Cerebral palsy research news

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Interventions and Management

1. Combined Selective Dorsal Rhizotomy and Single-Event Multilevel Surgery in a Child with Spastic Diplegic Cerebral Palsy: A Case Report
Kayli Gimarc, Suzanne Yandow, Samuel Browd, Connie Leibow, Kelly Pham

Case Reports Pediatr Neurosurg. 2021 Aug 12;1-6. doi: 10.1159/000517756. Online ahead of print.

Introduction: Children with spastic diplegic cerebral palsy (CP) often have functional and gait impairments related to spasticity and loss of range of motion (ROM). Selective dorsal rhizotomy (SDR) and single-event multilevel surgery (SEMLS) are surgical interventions that are used to manage spasticity and functional gait impairments, respectively. This is the first known case report of a child with spastic diplegic CP who underwent combined SDR and SEMLS. Case report: Our patient is a 7-year-old girl with spastic diplegic CP, functioning at the Gross Motor Function Classification System (GMFCS) level II, who presented with spasticity and contractures in bilateral lower extremities leading to functional gait impairments, despite conservative management. Combined SDR/SEMLS was offered with the goal of simultaneously managing spasticity and contractures while reducing the need for multiple procedures. Postoperatively, the patient's functional mobility, ROM, spasticity, and strength were assessed at various follow-up intervals. The patient had increased lower extremity weakness and functional decline postoperatively. Persistent genu recurvatum and knee instability required prolonged rehabilitation services, and she demonstrated functional gains with these interventions. At follow-ups, spasticity was resolved and ROM improved. By the 12-month follow-up, the Gross Motor Function Measure-66 was improved to 68.9 (55th percentile) from the preoperative level of 62.1 (35th percentile). By the 30-month follow-up, she was able to participate in novel recreational activities. Discussion/conclusion: Multidisciplinary teams may consider combined SDR/SEMLS for management of spasticity, gait impairment, and contracture in carefully selected patients with spastic CP.

PMID: 34384084

2. The effectiveness of adding guided growth to soft tissue release in treating spastic hip displacement
Huan Sheu, Wei C Lee, Hsuan K Kao, Wen E Yang, Chia H Chang

J Orthop Sci. 2021 Aug 3;S0949-2658(21)00216-5. doi: 10.1016/j.jos.2021.06.019. Online ahead of print.

Background: Guided growth at the proximal femur using one transphyseal screw corrects coxa valga and improves hip displacement in cerebral palsy. This study aimed to validate the effects of adding guided growth (GG) to soft tissue release (STR), in terms of decreasing the migration percentage (MP), compared to those with soft tissue alone. Methods: This retrospective study comprised patients with cerebral palsy who underwent soft tissue release alone (Group STR) or soft tissue release plus guided growth (Group GG) for hip displacement (mean age, 8.1 years; mean follow-up, 4.9 years). Difference in the MP and rate of controlling MP <40% at 2 years postoperatively and rate of revision surgeries at 5 years postoperatively

were compared between the groups. Results: The two groups were comparable in age, side, and gross motor function level, but Group GG (n = 24) had more severe hip displacement preoperatively than did Group STR (n = 64). Group GG had a significantly greater 2-year decrease in the MP (-14.8% vs. -11.8%, p < 0.05) than did Group STR. Among patients with a pre-operative MP >50%, the rate of MP <40% was greater in Group GG (73%) than in Group STR (41%). Revision surgeries, mainly repeated guided growth and soft tissue release, were comparable between the groups. Conclusions: This is the first comparative study to support adding guided growth to soft tissue release, as it results in greater improvements in hip displacement than that with soft tissue release alone. Non-ambulatory patients or severe hip displacement with MP 50%-70% could benefit from this less aggressive surgery by controlling the MP under 40% without femoral osteotomy.

PMID: 34362633

3. Functional and Clinical Outcomes of Combined Simultaneous Bilateral Anterior Distal Femoral Plate Hemiepiphysiodesis and Hamstrings Release in Management of Knee Flexion Contractures in Children With Neuromuscular Disorders
Ahmed Zaghloul, Dimitrios Manoukian, Matthew C Barrett, Ilektra Geronta, Claudia Maizen

J Pediatr Orthop. 2021 Aug 12. doi: 10.1097/BPO.0000000000001942. Online ahead of print.

Background: We examined the clinical and functional outcomes of the simultaneous anterior distal femoral 8-plate hemiepiphysiodesis (ADF8PH) and hamstring release, for fixed knee flexion deformity in children with neuromuscular disease. To our knowledge, no published evidence is available that reports the outcomes of this combined techniques. Methods: Electronic medical records were retrospectively reviewed for 19 consecutive children who underwent bilateral ADF8PH and concomitant hamstrings release in our institution from 2012 to 2019. Relevant demographics, Gross Motor Functional Classification Score and preoperative and postoperative knee flexion contractures and popliteal angles were documented. Results: The average age at the time of operation was 12±2.1 years. There were 15 males and 4 females. Diagnoses included cerebral palsy (n=16), Cornelia de Lange syndrome (n=1), hereditary spastic paraplegia type 56 (n=1) and fructose-1,6 bisphosphonate aldose B deficiency (n=1). Mean length of follow-up was 3.8 years (range: 1.5 to 7 y). Mean fixed knee flexion deformity improved from 28.9 to 13.4 degrees (P<0.001) at an average correction rate of 0.94 degrees per month. Mean popliteal angle improved from 81.8 to 44.4 degrees (P<0.001) in the early postoperative phase and to 51.8 degrees (P<0.001) in latest clinic review. Mean time to correction was 18.9 months. The agreed treatment goals of maintaining or promoting the use of standing frame and spinal/postural symmetry was attained in 18 patients (94.7%). Postoperative knee pain was reported in 2 cases (10.5%). We report 2 complications; 1 case of neurapraxia and 1 case of sepsis because of respiratory infection. Conclusion: Simultaneous bilateral ADF8PH with hamstrings release is a promising effective technique for correction of knee flexion contractures in skeletally immature individuals with neuromuscular disabilities. Our findings demonstrate improvement in clinical outcomes and maintaining functional outcomes, indicating the validity of this approach as a satisfactory, less invasive alternative in the management of this deformity. Level of evidence: Level IV-therapeutic study.

PMID: 34387232

4. Evaluation of factors affecting external tibial torsion in patients with cerebral palsy
Jae Jung Min, Soon-Sun Kwon, Kyu Tae Kim, Young Choi, Ki Hyuk Sung, Kyoung Min Lee, Moon Seok Park

BMC Musculoskelet Disord. 2021 Aug 12;22(1):684. doi: 10.1186/s12891-021-04570-5.

Background: Gait deviation and associated torsional problems are common in patients with cerebral palsy (CP). Although femoral anteversion in CP has been extensively reviewed in previous studies, only a few studies have focused on tibial torsion. Therefore, this study aimed to evaluate tibial torsion in patients with CP and investigate the affecting factors. Methods: Consecutive patients with cerebral palsy who underwent 3-dimensional computed tomography for the assessment of rotational profiles were reviewed. Femoral anteversion and tibial torsion were measured, and the demographic characteristics of the patients were recorded. A linear mixed model was implemented to overcome the retrospective nature of the study. Results: After the implementation of inclusion and exclusion criteria, 472 patients were enrolled for this study. With age, external tibial torsion increased, while femoral anteversion decreased. The factors affecting external tibial torsion were increased femoral anteversion (p = 0.0057), increased age (p < 0.0001), higher Gross Motor Function Classification System (GMFCS) level (p < 0.0001), and involved/uninvolved limbs of hemiplegia (p = 0.0471/p = 0.0047). Conclusions: Older age, GMFCS level IV/V, hemiplegia, and increased femoral anteversion were the independent risk factors of increased external tibial torsion; therefore, performing an imaging study is recommended for assessing the extent of tibial torsion in patients with such characteristics.

PMID: 34384415

5. The Contribution of Decreased Muscle Size to Muscle Weakness in Children With Spastic Cerebral Palsy
Britta Hanssen, Nicky Peeters, Ines Vandekerckhove, Nathalie De Beukelaer, Lynn Bar-On, Guy Molenaers, Anja Van Campenhout, Marc Degelaen, Christine Van den Broeck, Patrick Calders, Kaat Desloovere

Front Neurol. 2021 Jul 26;12:692582. doi: 10.3389/fneur.2021.692582. eCollection 2021.

Muscle weakness is a common clinical symptom in children with spastic cerebral palsy (SCP). It is caused by impaired neural ability and altered intrinsic capacity of the muscles. To define the contribution of decreased muscle size to muscle weakness, two cohorts were recruited in this cross-sectional investigation: 53 children with SCP [median age, 8.2 (IQR, 4.1) years, 19/34 uni/bilateral] and 31 children with a typical development (TD) [median age, 9.7 (IQR, 2.9) years]. Muscle volume (MV) and muscle belly length for m. rectus femoris, semitendinosus, gastrocnemius medialis, and tibialis anterior were defined from three-dimensional freehand ultrasound acquisitions. A fixed dynamometer was used to assess maximal voluntary isometric contractions for knee extension, knee flexion, plantar flexion, and dorsiflexion from which maximal joint torque (MJT) was calculated. Selective motor control (SMC) was assessed on a 5-point scale for the children with SCP. First, the anthropometrics, strength, and muscle size parameters were compared between the cohorts. Significant differences for all muscle size and strength parameters were found ($p \leq 0.003$), except for joint torque per MV for the plantar flexors. Secondly, the associations of anthropometrics, muscle size, gross motor function classification system (GMFCS) level, and SMC with MJT were investigated using univariate and stepwise multiple linear regressions. The associations of MJT with growth-related parameters like age, weight, and height appeared strongest in the TD cohort, whereas for the SCP cohort, these associations were accompanied by associations with SMC and GMFCS. The stepwise regression models resulted in ranges of explained variance in MJT from 29.3 to 66.3% in the TD cohort and from 16.8 to 60.1% in the SCP cohort. Finally, the MJT deficit observed in the SCP cohort was further investigated using the TD regression equations to estimate norm MJT based on height and potential MJT based on MV. From the total MJT deficit, 22.6-57.3% could be explained by deficits in MV. This investigation confirmed the disproportional decrease in muscle size and muscle strength around the knee and ankle joint in children with SCP, but also highlighted the large variability in the contribution of muscle size to muscle weakness.

PMID: 34381414

6. Acute responses to locomotor tasks differ according to gait-asymmetry patterns in children with hemiplegic cerebral palsy: An exploratory analysis
Ragab K Elnaggar

Hum Mov Sci. 2021 Aug 9;79:102860. doi: 10.1016/j.humov.2021.102860. Online ahead of print.

This study aimed at determining if differential responses to locomotor tasks in children with spastic hemiplegia occur on account of step-length asymmetry patterns [symmetrical step-length (S-SL); affected side short (AFFshort), and non-affected short (Non-AFFshort)] observed during on-ground walking. Thirty-two children (5-8 years) were assessed for spatial/temporal measures of gait while walking on the ground with self-selected speed. Data from on-ground walking were compared against three locomotor tasks that were examined on a treadmill: self-imposed walking velocity with bodyweight support of 0% (BWS-0%), self-imposed walking velocity with a BWS of 20% (BWS-20%), and fastest walking velocity with a BWS of 20% and a manually-guided response of the non-affected leg (MGRnon-affected). The primary outcome measures were the spatial (step length) and temporal (single-limb support time) symmetry indices. The step-length asymmetry subgroups responded differently to the locomotor tasks. The MGRnon-affected produced spatial symmetry in the S-SL and Non-AFFshort groups and temporal symmetry in the AFFshort group. The BWS-0% and BWS-20% treadmill walking conditions were insufficient to remediate either spatial or temporal walking asymmetry. In conclusion, acute responses to locomotor tasks are not consistent among asymmetry subgroups, suggesting that they might need individual treatment plans. In spite of the differences in walking characteristics between asymmetry subgroups, the improvement in gait-symmetry arose out of changes in affected and non-affected sides together.

PMID: 34385053

7. Is botulinum toxin type A more effective and safer than other treatments for the management of lower limb spasticity in children with cerebral palsy? A Cochrane Review summary with commentary
Heakyung Kim, Kat Kolaski

NeuroRehabilitation. 2021 Aug 2. doi: 10.3233/NRE-218003. Online ahead of print.

Background: Botulinum toxin A (BoNT-A) is a well-accepted treatment for the medical management of spasticity in children with cerebral palsy (CP). Objective: To assess the efficacy and safety of BoNT-A compared with other treatment options in managing lower limb spasticity in children with CP. Methods: A summary of the Cochrane Review update by Blumetti et al. (2019), with comments. Results: This review included 31 randomized controlled trials (1508 participants). Compared with usual care/physiotherapy, the evidence is very uncertain about the effect of BoNT-A on gait, function, ankle joint range of motion (ROM), satisfaction, and ankle spasticity in children with CP. Compared with placebo/sham, BoNT-A probably benefits these same outcomes, although the results for function are contradictory. BoNT-A may not be more effective than serial casting at improving gait, function, ankle ROM and spasticity at any time point. However, it may be more effective than an orthosis at medium-term follow-up for hip ROM and adductor spasticity, but not function. The rate of adverse events with BoNT-A is similar to placebo/sham and serial casting. Conclusions: Evidence for the effectiveness and safety of BoNT-A for the management of lower limb spasticity in children with CP is uncertain, with better quality evidence available from studies of placebo/sham than non-placebo controls. To produce high-quality evidence, future studies need to improve their methodological quality and increase sample sizes.

PMID: 34366300

8. Assessment of Swallowing Disorders, Nutritional and Hydration Status, and Oral Hygiene in Students with Severe Neurological Disabilities Including Cerebral Palsy
Alicia Costa, Alberto Martin, Viridiana Arreola, Stephanie A Riera, Ana Pizarro, Cristina Carol, Laia Serras, Pere Clavé

Nutrients. 2021 Jul 14;13(7):2413. doi: 10.3390/nu13072413.

Background: Special needs schools (SNS) educate children and young people with major neurological disabilities who are at high risk of oropharyngeal dysphagia (OD) and malnutrition (MN). We aimed to assess the prevalence of OD, MN, dehydration (DH), and oral health (OH) in students at an SNS. Methods: A cross-sectional observational study was conducted at SNS L'Arboç, Catalonia, Spain. We assessed (a) demographics, health status, comorbidities, and gross motor function classification system (GMFCS), (b) swallowing function, oral-motor evaluation, masticatory capacity, and EDACS classification for eating and drinking abilities, (c) nutritional and DH status (anthropometry, bioimpedance and dietary records), and (d) OH (Oral Hygiene Index Simplified). Results: A total of 33 students (mean age 13.3 years; 39.4% level V of GMFCS) were included. Main diagnosis was cerebral palsy at 57.6%. All students presented OD, 90.6% had impaired safety, 68.7% were at levels II-III of EDACS, and 31.3% required PEG; furthermore, 89.3% had chronic MN, 21.4% had acute MN, 70% presented intracellular DH, and 83.9% presented impaired OH. Conclusion: MN, DH, OD, and poor OH are highly prevalent conditions in students with cerebral palsy and other neurological disabilities and must be specifically managed through nutritional and educational strategies. The multidisciplinary team at SNS should include healthcare professionals specifically trained in these conditions.

PMID: 34371923

9. Musculoskeletal Health in Active Ambulatory Men with Cerebral Palsy and the Impact of Vitamin D
Christina Kate Langley, Gladys Leopoldine Onambélé-Pearson, David Thomas Sims, Ayser Hussain, Aidan John Buffey, Holly Leigh Bardwell, Christopher Ian Morse

Nutrients. 2021 Jul 20;13(7):2481. doi: 10.3390/nu13072481.

Purpose: (1) To determine the contribution of diet, time spent outdoors, and habitual physical activity (PA) on vitamin D status in men with cerebral palsy (CP) compared to physical activity matched controls (TDC) without neurological impairment; (2) to determine the role of vitamin D on musculoskeletal health, morphology, and function in men with CP compared to TDC. Materials and methods: A cross-sectional comparison study where 24 active, ambulant men with CP aged 21.0 ± 1.4 years

(Gross Motor Function Classification Score (I-II) and 24 healthy TDC aged 25.3 ± 3.1 years completed in vivo assessment of musculoskeletal health, including: vastus lateralis anatomical cross-sectional area (VL ACSA), isometric knee extension maximal voluntary contraction (KE iMVC), 10 m sprint, vertical jumps (VJ), and radius and tibia bone ultrasound (US) Tus and Zus scores. Assessments of vitamin D status through venous samples of serum 25-hydroxyvitamin D (25(OH)D) and parathyroid hormone, dietary vitamin D intake from food diary, and total sun exposure via questionnaire were also taken. Results: Men with CP had 40.5% weaker KE iMVC, 23.7% smaller VL ACSA, 22.2% lower VJ, 14.6% lower KE iMVC/VL ACSA ratio, 22.4% lower KE iMVC/body mass (BM) ratio, and 25.1% lower KE iMVC/lean body mass (LBM) ratio (all $p < 0.05$). Radius Tus and Zus scores were 1.75 and 1.57 standard deviations lower than TDC, respectively ($p < 0.05$), whereas neither tibia Tus nor Zus scores showed any difference compared to TDC ($p > 0.05$). The 25(OH)D was not different between groups, and 90.9% of men with CP and 91.7% of TDC had low 25(OH)D levels when compared to current UK recommendations. The 25(OH)D was positively associated with KE iMVC/LBM ratio in men with CP ($r = 0.500$, $p = 0.020$) but not in TDC ($r = 0.281$, $p = 0.104$). Conclusion: Musculoskeletal outcomes in men with CP were lower than TDC, and despite there being no difference in levels of 25(OH)D between the groups, 25 (OH)D was associated with strength (KE iMVC/LBM) in the CP group but not TDC. The findings suggest that vitamin D deficiency can accentuate some of the condition-specific impairments to musculoskeletal outcomes.

PMID: 34371988

10. Effectiveness and Determinant Variables of Augmentative and Alternative Communication Interventions in Cerebral Palsy Patients with Communication Deficit: a Systematic Review
Armenuhi Avagyan, Hasmik Mkrtchyan, Fatemeh Alsadat Shafa, Joan Alexandra Mathew, Tigran Petrosyan

Meta-Analysis Codas. 2021 Aug 4;33(5):e20200244. doi: 10.1590/2317-1782/20202020244. eCollection 2021.

Purpose: Assess the effectiveness of augmentative and alternative communication (AAC) interventions in patients with CP and to reveal determinant variables of main intervention outcomes: receptive and expressive language. Research strategies: The search was performed in following databases: MEDLINE (Ovid); PubMed (NLM); Embase (Ovid); Cochrane Database of Systematic Reviews; Cumulative Index to Nursing and Allied Health Literature; Database of Abstracts of Reviews of Effects; Cochrane Central Register of Controlled Trials; Health Technology Assessment database and PEDro. Selection criteria: Full-text and peer-reviewed studies in English studying the effectiveness of AAC in patients with cerebral palsy were included. Studies with patients (<18 years) diagnosed with CP were included. Data analysis: A narrative analysis was conducted to evaluate the efficacy of AAC methods. A random-effects model meta-analysis was used to assess determinants of AAC intervention outcomes. Results: The online database and manual reference search revealed 445 records. Nine studies investigating a total of 294 subjects with CP met predefined eligibility criteria: 4 studies with single subject, multiple baseline research designs, 3 longitudinal cohort studies, 1 case control study and 1 case series. Results revealed moderate-quality evidence that AAC interventions improve the receptive and expressive communication skills in patients with CP. The random-effects model meta-analysis revealed the power of identified determinant variables affecting the AAC intervention outcomes. Conclusion: Diversity of CP patients requires proper analysis of determinant variables to ensure the efficacy of AAC assessment and intervention. More studies of high methodological and practical quality assessing the efficacy of AAC interventions are needed to clarify the evidence.

PMID: 34378726

11. Exergaming improves balance in children with spastic cerebral palsy with low balance performance: results from a multicenter controlled trial
Pieter Meyns, Ian Blanckaert, Chloé Bras, Nina Jacobs, Jaap Harlaar, Laura van de Pol, Frank Plasschaert, Hilde Van Waelvelde, Annemieke I Buizer

Disabil Rehabil. 2021 Aug 9;1-10. doi: 10.1080/09638288.2021.1954704. Online ahead of print.

Purpose: Previous studies investigating the effectiveness of exergame balance-training (using video-games) in children with cerebral palsy (CP) yielded inconsistent results that could be related to underpowered studies. Therefore, in this multicenter intervention study, we investigated whether exergaming improves balance clinically in spastic CP. Materials and methods: In total, 35 children with unilateral or bilateral spastic CP (GMFCS-level I-II) were included (age-range: 7-16 years); 16 at VUMC (trial: NTR6034), 19 at UHG (trial: NCT03219112). All participants received care as usual. The intervention group (n = 24) additionally performed exergame-training; 6-8 weeks home-based X-box One Kinect training focused on balance.

Balance performance was assessed with the pediatric balance scale (PBS) and two subscales of the Bruininks-Oseretsky Test of Motor Proficiency-2nd edition ("balance" [BOTbal] and "running speed and agility" [BOTrsa]). Mixed model ANOVAs with between and within factors were used to test differences between and within groups. Results: On group level, no post-intervention differences were found between the intervention and control group (PBS: $p = 0.248$, $\eta p2 = 0.040$; BOTbal: $p = 0.374$, $\eta p2 = 0.024$; BOTrsa: $p = 0.841$, $\eta p2 = 0.001$). Distribution of CP-symptoms (unilateral versus bilateral) did not affect training (PBS: $p = 0.373$, $\eta p2 = 0.036$; BOTbal: $p = 0.127$, $\eta p2 = 0.103$; BOTrsa: $p = 0.474$, $\eta p2 = 0.024$). Children with low baseline balance performance (based on PBS) in the intervention group showed improvements in balance performance after training (PBS: $p = 0.003$, $\eta p2 = 0.304$; BOTbal: $p = 0.008$, $\eta p2 = 0.258$), whereas children with high baseline balance performance did not. Conclusions: This exergame-training resulted in balance improvements for the current population of CP that had a low baseline function. IMPLICATIONS FOR REHABILITATION: Exergame-training (training using video-games) shows mixed results in children with cerebral palsy (CP).Children with spastic CP (GMFCS level I-II) with a high baseline balance-level did not show functional balance improvements after this home-based exergame-training, suggesting that these children should not be enrolled in this type of exergame-training protocol. Children with spastic CP (GMFCS level I-II) with a low baseline balance-level showed clinically relevant functional balance improvements after this home-based exergame-training, suggesting that these children can benefit from enrolment in this type of exergame-training protocol to improve their balance. The distribution of CP-symptoms did not affect the effectiveness of this balance exergame-training in children with spastic CP with GMFCS-level I and II.

PMID: 34365883

12. Virtual Reality Intervention to Help Improve Motor Function in Patients Undergoing Rehabilitation for Cerebral Palsy, Parkinson's Disease, or Stroke: A Systematic Review of Randomized Controlled Trials
Jashvini Amirthalingam, Gokul Paidi, Khadija Alshowaikh, Anuruddhika Iroshani Jayarathna, Divya Bala Anthony Manisha R Salibindla, Katarzyna Karpinska-Leydier, Huseyin Ekin Ergin

Review Cureus. 2021 Jul 30;13(7):e16763. doi: 10.7759/cureus.16763. eCollection 2021 Jul.

There are many successful interventions in medicine, especially in neurology and rehabilitation. The neurosciences represent an area of medicine with tremendous recent research innovations, one of which is virtual reality. This paper aims to discover the powerful relationship between virtual reality and rehabilitation. We assessed the effectiveness of virtual reality-based rehabilitation compared to conventional rehabilitation on motor function recovery of three patient groups: patients with a diagnosis of cerebral palsy, Parkinson's disease, or stroke. We conducted a systematic review using PubMed and included only articles that were randomized controlled trials that were published in the last five years. We used a general search in combination with a more focused Medical Subject Headings (MeSH) search. After thorough assessment and risk of bias evaluation using the Cochrane risk of bias tool, we included thirteen studies in this review. The majority of the clinical trials showed a statistically significant effect for improved motor function. More specifically, improvements in upper extremity motor function, gait, and balance in patients diagnosed with stroke were seen. Similarly, when evaluating patients with Parkinson's disease, improved gait and posture were also seen. When it came to cerebral palsy, however, there were no significant differences between the experimental group and the control. The level of improvement in motor function with a virtual reality intervention was striking, particularly since a few studies demonstrated sustained motor improvement a few months post-trial as well. Virtual reality-based rehabilitation has promising results for adult patients diagnosed with stroke or Parkinson's disease. For pediatric patients, on the other hand, a larger number of clinical trials would still need to be conducted to validate if virtual reality interventions have the capability of providing improved motor function recovery.

PMID: 34367835

13. Nonimmersive Virtual Reality as Complementary Rehabilitation on Functional Mobility and Gait in Cerebral Palsy: A Randomized Controlled Clinical Trial
Joice Luiza Bruno Arnoni, Ana Francisca Rozin Kleiner, Camila Resende Gâmbaro Lima, Ana Carolina de Campos, Nelci Adriana Cicuto Ferreira Rocha

Games Health J. 2021 Aug;10(4):254-263. doi: 10.1089/g4h.2021.0009.

Objective: This study aimed to investigate the effects of nonimmersive virtual reality (VR) as complementary rehabilitation on functional mobility and gait in children with mild unilateral cerebral palsy (CP). Methods: Prospective, randomized, controlled, clinical trial. Twenty-two children with unilateral CP were randomized into two groups: intervention group (IG) (n = 11) and

control group (n = 11). After baseline assessments, the participants either started the VR intervention (IG) associated with conventional therapy, or continued conventional physical therapy (control group). Participants in the IG attended 45-minute training sessions twice a week for 8 weeks (total: 16 sessions and 12 hours of training). Participants in the control group underwent standard therapy for 50 minutes, twice a week. Timed Up and Go test (TUG), gait spatiotemporal variables, and pelvic angles were measured at baseline and after treatment sessions. Results: When compared with the control group, the IG performed the following activities in decreased time: TUG, and stride time. Also, the IG increased the velocity of walking and the pelvis retroversion, and decreased the pelvis interval/external rotations and amplitude of pelvis rotation while walking. Conclusions: A rehabilitative approach based on a nonimmersive VR as complementary rehabilitation may improve functional mobility and change joint mobility functions during gait of children with mild unilateral CP. The results of the study demonstrate that the insertion of a therapy based on VR may help in better strategies in the gait of children with CP. Thus, rehabilitation professionals can use this tool combined with conventional therapy.

PMID: 34370612

14. What is the effect of mechanically assisted walking training on walking, participation, and quality of life in children with cerebral palsy? A Cochrane Review summary with commentary
Ayesha Afridi, Farooq Azam Rathore

Dev Med Child Neurol. 2021 Aug 7. doi: 10.1111/dmcn.15013. Online ahead of print.

PMID: 34363698

15. Defining and grouping children's therapeutic footwear and criteria for their prescription: an international expert Delphi consensus study
Matthew Hill, Aoife Healy, Nachiappan Chockalingam

BMJ Open. 2021 Aug 9;11(8):e051381. doi: 10.1136/bmjopen-2021-051381.

Objectives: This study aimed to achieve an expert consensus on how to define and group footwear interventions for children, with a further focus on the design characteristics and prescription of off-the-shelf stability footwear for children with mobility impairment. Setting: A group of multinational professionals, from clinicians to those involved in the footwear industry, were recruited to ensure a spectrum of opinions. Participants: Thirty panellists were contacted, of which 24 consented to participate and six withdrew before round 1, a further two withdrew after round 1. Sixteen panellists completed the consensus exercise. Primary and secondary outcome measures: A Delphi consensus method was employed with round 1 split into three sections: (1) terms and definitions, (2) specifics of off-the-shelf stability footwear design and (3) criteria for clinical prescription of off-the-shelf stability footwear. The panel was asked to rate their level of agreement with statements and to provide further insights through open-ended questions. The opinions of the experts were analysed to assess consensus set at 75% agreement or to modify or form new statements presented through the subsequent two rounds. Results: Therapeutic footwear was the agreed term to represent children's footwear interventions, with grouping and subgrouping of therapeutic footwear being dependent on their intended clinical outcomes (accommodative, corrective or functional). Both the heel counter and topline as well as the stiffness and width of the sole were identified as potentially influencing mediolateral stability in children's gait. A consensus was achieved in the prescription criteria and outcome measures for off-the-shelf stability therapeutic footwear for cerebral palsy, mobile symptomatic pes planus, Duchenne muscular dystrophy, spina bifida and Down's syndrome. Conclusions: Through a structured synthesis of expert opinion, this study has established a standardisation of terminology and groupings along with prescription criteria for the first time. Reported findings have implications for communication between stakeholders, evidence-based clinical intervention and standardised outcome measures to assess effectiveness.

PMID: 34373314

16. Artificial intelligence to improve efficiency of administration of gross motor function assessment in children with cerebral palsy
Ibrahim Duran, Christina Stark, Ahmet Saglam, Alexandra Semmelweis, Heidrun Lioba Wunram, Karoline Spiess, Eckhard Schoenau

Dev Med Child Neurol. 2021 Aug 13. doi: 10.1111/dmcn.15010. Online ahead of print.

Aim: To create a reduced version of the 66-item Gross Motor Function Measure (rGMFM-66) using innovative artificial intelligence methods to improve efficiency of administration of the GMFM-66. Method: This study was undertaken using information from an existing data set of children with cerebral palsy participating in a rehabilitation programme. Different self-learning approaches (random forest, support vector machine [SVM], and artificial neural network) were evaluated to estimate the GMFM-66 score with the fewest possible test items. Test agreements were evaluated (among other statistics) by intraclass correlation coefficients (ICCs). Results: Overall, 1217 GMFM-66 assessments (509 females, mean age 8y 10mo [SD 3y 9mo]) at a single time and 187 GMFM-66 assessments and reassessments (80 females, mean age 8y 5mo [SD 3y 10mo]) after 1 year were evaluated. The model with SVM predicted the GMFM-66 scores most accurately. The ICCs of the rGMFM-66 and the full GMFM-66 were 0.997 (95% confidence interval [CI] 0.996-0.997) at a single time and 0.993 (95% CI 0.993-0.995) for the evaluation of the change over time. Interpretation: The study shows that the efficiency of the full GMFM-66 assessment can be increased by using machine learning (self-learning algorithms). The presented rGMFM-66 score showed an excellent agreement with the full GMFM-66 score when applied to a single assessment and when evaluating the change over time.

PMID: 34387869

17. Neuroimaging findings in children with cerebral palsy with autism and/or attention-deficit/hyperactivity disorder: a population-based study

Magnus Påhlman, Christopher Gillberg, Kate Himmelmann

Dev Med Child Neurol. 2021 Aug 9. doi: 10.1111/dmcn.15011. Online ahead of print.

Aim: To compare neuroimaging patterns according to the Magnetic Resonance Imaging Classification System (MRICS) in children with cerebral palsy (CP) with and without autism and/or attention-deficit/hyperactivity disorder (ADHD). Method: This population-based study assessed 184 children (97 males, 87 females) with CP born from 1999 to 2006 from the CP register of western Sweden, who had completed comprehensive screening and clinical assessment for neuropsychiatric disorders and undergone neuroimaging. Results: Autism (total prevalence 30%) and ADHD (31%) were common in all neuroimaging patterns, including normal. Autism and ADHD were not more prevalent in children with bilateral than unilateral lesions, contrary to other associated impairments. Children with predominant white matter injury, related to insults in the late second or early third trimester, had the highest prevalence of autism (40%). Children who had sustained a middle cerebral artery infarction had the highest prevalence of ADHD (62%). Interpretation: Although autism and ADHD are common regardless of neuroimaging patterns, timing and localization of insult appear to be of importance for the occurrence of autism and ADHD in children with CP. Neuroimaging may be of prognostic value for these associated impairments. Further in-depth neuroimaging studies may lead to a better understanding of the association between CP and neuropsychiatric disorders.

PMID: 34370307

18. Survival of South African children with cerebral palsy

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S Afr Med J. 2021 May 31;111(6):591-594. doi: 10.7196/SAMJ.2021.v111i6.15272.

Background: The South African (SA) public healthcare sector has experienced a surge in birth injury claims in recent years, particularly in respect of cerebral palsy (CP). The lump sum settlements in these matters are a function of the expected survival curve of the individual concerned. It is known from international studies that the life expectancy of children with CP is shorter than that of the general population, and depends on the pattern and severity of their disabilities. However, empirical estimates of survival for children with CP in SA are not available. Objectives: To construct survival curves according to the pattern of gross motor skills for CP children in SA and compare these with international studies. Methods: We collected data on mortality and functional status for 339 CP children on whose behalf claims for medical negligence had been instituted. Motor disabilities were classified according to the five-level Gross Motor Function Classification System (GMFCS). Children who were unable to walk unaided were further classified according to more basic motor skills, including the ability to lift their heads or chests in the prone position, rolling and sitting. Mortality rates were calculated and survival curves were estimated using the Kaplan-Meier method. Results: No deaths were observed among 119 children in GMFCS levels I - IV. Among the 220 children in GMFCS V, there were 20 observed deaths. The proportions surviving to ages 10 and 15 years were 85% (standard error (SE)

5%) and 55% (SE 11%), respectively. The former is comparable to what has been reported for children in California and Sweden, but the survival to age 15 is lower. Among 82 children who could not lift their heads in the prone position, there were 11 observed deaths for a mortality rate of 48.5 (95% confidence interval (CI) 24.2 - 86.9) deaths per 1 000 person-years. Among 72 children who could lift their heads but not their chests, there were 6 observed deaths for a mortality rate of 33.5 (95% CI 12.3 - 73.0) deaths per 1 000 person-years. These mortality rates are 22% and 15% higher than the corresponding figures documented for children with comparable abilities and disabilities in California. Conclusions: Life expectancy of children with CP in SA is lower than that of children with comparably severe disabilities in high-income countries.

PMID: 34382573

19. Neurodevelopmental outcome of preterm very low birth weight infants admitted to an Italian tertiary center over an 11-year period

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Sci Rep. 2021 Aug 11;11(1):16316. doi: 10.1038/s41598-021-95864-0.

Preterm very low birth weight infants (VLBWi) are known to be at greater risk of adverse neurodevelopmental outcome. Identifying early factors associated with outcome is essential in order to refer patients for early intervention. Few studies have investigated neurodevelopmental outcome in Italian VLBWi. The aim of our longitudinal study is to describe neurodevelopmental outcome at 24 months of corrected age in an eleven-year cohort of 502 Italian preterm VLBWi and to identify associations with outcome. At 24 months, Griffiths' Mental Developmental Scales were administered. Neurodevelopmental outcome was classified as: normal, minor sequelae (minor neurological signs, General Quotient between 76 and 87), major sequelae (cerebral palsy; General Quotient ≤ 75; severe sensory impairment). 75.3% showed a normal outcome, 13.9% minor sequelae and 10.8% major sequelae (3.8% cerebral palsy). Male gender, bronchopulmonary dysplasia, abnormal neonatal neurological assessment and severe brain ultrasound abnormalities were independently associated with poor outcome on multivariate ordered logistic regression. Rates of major sequelae are in line with international studies, as is the prevalence of developmental delay over cerebral palsy. Analysis of perinatal complications and the combination of close cUS monitoring and neurological assessment are still essential for early identification of infants with adverse outcome.

PMID: 34381139

20. Orthopaedic Disorders in Cerebral Palsy in International Cooperation Projects: A Descriptive Cross-Sectional Study

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Observational Study Int J Environ Res Public Health. 2021 Jul 25;18(15):7872. doi: 10.3390/ijerph18157872.

Background: In international cooperation projects that are carried out in less developed and developing countries, a large number of children with disabilities present cerebral palsy (CP). Orthopaedic disorders are frequent complications associated with this disorder. Their prevention and early intervention are essential to achieve an appropriate therapeutic approach for children with PC and to improve their quality of life. Objective: To describe the treatment approach that is currently used in international cooperation projects for the rehabilitation management of the orthopaedic disorders in children with cerebral palsy. Methods: This is an observational, descriptive, cross-sectional study, carried out by means of an online questionnaire to professionals in the field of Physiotherapy and Rehabilitation working in international cooperation projects. The inclusion criteria were professionals working in the rehabilitation field in development aid, humanitarian action or emergency projects that provided rehabilitation services, working with children with cerebral palsy from 0 to 18 years old. Results: Ninety-eight questionnaires were analysed. The average age of the participants was 33.2 years, they were mainly working in development cooperation projects (83.33%) that were implemented in rehabilitation centres and through community-based rehabilitation services (60%). The projects were located in countries all over the world but mainly on the Asian continent (71.4%). Physiotherapists and orthopaedic technicians (72.22%) were the main professionals working in these projects, followed by occupational therapists and social workers (55.56%). The results indicated that the orthopaedic disorders were very frequent in the sample (66.67%), with hip subluxation (50%), scoliosis (77.78%), kyphosis (61.1%), clubfoot (88.7%) and varus foot (61.11%) standing out. The most commonly used treatment approaches were positioning (88.89%) and the Bobath concept

(83.33%). The technical aids that were used by the professionals were ankle foot orthosis (AFO) (94.44%), bracing (66.67%), standing frames (83.33%), moulded seats (100%), corner seats (93.75%) and adapted seats (92.85%). Conclusions: In international cooperation projects, the rehabilitation treatment of children with cerebral palsy is based on a holistic approach. This is reflected in the interventions that are carried out to treat their orthopaedic disorders and in locally produced devices, awareness raising and community education. However, the professionals surveyed considered that the aids or orthoses used are insufficient in the treatment and prevention of orthopaedic disorders in cerebral palsy.

PMID: 34360167

21. Perinatal arterial ischemic stroke and periventricular venous infarction in infants with unilateral cerebral palsy
Melissa Vitagliano, Mary Dunbar, Sasha Dyck Holzinger, Nicole Letourneau, Deborah Dewey, Maryam Oskoui, Michael Shevell, Adam Kirton

Dev Med Child Neurol. 2021 Aug 10. doi: 10.1111/dmcn.15000. Online ahead of print.

Aim: To explore clinical factors associated with perinatal arterial ischemic stroke (AIS) and periventricular venous infarction (PVI) in infants who develop unilateral cerebral palsy (CP).Method: This was a case-control study. Data current to 2019 was extracted from the Canadian Cerebral Palsy Registry (CCPR). Cases were infants born at term with confirmed unilateral CP. Magnetic resonance images were stratified by expert review of reports as definitive perinatal stroke (AIS or PVI). Controls with common data elements were recruited from a population-based study in Alberta. Multivariable regression analyses were performed to estimate associations expressed as odds ratios with 95% confidence intervals. Results: Of 2093 cases from the CCPR, 662 had unilateral CP, of whom 299 (45%) had perinatal stroke: AIS 169 (57%) and PVI 130 (43%). Median age at diagnosis for AIS was 11.9 months (interquartile range: 6.2-25.7mo; range 0.17-104.1mo), and 58.6% were male. Median age at diagnosis for PVI was 25.3 months (interquartile range: 14.5-38mo, range 0.7-114.7mo) and 57.7% were male. Independent associations for both AIS and PVI on multivariable analysis were chorioamnionitis, illicit drug exposure, diabetes, gestational age, and maternal age. Variables associated with AIS alone were low Apgar score and prolonged rupture of membranes. Variables associated with PVI alone were small for gestational age and primigravida. Interpretation: Controlled analysis of disease-specific unilateral CP may offer unique perspectives on its pathophysiology. Acute intrapartum factors are mainly associated with AIS, while in utero factors are associated with PVI.

PMID: 34374437

22. Genomics in Cerebral Palsy phenotype across the lifespan: Comparison of diagnostic yield between children and adult population
Haifa Al Zahrani, Komudi Siriwardena, Dana Young, Anna Lehman, Gabriella A Horvath, Helly Goez

Review Mol Genet Metab. 2021 Jul 21;S1096-7192(21)00758-7. doi: 10.1016/j.ymgme.2021.07.007. Online ahead of print.

Purpose: The presentation and underlying etiology of Cerebral Palsy (CP) in general are heterogenous. Clinical features present differently in pediatric versus adult patient populations. Many metabolic and genetic conditions present with clinical symptoms suggestive of CP. Precision medicine practices are currently a standard of care, and Next-Generation-Sequencing (NGS) tools are used for the purpose of diagnosis and management. We describe the diagnostic yield and impact on management of NGS comparing a cohort of 102 children and 37 adults with CP, referred to two tertiary care centres between 2015 and 2020 (adult cohort) and 2017-2020 (pediatric cohort) respectively. Principal results: In the adult cohort, 28 patients had a positive genetic diagnosis, giving a yield of 75.6%. Their age varied between 18 and 59 years, with a median of 28 years. Out of the positive diagnoses, 12 were consistent with an inborn error of metabolism and in 9 patients (32.1%) some form of treatment or management guideline was recommended. In the pediatric cohort 21 patients had a positive genetic diagnosis and 22 results are still pending, giving a yield of 32.8%. Age at diagnosis ranged between 18 months and 12 years. In 15 patients (71.4%) there was some form of management recommendation. All families benefited from genetic counseling. Major conclusions: Given the combined high yield of positive genetic diagnosis in pediatric and adult cases presenting with symptoms of Cerebral Palsy, and the more readily available Next Generation Sequencing testing in major academic centres, we recommend that either a referral to a pediatric or adult neurometabolic centre to be made, or genetic testing to be initiated where this is available.

PMID: 34364746

23. Biallelic loss-of-function variants in the splicing regulator NSRP1 cause a severe neurodevelopmental disorder with spastic cerebral palsy and epilepsy

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Genet Med. 2021 Aug 12. doi: 10.1038/s41436-021-01291-x. Online ahead of print.

Purpose: Alternative splicing plays a critical role in mouse neurodevelopment, regulating neurogenesis, cortical lamination, and synaptogenesis, yet few human neurodevelopmental disorders are known to result from pathogenic variation in splicing regulator genes. Nuclear Speckle Splicing Regulator Protein 1 (NSRP1) is a ubiquitously expressed splicing regulator not known to underlie a Mendelian disorder. Methods: Exome sequencing and rare variant family-based genomics was performed as a part of the Baylor-Hopkins Center for Mendelian Genomics Initiative. Additional families were identified via GeneMatcher. Results: We identified six patients from three unrelated families with homozygous loss-of-function variants in NSRP1. Clinical features include developmental delay, epilepsy, variable microcephaly (Z-scores -0.95 to -5.60), hypotonia, and spastic cerebral palsy. Brain abnormalities included simplified gyral pattern, underopercularization, and/or vermian hypoplasia. Molecular analysis identified three pathogenic NSRP1 predicted loss-of-function variant alleles: c.1359_1362delAAAG (p.Glu455AlafsTer20), c.1272dupG (p.Lys425GlufsTer5), and c.52C>T (p.Gln18Ter). The two frameshift variants result in a premature termination codon in the last exon, and the mutant transcripts are predicted to escape nonsense mediated decay and cause loss of a C-terminal nuclear localization signal required for NSRP1 function. Conclusion: We establish NSRP1 as a gene for a severe autosomal recessive neurodevelopmental disease trait characterized by developmental delay, epilepsy, microcephaly, and spastic cerebral palsy.

PMID: 34385670

24. The assessment of general movements in term and late-preterm infants diagnosed with neonatal encephalopathy, as a predictive tool of cerebral palsy by 2 years of age-a scoping review

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Syst Rev. 2021 Aug 12;10(1):226. doi: 10.1186/s13643-021-01765-8.

Background: The General Movements Assessment is a non-invasive and cost-effective tool with demonstrated reliability for identifying infants at risk for cerebral palsy. Early detection of cerebral palsy allows for the implementation of early intervention and is associated with better functional outcomes. No review to date has summarized the utility of the General Movements Assessment to predict cerebral palsy in term and late-preterm infants diagnosed with neonatal encephalopathy. Methods: We conducted a scoping review involving infants born greater than or equal to 34 weeks gestational age to identify all available evidence and delineate research gaps. We extracted data on sensitivity, specificity, and positive and negative predictive values and described the strengths and limitations of the results. We searched five databases (MEDLINE, Embase, PsychINFO, Scopus, and CINAHL) and the General Movements Trust website. Two reviewers conducted all screening and data extraction independently. The articles were categorized according to key findings, and a critical appraisal was performed. Results: Only three studies, a cohort and two case series, met all of the inclusion criteria. The total number of participants was 118. None of the final eligible studies included late-preterm neonates. All three studies reported on sensitivity, specificity, and positive predictive and negative predictive values. An abnormal General Movement Assessment at 3-5 months has a high specificity (84.6-98%) for cerebral palsy with a similarly high negative predictive value (84.6-98%) when it was normal. Absent fidgety movements, in particular, are highly specific (96%) for moderate to severe cerebral palsy and carry a high negative predictive value (98%) when normal. In the time period between term and 4-5 months post-term, any cramped synchronized movements had results of 100% sensitivity and variable results for specificity, positive predictive value, and negative predictive value. Conclusions: A normal General Movements Assessment at 3 months in a term high-risk infant is likely associated with a low risk for moderate/severe cerebral palsy. The finding of cramped synchronized General Movements is a strong predictor for the diagnosis of cerebral palsy by 2 years of age in the term population with neonatal encephalopathy. The deficit of high-quality research limits the applicability, and so the General Movements Assessment should not be used in isolation when assessing this population.

PMID: 34384482

25. Inter-observer reliability using the General Movement Assessment is influenced by rater experience
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Early Hum Dev. 2021 Aug 2;161:105436. doi: 10.1016/j.earlhumdev.2021.105436. Online ahead of print.

Objective: To describe the inter-observer reliability of the General Movement Assessment (GMA) among a sample of infants at high-risk of cerebral palsy (CP) among raters with various levels of experience. Methods: Video assessments of 150 high-risk infants at 10-15 weeks corrected age were rated by three Prechtl GMA-certified observers with varied experience using the assessment. Videos were scored based on temporal organization of fidgety movements (FMs), presence of abnormal FMs, or absence of FMs. Inter-observer agreements were analyzed with Gwet's AC1 statistic. Results: We found fair to moderate agreement when subcategories of normal FMs (continuous and intermittent) were included (AC1 = 0.32-0.57) and moderate to near perfect agreement when normal categories of FMs were combined (AC1 = 0.60-0.95). Reliability was higher among observers with more experience using the GMA (AC1 = 0.57-0.98) than the observer with less experience (AC1 = 0.32-0.61). Conclusions: Caution may be warranted when the GMA is used to differentiate "continuous and intermittent" FMs temporal organization. The GMA is highly reliable among experienced raters when comparing normal FMs to other FMs categorizations.

PMID: 34375936

26. Botulinum Toxin Type A in the Spasticity of Cerebral Palsy Related to Congenital Zika Syndrome: An Observational Study
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Dev Neurorehabil. 2021 Aug 13;1-8. doi: 10.1080/17518423.2021.1960917. Online ahead of print.

Purpose: Investigate the effect of botulinum toxin type-A (BoNT-A) on spasticity and motor performance in children with Cerebral Palsy (CP) related to Congenital Zika Syndrome (CZS). Methods: Prospective longitudinal observational study of 34 children with CP referred for BoNT-A treatment. Outcomes were evaluated with a muscle tone assessment scale (Modified Ashworth Scale - MAS) and the Patients' Global Impression of Improvement (PGI-I) scale. Results: Mean age was 32.06 ± 3.07 months and 85% were classified as Gross Motor Function Classification System (GMFCS) V. Primitive reflexes were present in 56% of the sample. The majority of the parents (97.9%) reported improvement in range of motion or reduction in spasticity after treatment with botulinum toxin. No side effects were recorded. When compared to the baseline, median reduction in the MAS was 0.5 (IQR = 0). Conclusions: The findings of this study suggest that BoNT-A may effectively promote functional improvements and reduce muscle tone, improving the child's and family's quality of life.

PMID: 34387523

27. Highly Selective Partial Neurectomies for Spasticity: A Single-Center Experience
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Neurosurgery. 2021 Aug 12;nyab303. doi: 10.1093/neuros/nyab303. Online ahead of print.

Background: Sedating antispastic medications and focal therapies like botulinum toxin are the most common therapies for spasticity but are temporary and must be performed continuously for a principally static neurological insult. Alternatively, highly selective partial neurectomies (HSPNs) may reduce focal spasticity more permanently. Objective: To quantify the change in spasticity after HSPN and assess patient satisfaction. Methods: We retrospectively reviewed the records of patients with upper- and/or lower-extremity spasticity treated with HSPN from 2014 to 2018. Only cases with a modified Ashworth scale (MAS) score independently determined by a physical therapist were included. Pre- and postoperative MAS, complications, and patient satisfaction were evaluated. Results: The 38 patients identified (24 male, 14 female; mean age 49 yr) underwent a total of 88 procedures for focal spasticity (73% upper extremity, 27% lower extremity). MAS scores were adjusted to a 6-point scale for evaluation. The mean preoperative and final postoperative follow-up adjusted MAS scores were 3.6 and 1.7, respectively ($P < .001$), which represents average MAS less than 1+. Positive, neutral, and worse results were described by

91%, 6%, and 3% of patients, respectively. Four patients requested revision surgery. No perioperative complications were encountered. Conclusion: This is the first North American series to analyze HSPN for spasticity and the only series based on independent evaluation results. HSPN surgery demonstrated objective short- and long-term reduction in spasticity with minimal morbidity and excellent patient satisfaction.

PMID: 34382654

28. Sensorimotor Integration in Childhood Dystonia and Dystonic Cerebral Palsy-A Developmental Perspective
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Review Front Neurol. 2021 Jul 23;12:668081. doi: 10.3389/fneur.2021.668081. eCollection 2021.

Dystonia is a disorder of sensorimotor integration, involving dysfunction within the basal ganglia, cortex, cerebellum, or their inter-connections as part of the sensorimotor network. Some forms of dystonia are also characterized by maladaptive or exaggerated plasticity. Development of the neuronal processes underlying sensorimotor integration is incompletely understood but involves activity-dependent modeling and refining of sensorimotor circuits through processes that are already taking place in utero and which continue through infancy, childhood, and into adolescence. Several genetic dystonias have clinical onset in early childhood, but there is evidence that sensorimotor circuit development may already be disrupted prenatally in these conditions. Dystonic cerebral palsy (DCP) is a form of acquired dystonia with perinatal onset during a period of rapid neurodevelopment and activity-dependent refinement of sensorimotor networks. However, physiological studies of children with dystonia are sparse. This discussion paper addresses the role of neuroplasticity in the development of sensorimotor integration with particular focus on the relevance of these mechanisms for understanding childhood dystonia, DCP, and implications for therapy selection, including neuromodulation and timing of intervention.

PMID: 34367047

29. A Self-Limited Childhood Epilepsy as Co-Incidental in Cerebral Palsy
Olga An, Lidia Mayumi Nagae, Steven Parrish Winesett

Case Reports Int Med Case Rep J. 2021 Aug 5;14:509-517. doi: 10.2147/IMCRJ.S315550. eCollection 2021.

Background: Cerebral palsy is the most frequent motor disability in childhood and is associated with a higher incidence of seizure disorders. In many instances, it is recognized that motor difficulties, as well as seizures, are from the same underlying brain lesion. However, self-limited childhood epilepsies, being a common group of epilepsy syndromes, would be expected to occur in patients with cerebral palsy merely on chance association and be unrelated to the structural brain imaging abnormality causing the motor impairment. Differential diagnosis in this case is important determining the long-term prognosis and need for anticonvulsant treatment. Case presentation: Here, we report two patients with cerebral palsy combined with epilepsy, whose age at onset, seizure semiology and electroclinical features were similar to children with self-limited childhood-specific seizure disorders (childhood epilepsy with centrotemporal spikes and Panayiotopoulos syndrome). Conclusion: These cases highlight the importance of comprehensive differential diagnosis of seizures in cerebral palsy. Co-existence of age-dependent focal epilepsies with an underlying brain pathology as white matter injury, not affecting the cerebral cortex, might take place in the case of children with impaired motor skills. With health systems increasingly utilizing clinical pathways, it is important to consider the possibility of a self-limited childhood epilepsy and avoid aggressive and unnecessary medication treatment in children with cerebral palsy.

PMID: 34385844

30. Lessons learned in the development of a nurse-led family centered approach to developing a holistic comprehensive clinic and integrative holistic care plan for children with cerebral palsy
Lamara Love, Amy Newmeyer, Nancy Ryan-Wenger, Garey Noritz, Micah A Skeens

J Spec Pediatr Nurs. 2021 Aug 9;e12354. doi: 10.1111/jspn.12354. Online ahead of print.

Clinical problem: Children with cerebral palsy (CP) typically receive care from multiple specialty providers including Developmental Pediatrics, Orthopedics, Physical Medicine, Occupational Therapy, Physical Therapy, Speech Therapy, Clinical Social Work, Clinical Nutrition, Nursing and Orthotists, which often require many individual visits to the hospital annually. The potential for conflicting plans of care is increased by this fragmented approach, which may lead to duplication of services and increased healthcare costs. Solution: To address the problem and alleviate burden for families, the Comprehensive Cerebral Palsy Program implemented a nurse-led comprehensive interdisciplinary team approach to provide optimal care coordination to patients and families, using an Integrative Holistic Care Plan (IHCP). During an annual 3-4 hour Comprehensive CP Clinic appointment, a team of specialists meets with the family, and a holistic, evidence-based plan of care is developed. The family-centered care plan includes summaries of each discipline's plan of care with individualized goals, recommendations, and evidence-based outcomes. After the visit, the plan of care is communicated with the family, primary care provider, and other community providers to ensure continuity of care. Results: Early in the program and electronic IHCP development stage, clinical, and financial outcomes were improved. In addition to significant cost savings, family satisfaction surveys showed continuous improvement in the areas of access, communication, and coordination of care. Practice implications: Nurses working in interdisciplinary clinics are in a position to facilitate improved outcomes by developing and implementing a family-centered care plan that provides a comprehensive holistic approach to impacting the areas of quality, effectiveness, and efficiency of care delivery. The use of an IHCP decreases fragmentation of care and duplication of services leading to healthcare cost savings and enhanced patient satisfaction.

PMID: 34374481

31. Physical responses by cerebral palsy footballers in matches played at sea level and moderate altitude
Matías Henríquez, Daniel Castillo, Javier Yanci, Aitor Iturricastillo, Raul Reina

Res Sports Med. 2021 Aug 12;1-13. doi: 10.1080/15438627.2021.1966011. Online ahead of print.

The main objective of this study was to compare the physical response of para-footballers with cerebral palsy (CP) in official international football matches played at moderate altitude and sea level locations. Eighty-seven international CP footballers participated in this study. We divided participants according to the place of the international competition [sea level group (SLG) and moderate altitude group (MAG)], sport classes (i.e., FT1, FT2, and FT3), and match playing time (i.e., <20 min, 20–40 min, and >40 min). We recorded the physical response using global position system devices during matches. This study showed that MAG described a lower physical response than SLG on total distance, distance covered at different intensities, and the number of accelerations and decelerations. FT2 and FT3 presented a similar pattern, where we found significant differences for total distance, distance covered at lower and high intensities and moderate accelerations, and decelerations. Considering the playing time during altitude matches, the 20–40 min and >40 min groups obtained more marked differences in the physical response variables. Para-footballers with CP who competed under altitude conditions showed a lower physical response during football matches, suggesting the implementation of specific preparation and training strategies to face the demanding environmental conditions.

PMID: 34383571

32. Informing the development of the Canadian Neurodiversity Platform (iCAN): What is important to parents of children with neurodevelopmental disabilities?
Miriam Gonzalez, Shikha Saxena, Farhin Chowdhury, Sasha Dyck Holzinger, Rachel Martens, Maryam Oskoui, Keiko Shikako-Thomas

Child Care Health Dev. 2021 Aug 9. doi: 10.1111/cch.12906. Online ahead of print.

Background: A crowd-sourced Canadian platform that collects information across neurodevelopmental disabilities (NDDs) can: (1) facilitate knowledge mobilization, (2) provide epidemiological data that can benefit knowledge, treatment, and advocacy, and (3) inform policy and resource allocation decisions. We obtained input from parents of children with NDDs about relevance and feasibility of questionnaire items as a first step to inform questionnaire development of a stakeholder-driven, national platform for data collection on children with neurodevelopmental disabilities. Methods: A parent of a teenager with NDDs was a research partner on the project. Through four focus groups and using a guided discussion consensus process, 16 participants provided feedback on whether questionnaire items from existing instruments related to function and disability

were feasible for parents to complete and important to include in the platform. Data were analysed using content analysis. Results: Participants: (1) indicated that questions about medical history, general health, body functioning, self-care, access to resources, and outcomes (e.g., quality of life) are important to include in the platform and are feasible for self-completion, (2) provided various suggestions for the questionnaire ranging from additional items to include, using non-medical language, and keeping completion time from 20 to 30 minutes, (3) identified incentives and knowing the purpose of the platform as strong motivators to platform participation, (4) spoke about the challenges of their caregiver experience including impact of caregiving on themselves and barriers to accessing services, and (5) highlighted the isolation experienced by their children. Conclusion: Through the focus groups, parent stakeholders contributed to questionnaire development and shared their caregiver experiences. Obtaining feedback from youths with NDDs and healthcare providers on the questionnaire is a next step to validating findings. Stakeholder engagement is fundamental to developing a platform that will inform research that is relevant to the needs of children with neurodevelopmental disabilities and their families.

PMID: 34374115

33. Content validation of common measures of functioning for young children against the International Classification of Functioning, Disability and Health and Code and Core Sets relevant to neurodevelopmental conditions
Emily D'Arcy , Kerry Wallace, Angela Chamberlain , Kiah Evans, Benjamin Milbourn, Sven Bölte, Andrew Jo Whitehouse, Sonya Girdler

Autism. 2021 Aug 8;13623613211036809. doi: 10.1177/13623613211036809. Online ahead of print.

Young children who have developmental delay, autism, or other neurodevelopmental conditions can have difficulties doing things in different areas of their life. What they can and cannot do is called their level of functioning. There are lots of assessment measures that aim to assess functioning. But, we are not sure if these measures assess all the things we need to know about these children's functioning. Other research has identified lists of items (codes) that need to be assessed to understand functioning for young children with different neurodevelopmental conditions fully. These lists include body functions (the things a child's body or brain can do), activities and participation (the activities and tasks a child does) and environmental factors (parts of the environment that can influence functioning). In this study, we looked at the items from these lists assessed by different functioning measures to see how they compared to what should be assessed. The measures that we looked at covered 21%-57% of all the codes and 19%-63% of the codes for lists specific to different conditions. Most of the measures focused on activity and participation codes, and they rarely assessed environmental factors. Knowing which codes and how much of the lists the measures assess can help researchers, clinicians and policymakers to choose measures that are more appropriate for young children with neurodevelopmental conditions.

PMID: 34369196

34. Today Is My Day: Analysis of the Awareness Campaigns' Impact on Functional Diversity in the Press, on Google, and on Twitter
Irene Gómez-Marí, Pilar Sanz-Cervera, Raúl Tárraga-Mínguez

Int J Environ Res Public Health. 2021 Jul 22;18(15):7789. doi: 10.3390/ijerph18157789.

(1) Every day, people with functional diversity face different kinds of difficulties that pose a barrier to their social inclusion. These difficulties often go unnoticed by most citizens. Social networks are a powerful tool to sensitize the population. With this objective, different organizations such as associations, federations, foundations, and other institutions have promoted campaigns through the celebration of world days for different types of functional diversity. This research aims to monitor and analyze the impact of these social campaigns in Spain, including Asperger's syndrome, rare diseases, Down syndrome, autism, hearing and visual impairment, cerebral palsy, dyslexia, ADHD, spina bifida, disability, and dyscalculia world days, between 2015 and 2020. (2) The impact of each campaign on the press, Google, and Twitter has been analyzed using: MyNews, Google Trends, and Trendinalia. (3) The results suggest a close relationship between the impact on the number of pieces of news generated in the press, the searches on Google, and the hashtags in high positions on Twitter. (4) The campaigns with the greatest levels of success are those whose diagnoses involve greater difficulties in adaptive behavior. These results can provide some practical implications for future campaigns.

PMID: 34360080

35. Safety of allogeneic umbilical cord blood infusions for the treatment of neurological conditions: a systematic review of clinical studies
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Review Cytotherapy. 2021 Aug 9;S1465-3249(21)00715-5. doi: 10.1016/j.jcyt.2021.07.001. Online ahead of print.

Background aims: Umbilical cord blood (UCB) infusion is being investigated as a treatment for a range of neurological conditions, primarily because of its potent immunomodulatory effects mediated via paracrine signaling. Although initial research mainly utilized autologous UCB, allogeneic samples from a sibling or unrelated donor have now become more common. With the use of allogeneic UCB, questions have arisen surrounding the necessity for human leukocyte antigen (HLA) matching, preparative regimens and immunosuppressant drugs. To investigate the safety of allogeneic UCB for the treatment of neurological conditions and the impact of HLA mismatching and immunosuppresion, the authors conducted a systematic review of the safety of allogeneic UCB infusion for neurological conditions. Methods: A systematic review of published and gray literature was conducted to investigate the safety of allogeneic UCB infusions for neurological conditions. Results: Authors identified 10 studies using allogeneic UCB to treat autism spectrum disorder, cerebral palsy, stroke, traumatic brain injury and various other conditions. A total of 361 participants (with at least 442 UCB infusions) received a range of HLA-matched/untyped allogeneic units and cell doses, with the majority not administered post-infusion immunosuppression. There were no reported serious adverse events definitely or probably related to the allogeneic UCB infusion, nor later potential complications such as graft-versus-host disease or teratoma formation. Conclusions: Although variability between studies is high, the available data do not identify safety concerns with allogeneic UCB infusion for the treatment of neurological conditions, even with variable HLA matching or no immunosuppression.

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36. Education can improve clinician confidence in information sharing and willingness to refer to stem cell clinical trials for cerebral palsy
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To progress stem cell therapies for cerebral palsy, clinicians need to openly engage with patients about emerging evidence and be willing to refer to relevant clinical trials, if and when appropriate. To assess whether education can change clinicians' confidence in information sharing and willingness to refer to relevant clinical trials, an online questionnaire was distributed at a scientific conference before and after a professional workshop on cell therapies for cerebral palsy. Of the 42 participants who completed the survey, 26 self-identified as clinicians. Of these, 81% had had patients ask about stem cells, yet in the pre-workshop questionnaire indicated they were not confident answering questions about cell therapies. Clinicians were most commonly asked about stem cell treatments provided by private clinics, stem cell research and current evidence. Post-workshop, knowledge and confidence regarding stem cells, as well as likelihood to refer to clinical trials using therapies with a strong evidence base (eg, umbilical cord blood/placental cells), significantly increased ($p<0.001$). This study highlights that by offering resources and education, clinician confidence and willingness to refer to cell therapy trials can improve; this may help drive the stem cell research landscape and support patient decision-making.

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Prevention and Cure

37. Clinical and imaging outcomes after intrathecal injection of umbilical cord tissue mesenchymal stem cells in cerebral palsy: a randomized double-blind sham-controlled clinical trial
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Background: This study assessed the safety and efficacy of intrathecal injection of umbilical cord tissue mesenchymal stem cells (UCT-MSC) in individuals with cerebral palsy (CP). The diffusion tensor imaging (DTI) was performed to evaluate the alterations in white-matter integrity. Methods: Participants (4-14 years old) with spastic CP were assigned in 1:1 ratio to receive either UCT-MSC or sham procedure. Single-dose (2 × 107) cells were administered in the experimental group. Small needle pricks to the lower back were performed in the sham-control arm. All individuals were sedated to prevent awareness. The primary endpoints were the mean changes in gross motor function measure (GMFM)-66 from baseline to 12 months after procedures. The mean changes in the modified Ashworth scale (MAS), pediatric evaluation of disability inventory (PEDI), and CP quality of life (CP-QoL) were also assessed. Secondary endpoints were the mean changes in fractional anisotropy (FA) and mean diffusivity (MD) of corticospinal tract (CST) and posterior thalamic radiation (PTR). Results: There were 36 participants in each group. The mean GMFM-66 scores after 12 months of intervention were significantly higher in the UCT-MSC group compared to baseline (10.65; 95%CI 5.39, 15.91) and control (β 8.07; 95%CI 1.62, 14.52; Cohen's d 0.92). The increase was also seen in total PEDI scores (vs baseline 8.53; 95%CI 4.98, 12.08; vs control: β 6.87; 95%CI 1.52, 12.21; Cohen's d 0.70). The mean change in MAS scores after 12 months of cell injection reduced compared to baseline (-1.0; 95%CI -1.31, -0.69) and control (β -0.72; 95%CI -1.18, -0.26; Cohen's d 0.76). Regarding CP-QoL, mean changes in domains including friends and family, participation in activities, and communication were higher than the control group with a large effect size. The DTI analysis in the experimental group showed that mean FA increased (CST 0.032; 95%CI 0.02, 0.03. PTR 0.024; 95%CI 0.020, 0.028) and MD decreased (CST -0.035 × 10-3; 95%CI -0.04 × 10-3, -0.02 × 10-3. PTR -0.045 × 10-3; 95%CI -0.05 × 10-3, -0.03 × 10-3); compared to baseline. The mean changes were significantly higher than the control group. Conclusions: The UCT -MSC transplantation was safe and may improve the clinical and imaging outcomes. Trial registration: The study was registered with ClinicalTrials.gov (NCT03795974).

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38. Microglia and Stem-Cell Mediated Neuroprotection after Neonatal Hypoxia-Ischemia
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Neonatal hypoxia-ischemia encephalopathy (HIE) refers to a brain injury in term infants that can lead to death or lifelong neurological deficits such as cerebral palsy (CP). The pathogenesis of this disease involves multiple cellular and molecular events, notably a neuroinflammatory response driven partly by microglia, the brain resident macrophages. Treatment options are currently very limited, but stem cell (SC) therapy holds promise, as beneficial outcomes are reported in animal studies and to a lesser degree in human trials. Among putative mechanisms of action, immunomodulation is considered a major contributor to SC associated benefits. The goal of this review is to examine whether microglia is a cellular target of SC-mediated immunomodulation and whether the recruitment of microglia is linked to brain repair. We will first provide an overview on microglial activation in the rodent model of neonatal HI, and highlight its sensitivity to developmental age. Two complementary questions are then addressed: (i) do immune-related treatments impact microglia and provide neuroprotection, (ii) does stem cell treatment modulates microglia? Finally, the immune-related findings in patients enrolled in SC based clinical trials are discussed. Our review points to an impact of SCs on the microglial phenotype, but heterogeneity in experimental designs and methodological limitations hamper our understanding of a potential contribution of microglia to SC associated benefits. Thorough analyses of the microglial phenotype are warranted to better address the relevance of the neuroimmune crosstalk in brain repair and improve or advance the development of SC protocols in humans.

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39. Targeting Complement C3a Receptor to Improve Outcome After Ischemic Brain Injury
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Review Neurochem Res. 2021 Aug 11. doi: 10.1007/s11064-021-03419-6. Online ahead of print.

Ischemic stroke is a major cause of disability. No efficient therapy is currently available, except for the removal of the occluding blood clot during the first hours after symptom onset. Loss of function after stroke is due to cell death in the

infarcted tissue, cell dysfunction in the peri-infarct region, as well as dysfunction and neurodegeneration in remote brain areas. Plasticity responses in spared brain regions are a major contributor to functional recovery, while secondary neurodegeneration in remote regions is associated with depression and impedes the long-term outcome after stroke. Hypoxic-ischemic encephalopathy due to birth asphyxia is the leading cause of neurological disability resulting from birth complications. Despite major progress in neonatal care, approximately 50% of survivors develop complications such as mental retardation, cerebral palsy or epilepsy. The C3a receptor (C3aR) is expressed by many cell types including neurons and glia. While there is a body of evidence for its deleterious effects in the acute phase after ischemic injury to the adult brain, C3aR signaling contributes to better outcome in the post-acute and chronic phase after ischemic stroke in adults and in the ischemic immature brain. Here we discuss recent insights into the novel roles of C3aR signaling in the ischemic brain with focus on the therapeutic opportunities of modulating C3aR activity to improve the outcome after ischemic stroke and birth asphyxia.

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