Cerebral palsy research news

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Interventions and Management

1. Early interventions in infants with unilateral cerebral palsy: A systematic review and narrative synthesis
Lisa Mailleux, Nathalie De Beukelaer, Maria-Belén Carbone, Els Ortibus

Review Res Dev Disabil. 2021 Aug 16;117:104058. doi: 10.1016/j.ridd.2021.104058. Online ahead of print.

Background: Recent systematic reviews have already provided an overview of the impact of early interventions on developmental outcomes in infants at risk for cerebral palsy. However, none has thus far focused specifically on how early interventions might improve motor outcome in infants diagnosed with unilateral cerebral palsy (uCP). Hence, the aim of this systematic review was to provide an overview of early intervention programs used in infants with uCP to improve motor outcome. Methods: A systematic literature search was performed in PubMed, Embase, Cochrane Central Register of Controlled trials, CINAHL and Web of Science following the PRISMA-statement guidelines. Risk of bias was assessed using the Cochrane risk-of-bias 2 tool. Results: Three single-blinded randomized controlled trials (RCTs) were identified, including 88 infants with uCP. These RCTs suggest that modified constraint-induced movement therapy (mCIMT) is effective and safe for improving upper limb function in infants with uCP. Bimanual training compared to mCIMT was found to be equally effective in one study. No clinical or neurological predictors of treatment response could be identified yet. Conclusion: Although more high-quality RCTs are urgently needed, early interventions seem effective, safe and feasible to apply in infants with uCP for improving upper limb motor function. This underlines the importance of prompt referral to diagnostic-specific centres to start up such early interventions.

PMID: 34412011

2. Between Limb Muscle Co-activation Patterns in the Paretic Arm During Non-paretic Arm Tasks in Hemiparetic Cerebral Palsy
Nayo M Hill, Theresa Sukal-Moulton, Julius P A Dewald

Front Neurosci. 2021 Jul 29;15:666697. doi: 10.3389/fnins.2021.666697. eCollection 2021.

Tasks of daily life require the independent use of the arms and hands. Individuals with hemiparetic cerebral palsy (HCP) often experience difficulty with fine motor tasks demonstrating mirrored movements between the arms. In this study, bilateral muscle activations were quantified during single arm isometric maximum efforts and submaximal reaching tasks. The magnitude and direction of mirrored activation was examined in 14 individuals with HCP and 9 age-matched controls. Participants generated maximum voluntary torques (MVTs) in five different directions and completed ballistic reaches while producing up to 80% of shoulder abduction MVT. Electromyography (EMG) signals were recorded from six upper extremity muscles bilaterally. Participants with HCP demonstrated more mirrored activation when volitionally contracting the non-paretic (NP) arm than the paretic arm ($F = 83.543$, $p < 0.001$) in isometric efforts. Increased EMG activation during reach

acceleration resulted in a larger increase in rest arm co-activation when reaching with the NP arm compared to the paretic arm in the HCP group ($t = 8.425$, $p < 0.001$). Mirrored activation is more pronounced when driving the NP arm and scales with effort level. This directionality of mirroring is indicative of the use of ipsilaterally terminating projections of the corticospinal tract (CST) originating in the non-lesioned hemisphere. Peripheral measures of muscle activation provide insight into the descending pathways available for control of the upper extremity after early unilateral brain injury.

PMID: 34393702

3. Exploring Clinical and Neurophysiological Factors Associated with Response to Constraint Therapy and Brain Stimulation in Children with Hemiparetic Cerebral Palsy
Hsing-Ching Kuo, Jennifer Litzenberger, Alberto Nettel-Aguirre, Ephrem Zewdie, Adam Kirton

Dev Neurorehabil. 2021 Aug 14;1-10. doi: 10.1080/17518423.2021.1964103. Online ahead of print.

Background: Perinatal stroke causes hemiparetic cerebral palsy (HCP) and lifelong disability. Constraint-induced movement therapy (CIMT) and neurostimulation may enhance motor function, but the individual factors associated with responsiveness are undetermined. Objective: We explored the clinical and neurophysiological factors associated with responsiveness to CIMT and/or brain stimulation within a clinical trial. Methods: PLASTIC CHAMPS was a randomized, blinded, sham-controlled trial ($n = 45$) of CIMT and neurostimulation paired with intensive, goal-directed therapy. Primary outcome was the Assisting Hand Assessment (AHA). Classification trees created through recursive partitioning suggested clinical and neurophysiological profiles associated with improvement at 6-months. Results: Both clinical (stroke side (left) and age >14 years) and neurophysiological (intracortical inhibition/facilitation and motor threshold) were associated with responsiveness across treatment groups with positive predictive values (PPV) approaching 80%. Conclusion: This preliminary analysis suggested sets of variables that may be associated with response to intensive therapies in HCP. Further modeling in larger trials is required.

PMID: 34392795

4. Combined intensive therapies at home in spastic unilateral cerebral palsy with high bimanual functional performance. What do they offer? A comparative randomised clinical trial
Rocío Palomo-Carrión, Cristina Lirio-Romero, Asunción Ferri-Morales, Patricia Jovellar-Isiegas, María-Dolores Cortés-Vega, Helena Romay-Barrero

Ther Adv Chronic Dis. 2021 Aug 12;12:20406223211034996. doi: 10.1177/20406223211034996. eCollection 2021.

Background: Children with unilateral spastic cerebral palsy (USCP) receive different treatments, including the application of modified constraint induced movement therapy (mCIMT) or bimanual intensive therapy (BIT) to increase affected upper limb functionality. The aim of this study was to compare the effectiveness of two protocols with different proportions and orders of mCIMT/BIT within combined intensive home-therapy in children with USCP (6-8 years old) with high bimanual functional performance, applied by the family. Methods: The protocols were performed on 20 children with an average age of 7.12 years [standard deviation (SD): 0.70], allocated to two different combined therapies. The protocols were designed by 100 h of dose for 10 weeks: 80 h of mCIMT followed by 20 h of BIT (mCIMT-B group) and 80 h of BIT followed by 20 h of mCIMT (BIT-mCI group). Bimanual functional performance was measured with Assisting Hand Assessment Scale (AHA) and the affected upper limb-use experience with Children's Hand-use Experience Questionnaire (CHEQ). Parent satisfaction and expectations with therapy were measured using a specific questionnaire. There were five assessment timepoints (week 0, week 4, week 8, week 10 and week 34). Results: There were no statistically significant ($p > 0.05$) inter- and intra-group changes in the bimanual functional performance of both groups. The affected upper limb-use experience obtained significant changes in BIT-mCI group, with statistically significant differences in the pairwise comparisons between week 0-10 and week 4-10 ($p = 0.028$) for use of the affected hand and the use of the affected hand to grasp between week 4 and week 8 ($p = 0.028$). Grasp efficacy and discomfort acquired statistically significant differences only in the BIT-mCI group for pairwise comparisons week 0-week 10/ week 4-week 10 ($p = 0.035$). Although task execution time compared with a typically developing child of the same age obtained statistically significant differences only in the group mCIMT-B for pairwise comparisons week 0-week 8 ($p = 0.03$), week 0-week 10 ($p = 0.03$), week 4-week 8 ($p = 0.04$) and week 4-week 10 ($p = 0.03$). Family satisfaction and expectations acquired an increase between week 0 and week 10 ($p \leqslant 0.02$). Conclusion: Applying 80 h of BIT for 8 weeks in children with high bimanual functional performance USCP (6-8 years old), executed at home with family involvement would be sufficient to obtain improvements in affected upper limb-use experience, without the need to use combined protocols of 100 h. However, no statistically significant increase in bimanual functional performance would be obtained, with the basal situation of the child

being a factor to consider for the execution of mCIMT and BIT. Registration number and name of trial registry: [ClinicalTrials.gov identifier: NCT03465046].

PMID: 34408823

5. In children with cerebral palsy, does spinal fusion surgery for scoliosis improve lung function?
Katherine Lehovsky

Arch Dis Child. 2021 Aug 18;archdischild-2021-322600. doi: 10.1136/archdischild-2021-322600. Online ahead of print.

PMID: 34407955

6. Effect of muscle strength training in children and adolescents with spastic cerebral palsy: A systematic review and meta-analysis
Javier Merino-Andrés, Agustín García de Mateos-López, Diane L Damiano, Alberto Sánchez-Sierra

Clin Rehabil. 2021 Aug 18;2692155211040199. doi: 10.1177/02692155211040199. Online ahead of print.

Objective: This systematic review and meta-analysis investigates the effects of strength training program in children and adolescents with cerebral palsy to improve function, activity, and participation. Data sources: Five electronic databases (MEDLINE-Pubmed, Cochrane Library, PEDro, CINAHL, and SPORTDiscus) were systematically searched for full-text articles published from inception to 30 June 2021. Review methods: Randomized controlled trials were included, who compared: (i) child population with spastic cerebral palsy population between 0 and 22 years; (ii) studies in which a muscle strength training program was performed and included dosing information; (iii) studies comparing strength training with other physical therapy technique(s) or untreated control group. Studies with similar outcomes were pooled by calculating standardized mean differences. Risk of bias was assessed with Cochrane Collaboration's tool for assessing the risk of bias and PROSPERO's registration number ID: CRD42020193535. Results: Twenty-seven studies, comprising 847 participants with spastic cerebral palsy. The meta-analyses demonstrated significant standardized mean differences in favor of strength training program compared to other physical therapy technique(s) or untreated control group(s) for muscle strength at the knee flexors, at the knee extensor, at the plantarflexors, maximum resistance, balance, gait speed, GMFM (global, D and E dimension) and spasticity. Conclusion: A strength training program has positive functional and activity effects on muscle strength, balance, gait speed, or gross motor function without increasing spasticity for children and adolescents with cerebral palsy in Gross Motor Function Classification System levels I, II, and III when adequate dosage and specific principles are utilized.

PMID: 34407619

7. Intraoperative Fracture of a Dual Modular Delta Ceramic Femoral Head During Total Hip Arthroplasty: A Case Report
Harold I Salmons, Sean P Ryan, Robert T Trousdale

JBJS Case Connect. 2021 Aug 16;11(3). doi: 10.2106/JBJS.CC.21.00215.

Case: A 39-year-old man with cerebral palsy and hip dysplasia status post right Chiari osteotomy presented with right hip osteoarthritis in consultation for total hip arthroplasty (THA). During THA, a Delta ceramic head was misaligned on the taper, but this was obscured by an overlying dual modular polyethylene shell. When we attempted to tap the head onto the taper, fracture occurred requiring revision to a cobalt-chromium head due to slight taper damage. Conclusion: To our knowledge, this is the first reported case of intraoperative fracture of a BIOLOX Delta dual modular head.

PMID: 34398843

8. Biomechanical assessment of patellar tendon advancement in patients with cerebral palsy and crouch gait
Derya Karabulut, Yunus Ziya Arslan, Firooz Salami, Sebastian I Wolf, Marco Götze

Knee. 2021 Aug 16;32:46-55. doi: 10.1016/j.knee.2021.07.010. Online ahead of print.

Background: Patellar height is a valuable measure to evaluate the effect of patellar tendon advancement (PTA) on knee function. In the literature, there is no validated procedure to measure the patellar height. In this study we aimed to (1) determine the patella position through musculoskeletal modeling, (2) investigate the effects of two surgical procedures applied for PTA, and (3) assess the effect of PTA in combination with single-event multilevel surgery (SEMLS) on the knee kinematics of patients with cerebral palsy (CP) and crouch gait. Method: Three-dimensional gait and X-ray data of children with CP and crouch gait were retrospectively analyzed if they had received a SEMLS in combination with PTA (PTA group, n = 18) or without PTA (NoPTA group, n = 18). A computational musculoskeletal model was used to quantify patella position, knee extension moment arm, and knee kinematics pre- and postoperatively. Results: Patellar height significantly decreased in the PTA group (P = 0.004), while there was no difference in the NoPTA group (P > 0.05). The bony procedure for PTA provided a better Insall-Salvati ratio than the soft tissue procedure. The peak knee extension moment arm significantly increased in the PTA group (P = 0.008). In terms of postoperative knee joint kinematics, the PTA group was closer to typically developed children than the NoPTA group. Conclusion: Musculoskeletal modeling was found to be an effective tool for the determination of the patellar height. PTA improved the patella position, knee extension moment arm, and knee kinematics and was an effective procedure for the surgical management of crouch gait in patients with CP.

PMID: 34411886

9. Acquisition and loss of best walking skills in children and young people with bilateral cerebral palsy
Gillian Baird, Susie Chandler, Adam Shortland, Elspeth Will, Emily Simonoff, David Scrutton, Charlie Fairhurst

Dev Med Child Neurol. 2021 Aug 19. doi: 10.1111/dmcn.15015. Online ahead of print.

Aim: To explore factors predicting acquisition and loss of best walking ability in young people with bilateral cerebral palsy (CP). Method: In our population cohort (Study of Hips And Physical Experience) of 338 children (201 males, 137 females) with bilateral CP, age at achieving walking was recorded and walking ability predicted from early motor milestones. Walking was assessed at 5 to 8 years (mean 7y) and in 228 of 278 survivors at 13 to 19 years (mean 16y). Parent carers reported their view of any loss of best achieved walking. Factors potentially associated with loss of best achieved walking were explored: severity and type of motor disorder; intellect and communication; manipulative skill; general health and comorbidity; pain; orthopaedic surgery; musculoskeletal spine and lower limb deformity; weight; fatigue; mood; and presence of regular exercise regime. Results: The ability to walk independently was reliably predicted by the motor milestone 'getting to sit and maintain sitting' by the age of 36 months (without aids) and 55 months (with aids). Forty-five per cent of the cohort never walked 10 steps independently. Not all who achieved walking without aids were still doing so by a mean age of 16 years, which was associated with later age at achieving walking and the degree of musculoskeletal deformity, as was the parent carers' report of loss of best walking. Interpretation: In this study, development of musculoskeletal deformity was a significant factor in not maintaining best achieved walking by mean age 16 years, which is most likely to occur in young people whose walking ability is with aids over short distances or in therapy only. Prediction of future walking ability in a child with bilateral CP can be made from early motor milestones.

PMID: 34410016

10. Factors associated with walking activity in adults with cerebral palsy
Nancy Lennon, Chris Church, Thomas Shields, M Wade Shrader, John Henley, Tim Niiler, Julieanne P Sees, Freeman Miller

Gait Posture. 2021 Aug 8;90:43-47. doi: 10.1016/j.gaitpost.2021.08.005. Online ahead of print.

Background: This prospective study used instrumented gait analysis, patient-reported outcomes, and portable accelerometers to examine walking activity in adults with cerebral palsy (CP). Research question: This study aimed to provide objective data and evaluate factors associated with walking activity in adults with CP. Methods: Participants with CP (ages 25-45 years) completed instrumented gait analysis and patient-reported outcomes, including the Patient Reported Outcome Measurement

Information System (PROMIS) and Satisfaction with Life Score (SWLS), and wore a StepWatch for 8 days. Average strides per day, stratified by Gross Motor Function Classification System (GMFCS), were compared with nondisabled adults ages 30-39 years utilizing Welch's t-tests with Bonferroni corrections. Correlation coefficients and stepwise multiple linear regression analyses examined relationships between walking activity and GMFCS, gait deviation index (GDI), gait velocity, PROMIS physical function, SWLS, body mass index (BMI), and employment. Results: Participants included 109 adults with CP, ages 29 ± 4 years, classified at GMFCS levels I/II (73 %) and III/IV (27 %). Compared with nondisabled adults, daily stride count was significantly lower in both groups of adults with CP ($p < 0.00025$), with a progressive decline according to GMFCS level. Walking activity correlated with PROMIS physical function ($r = .42$), GDI ($r = .48$), and gait velocity ($r = .58$). Association for employment was lower ($r = 0.27$) but significant, while age, SWLS, and BMI were not individually correlated with walking activity. Stepwise, multiple linear regression modeled with Akaike information criterion explained 40.9 % of the observed variability in walking activity in this cohort of adults with CP. Significance: Physical function, as classified by GMFCS or measured by PROMIS and self-selected walking velocity, has the strongest association with and is the most significant predictor of walking activity in adults with CP. After accounting for physical function, a small amount of the variation in walking activity can be explained by GDI, employment, and age.

PMID: 34390921

11. Effectiveness of a Multi-Modal Exercise Program Incorporating Plyometric and Balance Training in Children With Hemiplegic Cerebral Palsy: A Three-Armed Randomized Clinical Trial
Ragab K Elnaggar, Waleed S Mahmoud, Saud F Alsubaie, Walaa A Abd El-Nabie

Phys Occup Ther Pediatr. 2021 Aug 15;1-17. doi: 10.1080/01942638.2021.1964674. Online ahead of print.

Aim: To evaluate the effectiveness of a multimodal exercise program incorporating plyometric and balance training on muscle strength and postural stability in children with spastic hemiplegic cerebral palsy (SHCP). Methods: A total of 57 children with SHCP were enrolled in the study and randomly allocated into three treatment-based groups: plyometric exercises (PLYO group; n = 19), balance exercises (BAL group, n = 19), and combined plyometric and balance exercises (PLYO-BAL group; n = 19). The maximum isometric muscle strength (IMSmax) and postural stability [anterior-posterior stability index (AP-SI), mediolateral stability index (ML-SI), and overall stability index (O-SI)] were measured pre- and post-intervention. Results: By applying the intention-to-treat analysis, the PLYO-BAL group showed greater post-treatment IMSmax than the PLYO and BAL groups for the quadriceps ($p=.03$ and $p=.0002$ respectively), hamstrings ($p=.018$ and $p<.0001$ respectively), and dorsiflexors ($p=.006$ and $p<.0001$ respectively). Also, the PLYO-BAL group achieved better post-intervention stability scores as compared to PLYO and BAL groups regarding AP-SI ($p<.0001$ and $p=.0001$ respectively), ML-SI ($p=.001$ and $p=.015$ respectively), and O-SI ($p=.011$ and $p=.04$ respectively). Conclusions: Incorporation of plyometric and balance exercises in a multimodal rehabilitation program could be an important consideration for enhancing muscle strength and boosting postural stability in children with SHCP.

PMID: 34396891

12. Safety and feasibility of symptom-limited cardiopulmonary exercise test using the modified Naughton protocol in children with cerebral palsy: An observational study
Ah-Ran Kim, Min-Hwa Suk, Jeong-Yi Kwon

Medicine (Baltimore). 2021 Jul 23;100(29):e26269. doi: 10.1097/MD.0000000000026269.

Variables derived from the cardiopulmonary exercise test (CPX) provide objective information regarding the exercise capacity of children with cerebral palsy (CP), which can be used as the basis for exercise recommendations. Performing maximal CPX might not be appropriate, safe, or practical for children with CP. In the present study, the safety and feasibility of symptom-limited CPX using the modified Naughton protocol, a submaximal protocol, were investigated in children with CP, Gross Motor Function Classification System (GMFCS) level I or II. The present study included 40 children aged 6 to 12 years with CP who underwent symptom-limited CPX. CPX was performed to measure cardiopulmonary fitness using a treadmill with a modified Naughton protocol. Motor capacity was assessed using the Gross Motor Function Measure (GMFM), Pediatric Balance Scale (PBS), Timed Up and Go (TUG) test, and 6-minute walk test. Thirty-seven children with CP successfully completed testing without any adverse events during or immediately after CPX (dropout rate 7.5%). The reason for test termination was dyspnea (51.4%) or leg fatigue (48.6%). Based on the respiratory exchange ratio (RER), 21 of 37 (56.8%) children chose premature termination. The relationship between the reason for test termination and RER was not statistically

significant (Spearman rho = 0.082, P = .631). CPX exercise time was strongly correlated with GMFM (Spearman rho = 0.714) and moderate correlation with PBS (Spearman rho = 0.690) and TUG (Spearman rho = 0.537). Peak oxygen uptake during CPX showed a weak correlation with GMFM and a moderate correlation with PBS. This study revealed that symptom-limited CPX using the modified Naughton protocol was safe and feasible for children with CP and GMFCS level I or II.

PMID: 34398001

13. Intensive repetitive motor training: how does it work in children with cerebral palsy?
Bernard Dan

Editorial Dev Med Child Neurol. 2021 Sep;63(9):1008. doi: 10.1111/dmcn.14970.

PMID: 34415626

14. Assessment of Hearing in Children with Cerebral Palsy
G S Khaydarova, A Madrimova, Kh E S Shaykhova

Int Tinnitus J. 2021 Mar 1;25(1):23-28. doi: 10.5935/0946-5448.2020006.

The objective of this study is to identify the prevalence and nature of auditory analyzer pathology in children with different forms of infant cerebral palsy by recording otoacoustic emission and recording short latency brainstem auditory evoked potentials. The subject group consisted of 75 children, 40 (53%) males and 35 (47%) were females, ranging from 3 to 14 years of age with a confirmed diagnosis of cerebral palsy on the basis of a psycho-neurological hospital in Tashkent. (Uzbekistan). The examination of children was carried out by the following methods: clinical examination of patients (general and otorhinolaryngological) and functional research methods of the auditory analyzer. All children underwent acoustic impedancemetry, including tympanometry with determination of the type of tympanogram and acoustic reflex. The data obtained revealed a bilateral lesion of the peripheral part of the auditory analyzer. Beilateral sensorineural hearing loss was detected in 21 - I - II degree, in 12 - III degree and in 15 - IV degree. Marked changes in the main parameters of BAEP were detected in the study of the stem structures of the auditory analyzer in children with cerebral palsy. Thus, disorganization, configuration disturbances of the component composition (I, III, V) were noted. Thus, the study revealed a disorder of auditory function by sound-detecting type and justified the need for hearing correction in these children. Evaluation of auditory function made it possible to determine the level of auditory analyzer injury and localization of the process from the results of a complex, objective examination.

PMID: 34410075

15. Unequal physical activity among children with cerebral palsy in Sweden-A national registry study
Frida Degerstedt, Martin Björklund, Britt-Inger Keisu, Birgit Enberg

Health Sci Rep. 2021 Aug 9;4(3):e342. doi: 10.1002/hsr2.342. eCollection 2021 Sep.

Aim: To examine the extent to which sex, country of birth, and functional aspects influence participation in physical education and physical leisure activity among children with cerebral palsy (CP) in Sweden. Methods: This national cross-sectional registry study included children with CP aged 6 to 18 years who participated in the Swedish national quality registry, the Cerebral Palsy Follow-up Program, CPUP, in 2015. Comparisons and associations between sex, country of birth, and functional aspects and physical leisure/physical education were examined using chi-squared and multivariable logistic regression analysis. Results: The study included 1935 children. Of them, 1625 (87%) reported participating in physical education and 989 (53%) reported participating in physical leisure activity. Children born in Sweden had higher odds of participating in physical education (OR: 1.99; 95% CI: 1.20-3.28) and physical leisure activity (OR: 2.51; 95% CI: 1.70-3.72) compared with children born outside Europe. Greater impairment of gross motor function was associated with lower participation levels. Boys participated slightly more frequently in leisure activities than girls. Conclusion: Enhancing social inclusion with regard to disability, birth country, and sex are important and achievable goals for policymakers and practitioners

for promoting participation in physical activity for children and adolescents with CP.

PMID: 34401523

16. Oligodendroglial ring finger protein Rnf43 is an essential injury-specific regulator of oligodendrocyte maturation
Jianqin Niu, Guangdan Yu, Xiaorui Wang, Wenlong Xia, Yuxin Wang, Kimberly K Hoi, Feng Mei, Lan Xiao, Jonah R Chan, Stephen P J Fancy

Neuron. 2021 Aug 5;S0896-6273(21)00539-0. doi: 10.1016/j.neuron.2021.07.018. Online ahead of print.

Oligodendrocyte (OL) maturation arrest in human white matter injury contributes significantly to the failure of endogenous remyelination in multiple sclerosis (MS) and newborn brain injuries such as hypoxic ischemic encephalopathy (HIE) that cause cerebral palsy. In this study, we identify an oligodendroglial-intrinsic factor that controls OL maturation specifically in the setting of injury. We find a requirement for the ring finger protein Rnf43 not in normal development but in neonatal hypoxic injury and remyelination in the adult mammalian CNS. Rnf43, but not the related Znrf3, is potently activated by Wnt signaling in OL progenitor cells (OPCs) and marks activated OPCs in human MS and HIE. Rnf43 is required in an injury-specific context, and it promotes OPC differentiation through negative regulation of Wnt signal strength in OPCs at the level of Fzd1 receptor presentation on the cell surface. Inhibition of Fzd1 using UM206 promotes remyelination following ex vivo and in vivo demyelinating injury.

PMID: 34390652

17. Are COL4A1 and COL4A2 gene polymorphisms associated with cerebral palsy?
Orhan Güvener, Melek Sezgin, Özlem Tezol, İbrahim Ömer Barlas, Asena Ayça Özdemir, Emine Arzu Kanık

Turk J Phys Med Rehabil. 2021 May 25;67(2):242-249. doi: 10.5606/tftrd.2021.5481. eCollection 2021 Jun.

Objectives: This study aims to investigate the association of COL4A1 and COL4A2 gene polymorphisms with susceptibility to risk of developing cerebral palsy (CP) and severity of CP. Patients and methods: Between December 2016 and June 2017, a total of 176 patients with CP (101 males, 75 females; mean age 71.8±37.9 months; range, 24 to 184 months) and age-, sex-, and ethnically-matched 178 (90 males, 88 females; mean age 69.3±55.2 months; range, 24 to 214 months) controls were included. Two polymorphisms of COL4A1 (rs1961495) and COL4A2 (rs9521733) genes were typed from genomic deoxyribonucleic acid. Genotype distributions and allelic frequencies were compared between the patient and control groups. Gross Motor Function Classification System, the use of medical drugs, type of involvement, number of affected limbs, accompanying conditions, birth weight, gestational age, and magnetic resonance imaging (MRI) findings were used to evaluate the disease severity and their relationships with the COL4A1 and COL4A2 gene polymorphisms. Results: There was no statistically significant difference between the groups in terms of genotype distribution and allele frequency of COL4A1 and COL4A2 gene polymorphisms ($p>0.05$). In addition, there was no relationship between severity of CP and two gene polymorphisms ($p>0.05$). A significant association was detected between the COL4A2 polymorphism and growth retardation in CP. The TT genotype (57.1%) and T allele (76.2%) were higher, compared to CC (4.8%) and CT genotypes (38.1%) and C allele (23.8%) in patients with CP with growth retardation ($p=0.03$ for genotype and $p=0.01$ for allele frequency). Conclusion: These findings suggest that COL4A1 and COL4A2 gene polymorphisms are not associated with susceptibility to CP in a group of Turkish populations, although COL4A2 gene polymorphism may be associated with growth retardation in patients with CP.

PMID: 34396076

18. Genetic counseling considerations in cerebral palsy
Alison M Elliott, Colleen Guimond

Review Mol Genet Metab. 2021 Jul 18;S1096-7192(21)00755-1. doi: 10.1016/j.ymgme.2021.07.004. Online ahead of print.

Genome-wide sequencing (exome and whole genome) has transformed our ability to diagnose patients with suspected genetic disorders. Cerebral palsy (CP), although historically thought to be due to birth injury (perinatal hypoxia), represents a clinical spectrum of disorders, many of which have been attributed to a genetic cause. GWS has elucidated the underlying single gene cause for many patients with CP and has important implications for the customization of treatment, management, and genetic counseling. International guidelines recommend genetic counseling for all families considering genome-wide sequencing. Genetic counselors educate and support families and help them to make testing decisions based on their values. They can help families adapt to, and understand the implications of a genomic diagnosis. Here, we review advances in sequencing for CP, clinical features suggestive of a genetic etiology of CP, practice guidelines for GWS, and a practical approach to the genetic counseling of these families. This includes: the content to be addressed in pre-test and post-test genetic counseling sessions, the benefits of a establishing a genetic cause and importantly, the need for ongoing support.

PMID: 34389249

19. Automating Quantitative Measures of an Established Conventional MRI Scoring System for Preterm-Born Infants Scanned between 29 and 47 Weeks' Postmenstrual Age

L van Eijk, M Seidel, K Pannek, J M George, S Fiori, A Guzzetta, A Coulthard, J Bursle, R S Ware, D Bradford, S Rose, P B Colditz, R N Boyd, J Fripp

AJNR Am J Neuroradiol. 2021 Aug 19. doi: 10.3174/ajnr.A7230. Online ahead of print.

Background and purpose: Conventional MR imaging scoring is a valuable tool for risk stratification and prognostication of outcomes, but manual scoring is time-consuming, operator-dependent, and requires high-level expertise. This study aimed to automate the regional measurements of an established brain MR imaging scoring system for preterm neonates scanned between 29 and 47 weeks' postmenstrual age. Materials and methods: This study used T2WI from the longitudinal Prediction of PREterm Motor Outcomes cohort study and the developing Human Connectome Project. Measures of biparietal width, interhemispheric distance, callosal thickness, transcerebellar diameter, lateral ventricular diameter, and deep gray matter area were extracted manually (Prediction of PREterm Motor Outcomes study only) and automatically. Scans with poor quality, failure of automated analysis, or severe pathology were excluded. Agreement, reliability, and associations between manual and automated measures were assessed and compared against statistics for manual measures. Associations between measures with postmenstrual age, gestational age at birth, and birth weight were examined (Pearson correlation) in both cohorts. Results: A total of 652 MRIs (86%) were suitable for analysis. Automated measures showed good-to-excellent agreement and good reliability with manual measures, except for interhemispheric distance at early MR imaging (scanned between 29 and 35 weeks, postmenstrual age; in line with poor manual reliability) and callosal thickness measures. All measures were positively associated with postmenstrual age ($r = 0.11$-0.94; $R2 = 0.01$-0.89). Negative and positive associations were found with gestational age at birth ($r = -0.26$-0.71; $R2 = 0.05$-0.52) and birth weight ($r = -0.25$-0.75; $R2 = 0.06$-0.56). Automated measures were successfully extracted for 80%-99% of suitable scans. Conclusions: Measures of brain injury and impaired brain growth can be automatically extracted from neonatal MR imaging, which could assist with clinical reporting.

PMID: 34413061

20. Rehabilitation after single-event multilevel surgery for children and young adults with cerebral palsy: A systematic review

Anne-Laure Guinet, Néjib Khouri, Eric Desailly

Am J Phys Med Rehabil. 2021 Aug 13. doi: 10.1097/PHM.0000000000001864. Online ahead of print.

This review sought to describe and analyze published protocols for rehabilitation after single-event multilevel surgery (SEMLS) for people with cerebral palsy (CP), to identify their differences and limits, and to introduce a common step-by-step framework for future descriptions and assessments of postoperative rehabilitation protocols. The MEDLINE, EMBASE, CINAHL, and the Cochrane Library databases were searched. Inclusion criteria were: (1) SEMLS, (2) full-text reports published after 1985, and (3) papers with a method section describing the rehabilitation protocol. Interventions were coded using the Oxford Levels of Evidence and the MINORS Index. Twenty-four articles were included in the review. Studies included patients aged 4-30 years with spastic CP (hemiplegia, diplegia, and quadriplegia). The mean postoperative rehabilitation duration was 4.5 months, with 4 sessions per week, and rehabilitation took place in a rehabilitation center. This review provides relevant information about the modalities, contents, limits, and difficulties associated with the post-SEMS rehabilitation protocol reported in the literature. Pain was identified as a major problem. A more precise and comprehensive

description of post-SEMS rehabilitation protocols would be useful. The proposed 5-step framework could be used by future studies to standardize their protocol description in terms of objective, content, and intensity.

PMID: 34393188

21. Aberrant somatosensory phase synchronization in children with hemiplegic cerebral palsy
Yanlong Song, Emmanuelle Renoul, Stephanie Acord, Yvette R Johnson, Warren Marks, George Alexandrakis, Christos Papadelis

Neurosci Lett. 2021 Aug 11;762:136169. doi: 10.1016/j.neulet.2021.136169. Online ahead of print.

Children with hemiplegic cerebral palsy (HCP) often show disturbances of somatosensation. Despite extensive evidence of somatosensory deficits, neurophysiological alterations associated with somatosensory deficits in children with HCP have not been elucidated. Here, we aim to assess phase synchrony within and between contralateral primary (S1) and secondary (S2) somatosensory areas in children with HCP. Intra-regional and inter-regional phase synchronizations within and between S1 and S2 were estimated from somatosensory evoked fields (SEFs) in response to passive pneumatic stimulation of contralateral upper extremities and recorded with pediatric magnetoencephalography (MEG) in children with HCP and typically developing (TD) children. We found aberrant phase synchronizations within S1 and between S1 and S2 in both hemispheres in children with HCP. Specifically, the less-affected (LA) hemisphere demonstrated diminished phase synchronizations after the stimulus onset up to ~120 ms compared to the more-affected (MA) hemisphere and the dominant hemisphere of TD children, while the MA hemisphere showed enhanced phase synchronizations after ~100 ms compared to the LA hemisphere and the TD dominant hemisphere. Our findings indicate abnormal somatosensory functional connectivity in both hemispheres of children with HCP.

PMID: 34390772

22. Kindy Moves: a protocol for establishing the feasibility of an activity-based intervention on goal attainment and motor capacity delivered within an interdisciplinary framework for preschool aged children with cerebral palsy
Dayna Pool, Catherine Elliott, Healthy Strides Research Advisory Council

BMJ Open. 2021 Aug 13;11(8):e046831. doi: 10.1136/bmjopen-2020-046831.

Introduction: Preschool aged children with cerebral palsy (CP) and like conditions are at risk of performing below their peers in key skill areas of school readiness. Kindy Moves was developed to support school readiness in preschool aged children with CP and like conditions that are dependent on physical assistance and equipment throughout the day. The primary aims are to determine the feasibility of motor-based interventions that are functional and goal directed, adequately dosed and embedded into a play environment with interdisciplinary support to optimise goal-driven outcomes. Methods and analysis: Forty children with CP and like conditions aged between 2 and 5 years with a Gross Motor Function Classification System (GMFCS) level of III-V or equivalent, that is, dependent on physical assistance and equipment will be recruited in Western Australia. Participants will undertake a 4-week programme, comprised three, 2-hour sessions a week consisting of floor time, gross motor movement and play (30 min), locomotor treadmill training (30 min), overground walking in gait trainers (30 min) and table-top activities (30 min). The programme is group based with 3-4 children of similar GMFCS levels in each group. However, each child will be supported by their own therapist providing an interdisciplinary and goal directed approach. Primary outcomes of this feasibility study will be goal attainment (Goal Attainment Scale) and secondary outcomes will include Canadian Occupational Performance Measure, 10 metre walk test, Children's Functional Independence Measure, Sleep Disturbance Scale, Infant and Toddler Quality of Life Questionnaire, Peabody Developmental Motor Scale and Gross Motor Function Measure. Outcomes will be assessed at baseline, post intervention (4 weeks) and retention at the 4-week follow-up. Ethics and dissemination: Ethical approval was obtained from Curtin University Human Ethics Committee (HRE2019-0073). Results will be disseminated through published manuscripts in peer-reviewed journals, conference presentations and public seminars for stakeholder groups. Trial registration number: Australian New Zealand Clinical Trials Registry (ACTRN12619000064101p).

PMID: 34389566

23. Reliability and construct validity of the Activities Scale for Kids in Italian children with cerebral palsy
Stefania Costi, Maria Cristina Filippi, Luca Braglia, Laura Beccani, Isabella Corradi, Elena Bruzzi, Chiara Signorelli, Elisa Pelosin

Disabil Rehabil. 2021 Aug 20;1-7. doi: 10.1080/09638288.2021.1966519. Online ahead of print.

Purpose: To investigate internal consistency and construct validity of the of the Activities Scale for Kids performance (ASKp) in Italian children with cerebral palsy (CP). Methods: This cross-sectional study was conducted from 2014 up to 2019 and consisted in the single self-administration of the Italian ASKp to 206 children aged 5-15, with unilateral or bilateral CP, classified on the basis of the Gross Motor Function Classification System (GMFCS). Results: The ASKp showed good internal consistency (Chronbach's α 0.91, 95% CI 0.89-0.93). It distinguished between children and adolescents (70.3 ± 16.6 versus 83.0 ± 18.0, respectively; $p < 0.001$), unilateral and bilateral CP clinical manifestations (82.5 ± 13.6 versus 72.4 ± 19.0, respectively; $p = 0.002$), children with and without intellectual disability (60.3 ± 18.3 versus 77.2 ± 17.3, respectively; $p < 0.001$). It also distinguished children using assistive devices for indoor mobility from children who did not use devices or those who use devices only for outdoor mobility (66.1 ± 18.3 versus 83.6 ± 12.8 and versus 80.4 ± 17.4, respectively; both $p < 0.001$). Conclusions: The ASKp could help integrate the perspective of children with CP in their rehabilitation process. Trial registration: ClinicalTrials.gov Identifier: NCT03325842 IMPLICATIONS FOR REHABILITATION: The ASKp is a valid and widely used measure for several ICF domains of activities and participation in pediatrics. It has never been formally validated in children with CP, although this disorder causes restrictions in everyday activities. Recently, the culturally adapted Italian version of the ASKp has been tested in typically developing Italian children, confirming its high acceptability and providing evidence of construct validity. This study confirms the internal consistency reliability and the construct validity of the Italian ASKp when applied to the population with CP. The ASKp can support rehabilitation professionals in planning therapeutic intervention targeted to relevant goals.

PMID: 34415225

24. Reliability and validity of the Eating and Drinking Ability Classification System (EDACS) for children with cerebral palsy in Taiwan
Hsiu-Ching Chiu, Katherine Buckeridge, Ta-An Lee, Diane Sellers

Disabil Rehabil. 2021 Aug 16;1-7. doi: 10.1080/09638288.2021.1962989. Online ahead of print.

Purpose: The study was to assess the inter- and intra-rater reliability, construct validity and utility of the Eating and Drinking Ability Classification System (EDACS). Methods: EDACS was translated into in Taiwan using an interactive process. Agreement between health professionals and teachers when using EDACS was assessed using Kappa and the Intraclass Correlation Co-efficient. Results: Paired ratings of 4 (13%) health professionals (either speech or occupational therapists) and 26 (87%) teachers were obtained for 53 children with CP aged 6.7 years (SD 4.1 years), who worked in six education institutions. The raters used EDACS independently to classify children's eating and drinking ability and re-classified children's eating and drinking abilities after one month. Pairs of raters showed substantial agreement for the EDACS level at the first assessment ($k = 0.75$; absolute agreement = 81%; ICC = 0.94) and the second assessment ($k = 0.70$; absolute agreement = 77%; ICC = 0.95). The intra-rater reliability of EDACS level showed almost perfect agreement at rater 1 ($k = 0.87$; absolute agreement = 91%) and rater 2 ($k = 0.87$; absolute agreement = 91%). Conclusions: We conclude that the Chinese version of EDACS is valid and reliable to be easily used by health professionals and teachers to classify functional eating and drinking abilities in children with cerebral palsy. IMPLICATIONS FOR REHABILITATION: The Chinese version of EDACS is valid and reliable to be easily used. EDACS can be used by health professionals and teachers to classify functional eating and drinking abilities in children with cerebral palsy. The EDACS is analogous to other functional classification systems (i.e., GMFCS, MACS and CFCS) and specifically represents eating and drinking ability.

PMID: 34396878

25. Effects of tracheostomy on mothers of children with cerebral palsy
Deniz Mavi, Zeynep Reyhan Onay, Elif Yuksel Karatoprak, Sinem Can Oksay, Yetkin Ayhan, Irem Bulut, Gülay Bilgin, Alperen Bikmazer, Saniye Girit

Pediatr Pulmonol. 2021 Aug 19. doi: 10.1002/ppul.25635. Online ahead of print.

Objective: We aimed to investigate psychosocial changes such as burnout, caregiver burden, depression, and coping in mothers of children with cerebral palsy (CP) after tracheostomy placement. Design: A total of 48 children with CP and chronic respiratory insufficiency and their mothers participated in the study. The children with tracheostomy were classified as T (+) (n=26) and those who did not have tracheostomy were classified as T (-) (n=22). The patients with tracheostomy through invasive mechanical ventilation were classified as TIV (+). The data about the clinical conditions of the patients and the sociodemographic characteristics of the mothers were recorded. Zarit caregiver burden, Maslach burnout, Beck depression, and Coping Orientation to Problems Experienced (COPE) questionnaires were applied to all mothers. Findings: Beck depression score was 14±8.24 in T (+) group and 16.09±9.65 in T (-) group(p=.576). There was no significant difference between the T (+) and T (-) groups in the Maslach burnout inventory, Zarit caregiver burden scale, and their subgroups. The first two methods from the COPE scales were identical. In the T (+) group, the third coping method was found as "planning" and in the T (-) group as "active coping". Maslach burnout inventory, Zarit 1, and Zarit 2 scores were higher in patients with only tracheostomy compared to those with TIV (p=.002, p =.018, p =.021). Conclusion: In the study presented, the placement of tracheostomy in children with CP does not increase mother's depression tendencies and mood changes.

PMID: 34411467

26. Social participation: the perspectives of adolescents with cerebral palsy and their mothers
Priscila Bianchi Lopes, Keiko Shikako-Thomas, Roberta Cardoso, Thelma Simões Matsukura

Int J Dev Disabil. 2019 Jul 31;67(4):263-272. doi: 10.1080/20473869.2019.1623596. eCollection 2021.

Background: Social participation is a complex construct, thus different factors may facilitate or restrict engagement. Adolescents with Cerebral Palsy (CP) and their mothers often experience barriers in social participation. Therefore, they are frequently facing challenges in order to engage in meaningful activities, in different contexts. Objective: We aimed at exploring the perspectives of mothers and adolescents with CP on their social participation. Method: This is a cross-sectional and exploratory study, with a qualitative design. Seven adolescents with CP, aged from 11 to17 years old and their mothers, participated in a semi-structured interview, in São Paulo, Brazil. Data from interviews were analyzed with the Collective Subject Discourse (CSD) technique. Results: Mothers believed that their parenting practices contribute to the social participation of their children. Mothers revealed concerns about how to support the autonomy of their children and how to help them to establish meaningful and mature relationships. Adolescents with CP reported to engage in a range of social activities, with friends in different contexts, such as restaurants, cinema, concerts, parks and school. They also reported to appreciate social participation and to look for strategies in order to engage. Conclusions: This work can contribute to the understanding of social participation of adolescents with CP, under the perspective of these people and their mothers by allowing them to express their thoughts and voice their fears and limitations. Healthcare providers should adopt a lifespan approach to disabilities and recognize the unique challenges of adolescence in the life of both child and parents.

PMID: 34408861

27. Altered Somatosensory Cortical Activity Is Associated with Cortical Thickness in Adults with Cerebral Palsy: Multimodal Evidence from MEG/sMRI
Michael P Trevarrow, Brandon J Lew, Rashelle M Hoffman, Brittany K Taylor, Tony W Wilson, Max J Kurz

Cereb Cortex. 2021 Aug 20;bhab293. doi: 10.1093/cercor/bhab293. Online ahead of print.

Somatosensory cortical activity is altered in individuals with cerebral palsy (CP). However, previous studies have focused on the lower extremities in children with CP and have given less attention to structural changes that may contribute to these alterations. We used a multimodal neuroimaging approach to investigate the relationship between somatosensory cortical activity and cortical thickness in 17 adults with CP (age = 32.8 ± 9.3 years) and 18 healthy adult controls (age = 30.7 ± 9.8 years). Participants performed a median nerve paired-pulse stimulation paradigm while undergoing magnetoencephalography (MEG) to investigate somatosensory cortical activity and sensory gating. Participants also underwent magnetic resonance imaging to evaluate cortical thickness within the area of the somatosensory cortex that generated the MEG response. We found that the somatosensory responses were attenuated in the adults with CP (P = 0.004). The adults with CP also hypergated the second stimulation (P = 0.030) and had decreased cortical thickness in the somatosensory cortex (P = 0.015). Finally, the strength of the somatosensory response was significantly correlated with the cortical thickness (P = 0.023). These findings demonstrate that the aberrant somatosensory cortical activity in adults with CP extends to the upper extremities and appears to

be related to cortical thickness.

PMID: 34416763

Prevention and Cure

28. Efficacy of Antenatal Magnesium Sulfate for Neuroprotection in Extreme Prematurity: A Comparative Observational Study
Vandana Bansal, Avinash Desai

J Obstet Gynaecol India. 2021 Aug 8;1-12. doi: 10.1007/s13224-021-01531-9. Online ahead of print.

Background: Survival of preterm infants has improved drastically. In addition to significant contribution to neonatal mortality, impact of prematurity among survivors may continue through life impairing long-term physical life through neuro-disability and increased risk of cerebral palsy. Maternal administration of magnesium sulfate prior to impending preterm birth is an effective strategy to reduce neuromorbidity. Aim: To investigate the effectiveness of antenatal magnesium sulfate for neuroprotection in preterm infants between 26 and 34 weeks in preventing early neonatal morbidity and mortality. Secondary objective was to assess any adverse events with the use of magnesium sulfate on the mother and neonate. Method: This was a prospective observational comparative study for 2 years at our tertiary care hospital of 100 pregnant women who gave preterm births. Fifty infants each were born to mothers who were either not given MgSO4 (Group 1) or given 4gm intravenous loading dose MgSO4 (Group 2), preferably 4 h prior to preterm birth. Results: Among all the preterm in our study, 81% delivered between 30 and 34 weeks. There was no significant difference in terms of maternal mortality or serious morbidity including postpartum hemorrhage, caesarian section rates or length of hospital stay among women receiving MgSO4 versus no MgSO4. Mild maternal side effects secondary to magnesium sulfate were experienced in 8% cases. There were no significant differences between both groups for low 5 min APGAR, need for NICU admission, neonatal convulsions, hyperbilirubinemia, necrotizing enterocolitis, periventricular leukomalacia and septicemia. There was a trend toward reduced risk in the magnesium sulfate group for need for mechanical ventilation and ongoing respiratory support, intraventricular hemorrhage, neonatal hypotension, hypothermia, length of NICU stay. IVH was less frequent and less severe in babies exposed to antenatal MgSO4 (8%) as compared to non-MgSO4 group (16%). Neonatal morbidities were more when antenatal MgSO4 was given less than 4 h from delivery. Conclusion: MgSO4 is a safe drug to use in antenatal women at risk for impending preterm. Antenatal magnesium sulfate given to women in established preterm labor conferred significant neuroprotective advantage to the neonate. MgSO4 also has protective effect on the need of invasive ventilatory support in preterm infants. Given the breadth of evidence in its favor, it is time for us to start using MgSO4 in clinical practice for neuroprotective intent in all our extreme preterm births.

PMID: 34393393

29. Is the search for cerebral palsy 'cures' a reasonable and appropriate goal in the 2020s?
Ingrid Honan, Megan Finch-Edmondson, Christine Imms, Iona Novak, Amy Hogan, Shannon Clough, Bruce Bonyhady, Sarah McIntyre, Catherine Elliott, Shirley Wong, Michael Bink, Nadia Badawi

Review Dev Med Child Neurol. 2021 Aug 17. doi: 10.1111/dmcn.15016. Online ahead of print.

In the field of disability research and advocacy, the notion of 'cures' is contentious. Cerebral palsy (CP) is no exception. In this narrative review, we combine perspectives gained during community consultation undertaken for the Australian and New Zealand Cerebral Palsy Strategy, 2020 with those published in the scientific and grey literature to understand whether 'cures for CP' is a reasonable and appropriate goal. We frame these perspectives through the lens of several ethical principles central to the discussion. These include maintaining hope while also being realistic, sensitivity to sharply different viewpoints amongst people with disability and their families, and responding to community priorities, societal attitudes, and identity. Through this exploration of the literature and perspectives, we arrived at a definition of 'cures for CP' that is pluralized and focuses on functional improvement and/or symptom reduction whilst still acknowledging the potential for neural repair/regeneration strategies.

PMID: 34402053