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Cerebral palsy research news

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Interventions and Management

1. Combinatorial Effects of Transcutaneous Spinal Stimulation and Task-Specific Training to Enhance Hand Motor Output after Paralysis

Jeonghoon Oh, Michelle S Scheffler, Erin E Mahan, Shane T King, Catherine A Martin, Jenny Dinh, Alexander G Steele, Marcia K O'Malley, Dimitry G Sayenko

Top Spinal Cord Inj Rehabil. 2023 Fall;29(Suppl):15-22. doi: 10.46292/sci23-00040S. Epub 2023 Nov 17.

Background: Despite the positive results in upper limb (UL) motor recovery after using electrical neuromodulation in individuals after cervical spinal cord injury (SCI) or stroke, there has been limited exploration of potential benefits of combining task-specific hand grip training with transcutaneous electrical spinal stimulation (TSS) for individuals with UL paralysis. Objectives: This study investigates the combinatorial effects of task-specific hand grip training and noninvasive TSS to enhance hand motor output after paralysis. Methods: Four participants with cervical SCI classified as AIS A and B and two participants with cerebral stroke were recruited in this study. The effects of cervical TSS without grip training and during training with sham stimulation were contrasted with hand grip training with TSS. TSS was applied at midline over cervical spinal cord. During hand grip training, 5 to 10 seconds of voluntary contraction were repeated at a submaximum strength for approximately 10 minutes, three days per week for 4 weeks. Signals from hand grip dynamometer along with the electromyography (EMG) activity from UL muscles were recorded and displayed as visual feedback. Results: Our case study series demonstrated that combined task-specific hand grip training and cervical TSS targeting the motor pools of distal muscles in the UL resulted in significant improvements in maximum hand grip strength. However, TSS alone or hand grip training alone showed limited effectiveness in improving grip strength. Conclusion: Task-specific hand grip training combined with TSS can result in restoration of hand motor function in paralyzed upper limbs in individuals with cervical SCI and stroke.

PMID: 38174129

2. Epidural Spinal Cord Stimulation for Spasticity: a Systematic Review of the literature

Youngkyung Jung, Sara Breitbart, Anahita Malvea, Anuj Bhatia, George M Ibrahim, Carolina Gorodetsky

Review World Neurosurg. 2024 Jan 3:S1878-8750(24)00001-9. doi: 10.1016/j.wneu.2023.12.158. Online ahead of print.

Objective: Spasticity is a form of muscle hypertonia secondary to various pathologies, including traumatic brain injury, spinal cord injury, cerebral palsy, and multiple sclerosis. Medical treatments are available however these often result in insufficient clinical response. This review evaluates the role of epidural spinal cord stimulation (SCS) in the treatment of spasticity and associated functional outcomes. Methods: A systematic review of the literature was performed using the Embase, CENTRAL, and MEDLINE databases. We included studies that utilized epidural SCS to treat spasticity. Studies investigating functional electrical stimulation, transcutaneous SCS, and animal models of spasticity were excluded. We also excluded studies that used SCS to treat other symptoms such as pain. Results: Thirty-four studies were included in the final analysis. The pooled rate of subjective improvement in spasticity was 78% (95% CI 64%-91%, I2 = 77%), 40% (95% CI 7%-73%, I2 = 88%) for increased H reflex threshold or decreased Hoffman-reflex/muscle response wave ratio, and 73% (65%-80%, I2 = 50%) for

improved ambulation. Patients with spinal aetiologies had better outcomes compared to cerebral aetiologies. Up to 10% of patients experienced complications including infections and hardware malfunction. Conclusions: Our review of the literature suggests that SCS may be a safe and useful tool for the management of spasticity, however there is significant heterogeneity amongst studies. The quality of studies is also very low. As such, further studies are needed to fully evaluate the utility of this technology, including various stimulation paradigms across different aetiologies of spasticity.

PMID: 38181878

3. The Impact of Operative Correction of Equinus in Cerebral Palsy on Gait Patterns

Axel Horsch, Lara Petzinger, Julian Deisenhofer, Maher Ghandour, Matthias Klotz, Tobias Renkawitz, Cornelia Putz

Foot Ankle Int. 2023 Dec 29:10711007231217273. doi: 10.1177/10711007231217273. Online ahead of print.

Background: This study aimed to evaluate gait outcomes and strength following the surgical correction of equinus in cerebral palsy (CP) based on different surgical procedures. We included the Baumann and Strayer procedures, as well as the Achilles tendon lengthening (ATL). Methods: A retrospective analysis was performed in patients with infantile, bilateral CP who received instrumental 3D gait analysis before and after surgical correction (18.66 months postoperatively). Patients were divided into 3 groups: Strayer surgery, Baumann surgery, and ATL. Gait performance and muscle strengths were compared between studied surgeries. Results: A total population of 204 patients (15.43 years) with 341 operated lower limbs (LLs) was analyzed. Dorsiflexion in swing and stance phases significantly improved in all groups postoperatively. The Strayer and the ATL group showed higher postoperative dorsiflexion than the Baumann group. However, no loss of strength was observed with the Baumann method. Maximum power improved in this group postoperatively. An 8.2% loss in calf muscle strength was recorded in the Strayer group. Conclusion: Operative pes equinus treatment successfully improved the gait of children and adults with CP postoperatively. There were differences in postoperative results between studied operative techniques regarding range of motion and power. Level of evidence: Level III, retrospective cohort study.

PMID: 38156624

4. Evaluating the Role of Gracilis Release in Correcting Spastic In-Toeing Gait in Spastic Cerebral Palsy: A Case Report

Saksham Goyal, Ratnakar Ambade, Suhas Landge, Adarsh Jayasoorya, Rohan Chandanwale

Case Reports Cureus. 2023 Dec 1;15(12):e49802. doi: 10.7759/cureus.49802. eCollection 2023 Dec.

Cerebral palsy (CP) encompasses a range of conditions that impact an individual's mobility, balance, and posture, making it the most prevalent motor impairment in children. In spastic cerebral palsy, muscle stiffness hinders walking and, if left untreated, may lead to complications such as hip dislocations or dysplasia. Adductor spasticity is a common challenge in these children, significantly impeding mobility and daily activities. The risk of hip dislocation escalates as gross motor function declines, particularly in children with severe impairments. This case report highlights the successful application of bilateral adductor tenotomy with gracilis release in a 9-year-old child diagnosed with spastic cerebral palsy, exhibiting a scissoring and in-toeing gait. Additionally, this report prompts consideration of the potential benefits of gracilis release in addressing the in-toeing gait observed in children affected by spastic cerebral palsy.

PMID: 38161526

5. Beyond pediatrics: noninvasive spinal neuromodulation improves motor function in an adult with cerebral palsy

Rahul Sachdeva, Kristin Girshin, Yousef Shirkhani, Parag Gad

Bioelectron Med. 2024 Jan 3;10(1):1. doi: 10.1186/s42234-023-00133-2.

Regaining motor function in individuals with cerebral palsy (CP) has been predominantly studied in children, resulting in an underrepresentation of adults in research efforts. We tested the efficacy of noninvasive spinal neuromodulation with neurorehabilitation (Spinal Cord Innovation in Pediatrics; SCiP™ therapy). A 60-year-old CP participant underwent 8 weeks of SCiP™ therapy, resulting in significant motor recovery measured by 14.2-points increase in gross motor function measure (GMFM-88) score, ~ three times the Minimal Clinically Important Difference (MCID) of 5-points. This represented gains in kneeling, sitting, and walking functions. The improvement in GMFM-88 score was maintained above the MCID at the follow up visit (10.3 points above the baseline), twenty weeks following the last therapy session, indicating a persistent effect of the therapy. Our preliminary findings support the therapeutic promise of SCiP™ therapy for enhancing motor function in CP adults. Broader investigations are needed to establish its wider applicability.

PMID: 38167312

6. Effect of core stabilization versus rebound therapy on balance in children with cerebral palsy

Alaa Al-Nemr, Alaa Noureldeen Kora

Acta Neurol Belg. 2024 Jan 5. doi: 10.1007/s13760-023-02430-8. Online ahead of print.

Objective: This study aimed to compare the effect of core stabilization exercises and rebound therapy on balance in children with hemiplegic cerebral palsy (CP). Methods: Fifty- two children of spastic hemiplegic CP aged 5 up to 8 years from both genders were assigned randomly into two groups: core stability and rebound therapy groups. Both groups received 3 sessions/ week, 1.5-h training per session, for 12 successive weeks. The measurement was performed at baseline and post-treatment. Balance as a primary outcome for this study was measured by a Biodex Balance System (BBS), and knee extensor strength and functional capacity as secondary outcomes were assessed using a hand-held dynamometer, and a six-minute walk test (6MWT), respectively. Results: All variables showed a significant improvement after intervention in each group ($p < 0.0001$), with significant improvement in all stability indices (overall, anteroposterior, and mediolateral) in core stability group when compared to rebound therapy group. Conclusion: Core stability exercises and rebound therapy are recommended in the rehabilitation of children with hemiplegic CP. Core stability exercises were more effective than rebound therapy for balance improvement. Trial registration number: NCT05739396.

PMID: 38177509

7. A good night's sleep: pain trajectories and sleep disturbance in children with cerebral palsy

Heather M Shearer, Pierre Côté, Sheilah Hogg-Johnson, Darcy L Fehlings

J Clin Sleep Med. 2024 Jan 3. doi: 10.5664/jcsm.10980. Online ahead of print.

Study objectives: Sleep quality is important during childhood and adolescence. Given the high prevalence of pain in children/ youth with cerebral palsy (CP), we aimed to measure the association between short-term pain trajectories and sleep disturbance in these individuals. Methods: We accrued the cohort between November 2019 and October 2020 and recruited children/youth who: 1) were 8-18 years old; 2) had CP with any gross motor function classification system (GMFCS) level; and 3) could self-report pain and sleep disturbance. We collected self-report baseline and weekly follow-up data using electronic questionnaires completed every week for five weeks. Sleep disturbance at five weeks was the primary outcome (paediatric Patient-Reported Outcomes Measurement Information System [PROMIS] short form (v1.0-4a)). We used general linear regression to assess the association between pain intensity trajectory group and sleep disturbance controlling for confounders. Results: 190 individuals were eligible, 102 were enrolled and 89 were included in our final analysis. Pain trajectory groups had estimated crude mean sleep disturbance scores at 5 weeks ranging from 56.0 (95% CI 51.8, 60.8) to 61.8 (55.7, 67.9). Compared to those with stable no/very mild pain, those in the stable high pain group had the greatest sleep disturbance (adjusted β=5.7; 95% CI 1.2, 10.2). Conclusions: Irrespective of pain trajectory, children and youth with CP reported sleep disturbances. Those with a stable, high pain intensity in the previous five weeks reported the greatest sleep disturbance. The results highlight the importance of considering pain trajectories and their impact on sleep in children with CP.

PMID: 38169433

8. Genomic analysis of presumed perinatal stroke in Saudi Arabia reveals a strong monogenic contribution

Muneera J Alshammari, Hanan E Shamseldin, Fahad Essbaiheen, Sara H Eltahir, Ashwag R Alruwaili, Firdous Abdulwahab, Fowzan S Alkuraya

Hum Genet. 2024 Jan 5. doi: 10.1007/s00439-023-02621-6. Online ahead of print.

Perinatal stroke is associated with significant short- and long-term morbidity and has been recognized as the most common cause of cerebral palsy in term infants. The diagnosis of presumed perinatal stroke (PPS) is made in children who present with neurological deficit and/or seizures attributable to focal chronic infarction on neuroimaging and have uneventful neonatal history. The underlying mechanism of presumed perinatal stroke remains unknown and thorough investigation of potential monogenic causes has not been conducted to date. Here, we describe the use of untargeted exome sequencing to investigate a cohort of eight patients from six families with PPS. A likely deleterious variant was identified in four families. These include the well-established risk genes COL4A2 and JAM3. In addition, we report the first independent confirmation of the recently described link between ESAM and perinatal stroke. Our data also highlight NID1 as a candidate gene for the condition. This study suggests that monogenic disorders are important contributors to the pathogenesis of PPS and should be investigated by untargeted sequencing especially when traditional risk factors are excluded.

PMID: 38180561

9. The diagnosis of cerebral palsy in two Danish national registries: a validation study

Mads L Larsen, Christina E Hoei-Hansen, Gija Rackauskaite

Scand J Public Health. 2024 Jan 5:14034948231219825. doi: 10.1177/14034948231219825. Online ahead of print.

Aims: To determine the quality of prospectively collected data from the highly specialized Danish Cerebral Palsy Follow-up Program (CPOP), and to establish the validity of a reported cerebral palsy (CP) diagnosis in the Danish National Patient Registry (NPR), regularly used as a proxy for neurodevelopmental disorders in epidemiological research. Methods: We compared data from the two registries on children with registered CP, born in Denmark between 2008 and 2009, with information from medical records verified by two experienced physicians specializing in pediatric neurology. Data accuracy was estimated by completeness, correctness, and reliability. Completeness was calculated as the number of cases with correctly registered CP diagnoses divided by the total number of true CP diagnoses (similar to sensitivity). Correctness was calculated as the number of cases with correct registrations divided by the total number of cases (similar to positive predictive value). Reliability was estimated using kappa statistics. Results: Registered CP diagnoses in the CPOP had high accuracy, with 94% correctness and 91% completeness. Furthermore, most key variables in the CPOP showed excellent reliability, especially variables defining the severity of the condition. In the Danish NPR, only 225 of 348 children with a noted CP diagnosis fulfilled the diagnostic criteria for CP, resulting in 65% correctness. Conclusions: Danish CPOP data are a valid source for epidemiological research. Conversely, a noted CP diagnosis in the Danish NPR was, at best, correct in only two out of three patients.

PMID: 38179995

10. Mapping the Current Research on Mindfulness Interventions for Individuals with Cerebral Palsy: A Scoping Review

Roberto Tedeschi

Neuropediatrics. 2024 Jan 5. doi: 10.1055/a-2239-1936. Online ahead of print.

Background Cerebral palsy (CP) is a chronic neurological disorder that can cause motor and cognitive disabilities. Mindfulness is a form of meditation that has gained attention as a potential therapeutic intervention for improving the health and well-being of patients with CP. Methods Four databases were searched until January 2023. A scoping review was conducted to explore the role of mindfulness in the management of CP by reviewing the available scientific literature. Studies that examined the effects of mindfulness on motor function, communication, and quality of life in patients with CP were analysed. Grey literature and reference lists of included articles were not identified. The results were presented in numerical and thematic form. Results From an initial pool of 30 registered studies, only 3 met the inclusion criteria. These selected studies reported positive effects of mindfulness interventions on communication abilities and stress management in patients with cerebral palsy (CP). Conclusions The available evidence suggests that mindfulness may have beneficial effects on motor function, communication, and quality of life in patients with CP. The findings of this review highlight the potential of mindfulness as a complementary therapy for improving the health and well-being of patients with CP.

PMID: 38181818

11. Levodopa for Dystonia in Children: A Case Series and Review of the Literature

Alexandra Lesenskyj DeArias, Nigel S Bamford

Pediatr Neurol. 2023 Dec 19:152:16-19. doi: 10.1016/j.pediatrneurol.2023.12.012. Online ahead of print.

Background: Levodopa is used to treat hyperkinetic movements in children with dopa-responsive dystonia. However, levodopa may also be helpful in treating other forms of dystonia when used beyond a brief trial period. Methods: We performed a retrospective review of all children referred to our institution for evaluation of generalized dystonia and subsequently treated with carbidopa-levodopa. Motor function was assessed using video recordings and examination notes, quantified with the Burke-Fahn-Marsden Dystonia Rating Scale. Results: Long-term treatment with carbidopa-levodopa moderately improved motor function, whereas short-term use did not. Carbidopa-levodopa was well tolerated without untoward effects. Conclusions: Dystonia is a significant cause of disability with limited effective treatment options. Published work is restricted but generally supports the findings of this review. A well-controlled study to examine the utility of carbidopa-levodopa treatment for dystonia is needed.

PMID: 38176223

12. Effect of ultra-early intervention of NDT therapy on nerve and motor development in infants at high risk of cerebral palsy

Meihua Li, Lihua Wang, Shujie Yu, Xuesong Guo, Bingbing Xun, Yu Zhang

Folia Neuropathol. 2024 Jan 4:51502. doi: 10.5114/fn.2023.131551. Online ahead of print.

Introduction: The aim of the study was to investigate the effect of ultra-early intervention of nerve and motor development in infants at high risk of cerebral palsy. Material and methods: One hundred and twenty cases of infants born in The Affiliated Hospital of Harbin Medical University from January 2017 to January 2019 and diagnosed with high risk of cerebral palsy were included in the observation group. In addition, 120 cases of infants at high risk of cerebral palsy (three to five months old) who were admitted to this hospital during the same period were included in the control group, and 120 healthy infants born in the same hospital were included in the healthy group. Intervention was performed on the observation group after diagnosis (within seven days of birth), mainly using neurodevelopmental therapy (NDT). Children in the control group underwent intervention after diagnosis (at three to five months old) using the same measures. The healthy group underwent no intervention. Changes in various indicators were compared among the observation group, healthy group, and control group. Results: At baseline and at three months, the developmental quotient (DQ) at all functional areas, total DQ, and GESELL development scale (GDS) scores were significantly lower in the observation and control groups than in the healthy group ($p < 0.05$). At six months, 12 months, 18 months, and 24 months, the DQ at all functional areas, total DQ, and GDS (adaptability, gross motor, fine motor, language, personal social interaction) scores in the observation and control groups were significantly lower than those in the healthy group ($p < 0.05$). However, the observation group scores were significantly higher than the control group scores ($p < 0.05$). In the observation group, the normalisation rate was higher than in the control group, and the incidence rate of cerebral palsy and full developmental delay was lower than in the control group ($p < 0.05$). Conclusions: Ultra-early diagnosis and NDT intervention can significantly accelerate the motor development of infants at high risk of cerebral palsy. The earlier, the better. Ultra-early intervention can promote the normalisation of infants at high risk of cerebral palsy and significantly reduce the risk of progression to cerebral palsy.

PMID: 38174677

13. Caregiver descriptions of dystonia in cerebral palsy

Fayza Jaleel, Alyssa Rust, Shirley Cheung, Toni S Pearson, Keisuke Ueda, Amy Robichaux-Viehoever, Katie Leger, Keerthana Chintalapati, Danielle Guez-Barber, Michele Shusterman, Bhooma Aravamuthan

Ann Clin Transl Neurol. 2024 Jan 4. doi: 10.1002/acn3.51941. Online ahead of print

Objective: To determine how caregivers describe dystonia in people with cerebral palsy (CP). Methods: In this prospective cohort study, paper surveys were administered to caregivers between September 7, 2021 and October 28, 2021 during CP Center visits at a large tertiary care center. Caregivers were asked to describe involuntary movements triggered by voluntary movement or triggered by tactile stimulation in the people with CP they cared for. Their CP Center medical provider separately assessed people with CP for dystonia. Movement features described exclusively by caregivers of people with CP and dystonia were determined using conventional content analysis. Results: 113 caregivers responded on behalf of 56 people with and 57 people without dystonia. If caregivers noted that both voluntary movement and tactile stimulation triggered involuntary movements, that had a 92% positive predictive value for a dystonia diagnosis. Movement features exclusively described in people with CP and dystonia included: (1) stiffening, tensing, or tightening (15% of respondents); (2) involvement of the head (10%), torso (5%), or feet (5%); and (3) triggers of stretching (12.5%), excitement (5%), or transfers (5%). Interpretation: In addition to a thorough exam, asking caregivers of people with CP to describe involuntary movements triggered by voluntary movement or tactile stimulation may inform clinical dystonia diagnosis.

PMID: 38174361

14. Therapeutic effects of extracorporeal shock wave therapy on patients with spastic cerebral palsy and Rett syndrome: clinical and ultrasonographic findings

Ting-Yu Su, Yu-Chi Huang, Jih-Yang Ko, Yi-Jung Hsin, Min-Yuan Yu, Pi-Lien Hung

Orphanet J Rare Dis. 2024 Jan 3;19(1):6. doi: 10.1186/s13023-023-03010-y.

Background: Extracorporeal shock wave therapy (ESWT) is reportedly effective for improving spasticity and motor function in children with cerebral palsy (CP). Because late-stage Rett syndrome has a similar presentation, this study aimed to investigate the effects of ESWT on these two diseases. Material and methods: Patients diagnosed with spastic CP and Rett syndrome received 1500 impulses of ESWT at 4 Hz and 0.1 mJ/mm2, on their spastic legs once weekly for a total of 12 weeks. Outcomes were assessed before and 4 and 12 weeks after ESWT. Clinical assessments included the Modified Ashworth Scale (MAS), passive range of motion (PROM), and Gross Motor Function Measure 88 (GMFM-88). Ultrasonographic assessments included muscle thickness, acoustic radiation force impulse (ARFI), and strain elastography. Results: Fifteen patients with CP and six

with Rett syndrome were enrolled in this study. After ESWT, patients with CP showed significant clinical improvement in the MAS (P = 0.011), ankle PROM (P = 0.002), walking/running/jumping function (P = 0.003), and total function (P < 0.001) of the GMFM-88. The patients with Rett syndrome showed improved MAS scores (P = 0.061) and significantly improved total gross motor function (P = 0.030). Under ARFI, patients with CP demonstrated decreased shear wave speed in the gastrocnemius medial head (P = 0.038). Conversely, patients with Rett syndrome show increased shear-wave speeds after ESWT. Conclusion: Our study provides evidence that a weekly course of low-dose ESWT for 12 weeks is beneficial for children with both CP and Rett syndrome, with the clinical effects of reducing spasticity and improving the gross motor function of the lower limbs. The ARFI sonoelastography reveals improvement of muscle stiffness in patients with CP after ESWT, but deteriorated in patients with Rett syndrome. The diverse therapeutic response to ESWT may be caused by the MECP2 mutation in Rett syndrome, having a continuous impact and driving the pathophysiology differently as compared to CP, which is secondary to a static insult. Trial registration IRB 201700462A3. Registered 22March 2017, https://cghhrpms.cgmh.org.tw/HRPMS/Default.aspx .

PMID: 38172891

15. Evaluating the Safety and Efficacy of Erythropoietin Therapy for Neonatal Hypoxic-Ischemic Encephalopathy: A Systematic Review and Meta-Analysis

Shayan Marsia, Danisha Kumar, Hamna Raheel, Ali Salman, Baseer Aslam, Armeen Ikram, Piresh Kumar, Aimun Aslam, Areeba Shafiq, Areeba Gul

Review Pediatr Neurol. 2023 Dec 14:152:4-10. doi: 10.1016/j.pediatrneurol.2023.12.008. Online ahead of print.

Background: Erythropoietin (EPO) is a proposed drug for the treatment of neonatal hypoxic-ischemic encephalopathy (HIE). Multiple studies have linked its use, either as a monotherapy or in conjunction with therapeutic hypothermia (TH), with improved neonatal outcomes including death and neurodisability. However, there is also evidence in the literature that raises concerns about its efficacy and safety for the treatment of neonatal encephalopathy (NE). Methods: We searched MEDLINE, Cochrane CENTRAL, and Embase for both observational studies and randomized controlled trials (RCTs) investigating the effectiveness of EPO in treating NE. Only studies in which at least 300 U/kg of EPO was used and reported any one of the following outcomes: death, death or neurodisability, and cerebral palsy, were included. Results: Seven studies with 903 infants with the diagnosis of NE were included in our meta-analysis. EPO did not reduce the risk of death or neurodisability (risk ratio 0.68 [95% confidence interval [CI]: 0.43 to 1.09]) (P = 0.11). Similarly, the risk of cerebral palsy was not reduced by the administration of EPO (risk ratio 0.68 [95% CI: 0.33 to 1.40]) (P = 0.30). The risk of death was also not reduced at any dose of EPO regardless of the use of TH. Conclusions: The results of our meta-analysis do not support the use of EPO for the treatment of neonatal encephalopathy. However, future large-scale RCTs are needed to strengthen these findings.

PMID: 38171084

16. Clinical utility of a genetic diagnosis in individuals with cerebral palsy and related motor disorders

Alexandra Santana Almansa, Dustin L Gable, Zoë Frazier, Abigail Sveden, Aisling Quinlan, Maya Chopra, Sara A Lewis, Michael Kruer, Annapurna Poduri, Siddharth Srivastava

Ann Clin Transl Neurol. 2024 Jan 2. doi: 10.1002/acn3.51942. Online ahead of print.

Objective: Evaluation of the clinical utility of a genetic diagnosis in CP remains limited. We aimed to characterize the clinical utility of a genetic diagnosis by exome sequencing (ES) in patients with CP and related motor disorders. Methods: We enrolled participants with CP and "CP masquerading" conditions in an institutional ES initiative. In those with genetic diagnoses who had clinical visits to discuss results, we retrospectively reviewed medical charts, evaluating recommendations based on the genetic diagnosis pertaining to medication intervention, surveillance initiation, variant-specific testing, and patient education. Results: We included 30 individuals with a molecular diagnosis and clinical follow-up. Nearly all (28 out of 30) had clinical impact resulting from the genetic diagnosis. Medication interventions included recommendation of mitochondrial multivitamin supplementation (6.67%, n = 2), ketogenic diet (3.33%, n = 1), and fasting avoidance (3.33%, n = 1). Surveillance-related actions included recommendations for investigating systemic complications (40%, n = 12); referral to new specialists to screen for systemic manifestations (33%, n = 10); continued follow-up with established specialists to focus on specific manifestations (16.67%, n = 5); referral to clinical genetics (16.67%, n = 5) to oversee surveillance recommendations. Variant-specific actions included carrier testing (10%, n = 3) and testing of potentially affected relatives (3.33%, n = 1). Patient education-specific actions included referral to experts in the genetic disorder (30%, n = 9); and counseling about possible changes in prognosis, including recognition of disease progression and early mortality (36.67%, n = 11). Interpretation: This study highlights the clinical utility of a genetic diagnosis for CP and "CP masquerading" conditions, evident by medication interventions, surveillance impact, family member testing, and patient education, including possible prognostic changes.

PMID: 38168508

17. Early detection of cerebral palsy using general movements assessment and MRIs - a sensible way forward

Nadia Badawi, Iona Novak, Catherine Morgan, Cathryn Crowle

Pediatr Res. 2024 Jan 3. doi: 10.1038/s41390-023-03008-z. Online ahead of print.

No abstract available

PMID: 38167645

18. Revving up possibilities: can psychostimulants enhance physical function in children with cerebral palsy?

Iona Novak, Michelle Jackman, Alexandra R Griffin, Remy Blatch-Williams, Esther Norfolk, Karin Lind, Daniel Polybank, Maria Mc Namara

Pediatr Res. 2024 Jan 2. doi: 10.1038/s41390-023-03010-5. Online ahead of print.

No abstract available

PMID: 38167643

19. Single-pulse transcranial magnetic stimulation for assessment of motor development in infants with early brain injury

Ellen N Sutter, Cameron P Casey, Bernadette T Gillick

Expert Rev Med Devices. 2024 Jan 3:1-8. doi: 10.1080/17434440.2023.2299310. Online ahead of print.

Introduction: Single-pulse transcranial magnetic stimulation (TMS) has many applications for pediatric clinical populations, including infants with perinatal brain injury. As a noninvasive neuromodulation tool, single-pulse TMS has been used safely in infants and children to assess corticospinal integrity and circuitry patterns. TMS may have important applications in early detection of atypical motor development or cerebral palsy. Areas covered: The authors identified and summarized relevant studies incorporating TMS in infants, including findings related to corticospinal development and circuitry, motor cortex localization and mapping, and safety. This special report also describes methodologies and safety considerations related to TMS assessment in infants, and discusses potential applications related to diagnosis of cerebral palsy and early intervention. Expert opinion: Single-pulse TMS has demonstrated safety and feasibility in infants with perinatal brain injury and may provide insight into neuromotor development and potential cerebral palsy diagnosis. Additional research in larger sample sizes will more fully evaluate the utility of TMS biomarkers in early diagnosis and intervention. Methodological challenges to performing TMS in infants and technical/equipment limitations require additional consideration and innovation toward clinical implementation. Future research may explore use of noninvasive neuromodulation techniques as an intervention in younger children with perinatal brain injury to improve motor outcomes.

PMID: 38166497

20. Genetic variants in the HLA region contribute to the risk of cerebral palsy

Ye Cheng, Yiran Xu, Hongwei Li, Yimeng Qiao, Yangong Wang, Yu Su, Jin Zhang, Xiaoyang Wang, Lili Song, Jian Ding, Dan Wang, Changlian Zhu, Qinghe Xing

Biochim Biophys Acta Mol Basis Dis. 2023 Dec 30;1870(3):167008. doi: 10.1016/j.bbadis.2023.167008. Online ahead of print.

Cerebral palsy (CP) is the most common physical disability in childhood, and genetic factors play an important role in its pathogenesis. However, the genetic contributions remain incompletely elucidated. Here, we conducted a two-stage association study between 1090 CP cases and 1100 healthy controls after whole exome sequencing. The human leukocyte antigen (HLA) allelic predispositions were further analyzed in overall CP and subgroups using multivariate logistic regression. We found a strong signal in the HLA region on chromosome 6, where rs3131787 harbored the most significant association with CP ($P = 2.05 \times 10\text{-}14$, OR = 2.22). In comparison to controls, the carrier frequencies of HLA-B*13:02 were significantly higher in children with CP (9.82 % in control vs 19.27 % in CP, $P = 1.03 \times 10\text{-}4$, OR = 2.17). Furthermore, the effect of HLA-B*13:02 on increasing the risk of CP mainly existed in cryptogenic CP without exposure to premature birth, low birth weight, birth asphyxia, or periventricular leukomalacia. This study indicated a strong association of HLA variants with CP, which implied that immune dysregulation resulting from immunogenetic variants might underlie the pathogenesis of CP. Our findings provide genetic evidence that an immunomodulator may serve as a promising therapeutic intervention for patients with CP by reinstating the neuroinflammation hemostasis.

PMID: 38163449

21. Whole Body Vibration Therapy for Children with Disabilities: A Survey of Potential Risks and Benefits

David Godley, John Csongradi

Arch Rehabil Res Clin Transl. 2023 Sep 29;5(4):100298. doi: 10.1016/j.arrct.2023.100298. eCollection 2023 Dec.

The purpose of this report is to remind providers of the potential risks of Whole Body Vibration Therapy (WBVT) for children with disabilities. We reviewed the current state of knowledge and learned that WBVT may have potential risk of injury for some children. To the best of our knowledge this review is the first to clarify WBVT risks. We believe WBVT may have therapeutic value but we recommend caution and offer suggestions for future research.

PMID: 38163033

22. Managing Fatigue: Experiences From a 6-week Course for Adults With Cerebral Palsy

Ellinor Nilsson, Séverine Hedberg Dubuc, Nazdar Ghafouri, Anne Söderlund Schaller

Arch Rehabil Res Clin Transl. 2023 Oct 2;5(4):100300. doi: 10.1016/j.arrct.2023.100300. eCollection 2023 Dec.

Objective: To explore experiences of a 6-week Fatigue Management course (FMC) in adults with cerebral palsy (CP). Design: A qualitative study using semi-structured interviews. The study process followed the Consolidated Criteria for Reporting Qualitative Research (COREQ). Setting: The study was conducted in southeastern Sweden in an out-patient setting. Participants: Adults (N=8) with CP who had participated in FMC. Interventions: Not applicable. Main outcome measure: Qualitative content analysis of the transcribed interviews led to identification of a main category, categories, and subcategories, describing the participants' experiences of FMC. Results: The analysis identified 2 categories: Awareness regarding fatigue, with the 2 subcategories: A better understanding, and The feeling of not being alone; and Perceive opportunities for changes, with the 3 subcategories: Understanding the need for changes, Demanding process, and Taking steps toward change. These categories were summed up in the main category describing the participants' experiences of FMC: A challenging and eye-opening course that gave deeper self-understanding and thoughts about making changes. Conclusions: Overall, the participants described positive experiences of FMC, with increased awareness regarding fatigue and insight regarding the possibilities for change. Nevertheless, there were challenges in coping with the extensive information and with the home assignments. This study gives promising results regarding the applicability of FMC for adults with CP. However, there is a need for course modifications with more targeted and differentiated content that is manageable and does not overload the participants. The modifications should include extended time, the addition of individual support, and follow-up between sessions, to increase participants' opportunities to implement new strategies and initiate behavioral change.

PMID: 38163030

23. Range of Motion Limitations in Middle-aged Adults With Cerebral Palsy

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Objective: To describe limitations in range of motion (ROM) in middle-aged adults with cerebral palsy (CP), and identify associations with CP subtype, gross motor function, sex and age. Design: Population-based cohort study. Setting: Local and regional referral centers. Participants: Inclusion criteria: diagnosis of CP, born 1959 to 1978 and living in the county of Västra Götaland, Sweden. In the population-based register of CP in Western Sweden, 417 subjects were identified and 139 volunteered to participate. Adults with CP, born elsewhere, who had moved into the area were invited through patient organizations and habilitation units, and eleven chose to participate. In total 150 participants, age 37-58 years (mean 48) 65 women (43%) (N=150). All CP subtypes and Gross Motor Function Classification (GMFCS) levels were represented. Interventions: Not applicable. Main outcome measures: Passive ROM was measured in the upper and lower extremity and was classified into 4 levels (inspired by The Spinal Alignment and Range of Motion Measure and adapted from the values of the American Academy of Orthopedic Surgeons); good=1, vs mild=2, moderate=3 or severe=4 limitation. The results were summarized to obtain a total score of the participants' ROM limitations. Results: Moderate to severe limitations were present in 98 % of the participants. There was a correlation to GMFCS level in both the upper and lower extremity (P<.001), but no correlation with age. Upper extremity limitations were most common in dyskinetic CP, lower extremity limitations were most common in dyskinetic CP and bilateral spastic CP. Men had more limitations in the lower extremity (P=.001). The most common limitation in the lower extremity was hamstrings tightness (82%) and hip abduction (80%), and in the upper extremity, limited shoulder abduction (57%). Conclusions: Limited ROM is common in adults with CP, most pronounced in shoulders, hip joints and hamstrings muscles, with no differences related to age in this age-span.

PMID: 38163028

24. A Call for Early Detection of Cerebral Palsy

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Neoreviews. 2024 Jan 1;25(1):e1-e11. doi: 10.1542/neo.25-1-e1.

Cerebral palsy (CP) is the most common physical disability across the lifespan, but historically, CP has not been diagnosed before the age of 2 years. Barriers to early diagnosis ranged from lack of available biomarkers, absence of curative treatments, perceived stigma associated with a lifelong diagnosis, and a desire to rule out other diagnoses first. Most importantly, the fundamental question that remained was whether children would benefit from earlier detection and intervention given the paucity of research. However, evidence-based guidelines published in 2017 demonstrated that the General Movements Assessment, the Hammersmith Infant Neurological Examination, and neuroimaging can be combined with other elements such as a clinical history and standardized motor assessments to provide the highest predictive value for diagnosing CP as early as age 3 months in high-risk newborns. Implementation of these guidelines has been successful in decreasing the age at CP diagnosis, particularly in high-risk infant follow-up clinics with expertise in performing these assessments. Early detection of CP allows for clinical and research opportunities investigating earlier interventions during a critical period of neuroplasticity, with the goal of improving developmental trajectories for children and their families. New guidelines and research are now being developed with a focus on early, targeted interventions that continue to be studied, along with global detection initiatives.

PMID: 38161182

25. Author Correction: Cerebellar growth, volume and diffusivity in children cooled for neonatal encephalopathy without cerebral palsy

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PMID: 38158414

26. Neurological and Visual Outcomes in Infants and Toddlers Following Therapeutic Hypothermia for Neonatal Hypoxic-Ischemic Encephalopathy

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Background: The majority of studies have investigated neurodevelopmental outcomes, whereas visual impairment is less explored in children with a history of neonatal (hypoxic-ischemic) encephalopathy. Our aim was to perform a detailed neurological and visual assessment and also to investigate the presence of cerebral visual impairment in infants and toddlers with neonatal encephalopathy. Methods: Thirty participants with a history of neonatal encephalopathy, who had been hospitalized for therapeutic hypothermia, underwent a detailed neurological examination at age five to 36 months. Age-matched, 30 healthy children were also enrolled as a control group. All children in the study and control groups received neurological and a comprehensive ophthalmologic examination, including visual field and visual acuity. Presence of cerebral visual impairment was also evaluated clinically. Results: Rates of cerebral palsy, severe motor impairment, cognitive impairment, epilepsy, and cerebral visual impairment were found to be 20%, 10%, 15.3%, 10%, and 20%, respectively. When compared with healthy controls, oculomotor functions, pupillary light response, refractive parameters, anterior/posterior segment examinations, ocular visual impairment rates, and last, visual acuities were found similar. However, we found a statistically significant increase in visual field defects in our study group. Conclusions: It could be better to perform a comprehensive ophthalmologic examination including visual field, visual acuity, and oculomotor functions by a pediatric ophthalmologist to accurately diagnose neurovisual deficits in infants following therapeutic hypothermia. Early identification and rehabilitation of the visual deficits might improve the neurodevelopment in these children.

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