. Birth outcomes affecting infants of mothers with intellectual and developmental disabilities Eric Rubenstein, Deborah B Ehrenthal, David C Mallinson, Lauren Bishop, Hsiang-Hui Kuo, Maureen S Durkin

Paediatr Perinat Epidemiol. 2021 May 6. doi: 10.1111/ppe.12765. Online ahead of print.

Background: Women with intellectual and developmental disabilities (IDD) face increased risk of adverse maternal pregnancy outcomes, yet less is known about infant outcomes. Objectives: To examine birth outcomes of infants born to mothers with IDD and assess associations with demographics and IDD-type. Methods: We used data from the Big Data for Little Kids project, which links Wisconsin birth records to Medicaid claims for live births covered by Medicaid from 2007 to 2016. We identified IDD using maternal prepregnancy Medicaid claims and ran Poisson regression (with a log link function) with robust variance clustered by mother to compare prevalence of outcomes between singleton births with and without mothers with IDD. We adjusted the associations for demographic factors and estimated prevalence ratios (PR) as the effect measure. We assessed outcomes by IDD-type (intellectual disability, genetic conditions, cerebral palsy, and autism spectrum disorder) to explore differences by categories of IDD. Results: Of 267,395 infants, 1696 (0.6%) had mothers with IDD. A greater percentage of infants with mothers with IDD were born preterm (12.8% vs 7.8%; PR 1.64, 95% confidence interval [CI] 1.42, 1.89), small for gestational age (8.5% vs 5.4%; PR 1.42, 95% CI 1.25, 1.61), and died within 12 months of birth (3.2% vs 0.7%; PR 4.93, 95% CI 3.73, 6.43) compared to infants of mothers with IDD. Prevalence ratios were robust to adjustment for demographics factors. Estimates did not meaningfully differ when comparing different IDD-types. Conclusions: A greater porportion of poor infant outcomes was greater for mothers with IDD even after accounting for demographic differences. It is imperative to understand why infants of mothers with IDD are at greater risk so interventions and management can be developed.

PMID: 33956997

32. Physical Performance Differences Between Spanish Selected and Nonselected Para-Footballers With Cerebral Palsy for the National Team

Iván Peña-González, José M Sarabia, Alba Roldan, Agustín Manresa-Rocamora, Manuel Moya-Ramón

Int J Sports Physiol Perform. 2021 May 5;1-8. doi: 10.1123/ijspp.2020-0842. Online ahead of print.

In regular football, the players' selection process involves an objective assessment based on their anthropometric and physical performance. However, available literature focused on players' selection process in cerebral palsy (CP) football is scarce. Purpose: To describe the anthropometrical and physical performance profiles of the International Spanish CP footballers and to compare them with the remaining CP football players from the national competition. Method: A total of 75 CP football players from the Spanish CP Football National Competition (classified into the 3 existing classes: football class [FT] 1 = 38; FT2 = 29; FT3 = 8) participated in the study. Participants were divided into 2 groups: selected players (n = 15) and nonselected players (n = 60) for the national team. Anthropometrical data and physical performance (countermovement jump, 20-m sprint, modified agility T-test [MAT], and dribbling test) were collected. Results: There were significant differences in the 20-m sprint, MAT, and dribbling for the total sample and in MAT and dribbling for FT2 and FT3 classes between selected players and nonselected players (P < .05), but there were no differences for FT1. The MAT and dribbling showed a positive correlation and a high percentage of player selection process, as they allow the evaluation of important aspects of the game, but they may also provide the technical staff with an idea of the functionality and the physical performance of the players in each sport class.

PMID: <u>33952712</u>

33. Quality of Life and Associated Factors Among Male Wheelchair Handball Athletes

David Dos Santos Calheiros, Jorge Lopes Cavalcante Neto, Flávio Anderson Pedrosa de Melo, Fábio Ítalo Pedrosa de Melo, Mey de Abreu van Munster

Percept Mot Skills. 2021 May 3;315125211014865. doi: 10.1177/00315125211014865. Online ahead of print.

Although scarce, some recent studies have observed good self-reported quality of life (QOL) among wheelchair users who are involved in adapted sports. These findings have encouraged further investigations, particularly investigations of combined sociodemographic and sport factors in the study of QOL. In this study we analyzed the association between sociodemographic and sport factors with QOL in a cross-sectional study of 105 male wheelchair handball (WH) athletes with higher and lower QOL. We used the World Health Organization Quality of Life - BREF (WHOQOL-BREF) scale to evaluate the respondents QOL; and we used a sociodemographic questionnaire to evaluate associated sociodemographic and sport factors. A logistic regression analysis found these athletes' good QOL to be generally characterized by stable marital status, disability due to cerebral palsy, the use of locomotion/mobility resources, full independence, bi-weekly training, and the use of a custom-made wheelchair for around 70% of their daily living activities. These findings reveal the important issues to be considered in the sport factors in determining QOL among these WH respondents. These findings reveal the important issues to be considered in the sport modality when attempting to improve the QOL and functionality of these participants and perhaps WH athletes worldwide.

PMID: 33940990

Prevention and Cure

34. Neuroprotective effect of helium after neonatal hypoxic ischemia: a narrative review Ru-Ming Deng, Hai-Ying Li, Xiang Li, Hai-Tao Shen, De-Gang Wu, Zhong Wang, Gang Chen

Review Med Gas Res. Jul-Sep 2021;11(3):121-123. doi: 10.4103/2045-9912.314332.

Neonatal hypoxic ischemia is one of the leading causes of permanent morbidity and mortality in newborns, which is caused by difficulty in supplying blood and oxygen to brain tissue and is often associated with epilepsy, cerebral palsy, death, short-term or long-term neurological and cognitive impairment. In recent years, the clinical therapeutic effects of noble gases have been

gradually discovered and recognized. Numerous studies have shown that noble gases have unique neuroprotective effects to restore damaged nerve and relieve symptoms in patients. Although research on the neuroprotective mechanisms of xenon and argon has yielded a lot of results, studies on helium have stalled. Helium is a colorless, odorless, monoatomic inert gas. The helium has no hemodynamic or neurocognitive side effects and can be used as an ideal pre-adaptor for future clinical applications. In recent years, studies have shown that heliox (a mixture of helium and oxygen) pretreatment can protect the heart, brain, liver and intestine from damage in several animal models, where a variety of signaling pathways have been proved to be involved. There are numerous studies on it even though the mechanism of helium for protecting newborns has not been fully elucidated. It is urgent to find an effective treatment due to the high death rate and disability rate of neonatal hypoxic ischemia. It is believed that helium will be approved safely and effectively for clinical use in the near future.

PMID: 33942783