Cerebral palsy research news

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Interventions and Management

1. Bimanual Movement Characteristics and Real-World Performance Following Hand-Arm Bimanual Intensive Therapy in Children with Unilateral Cerebral Palsy

Shailesh S Gardas, Christine Lysaght, Amy Gross McMillan, Shailesh Kantak, John D Willson, Charity G Patterson, Swati M Surkar

Behav Sci (Basel). 2023 Aug 13;13(8):681. doi: 10.3390/bs13080681.

The purpose of this study was to quantify characteristics of bimanual movement intensity during 30 h of hand-arm bimanual intensive therapy (HABIT) and bimanual performance (activities and participation) in real-world settings using accelerometers in children with unilateral cerebral palsy (UCP). Twenty-five children with UCP participated in a 30 h HABIT program. Data were collected from bilateral wrist-worn accelerometers during 30 h of HABIT to quantify the movement intensity and three days pre- and post-HABIT to assess real-world performance gains. Movement intensity and performance gains were measured using six standard accelerometer-derived variables. Bimanual capacity (body function and activities) was assessed using standardized hand function tests. We found that accelerometer variables increased significantly during HABIT, indicating increased bimanual symmetry and intensity. Post-HABIT, children demonstrated significant improvements in all accelerometer metrics, reflecting real-world performance gains. Children also achieved significant and clinically relevant changes in hand capacity following HABIT. Therefore, our findings suggest that accelerometers can objectively quantify bimanual movement intensity during HABIT. Moreover, HABIT enhances hand function as well as activities and participation in real-world situations in children with UCP.

PMID: 37622821

2. Efficacy of Constraint-Induced Movement Therapy Versus Bimanual Intensive Training on Motor and Psychosocial Outcomes in Children With Unilateral Cerebral Palsy: A Randomized Trial

Kai-Jie Liang, Hao-Ling Chen, Chen-Wei Huang, Tien-Ni Wang

Randomized Controlled Trial Am J Occup Ther. 2023 Jul 1;77(4):7704205030. doi: 10.5014/ajot.2023.050104.

Importance: Emerging research has demonstrated that constraint-induced movement therapy (CIMT) and bimanual intensive training (BIT) show promising effectiveness for children with unilateral cerebral palsy (UCP). Considering that neurorehabilitative programs have always been designed with long training periods, psychosocial outcomes have received scarce attention and thus have not been investigated sufficiently. Objective: To compare the efficacy of CIMT and BIT with 36-hr interventional dosages for both motor and psychosocial outcomes. Design: Randomized trial. Setting: Community. Participants: Forty-eight children with UCP, ages 6 to 12 yr. Intervention: Both CIMT and BIT delivered via individual intervention for 2.25 hr/day, twice a week, for 8 wk. Outcomes and measures: The Melbourne Assessment 2, Pediatric Motor Activity Log-Revised, Bruininks-Oseretsky Test of Motor Proficiency, ABILHAND-Kids measure, and Parenting Stress Index-Short Form were administrated at pretreatment, midterm, posttreatment, and 6 mo after intervention. An engagement questionnaire for investigating the child's engagement in the intervention was used to collect the perspectives of the children and the parents weekly. Results: Children with UCP who received either CIMT or BIT achieved similar motor improvements.

The only difference was that CIMT yielded larger improvements in frequency and quality of use of the more affected hand at the 6-mo follow-up. Similar child engagement and parental stress levels were found in the two groups. Conclusions and relevance: This study comprehensively compared the efficacy of motor and psychosocial outcomes for 36-hr dosages of CIMT and BIT. The promising findings support the clinical efficacy and feasibility of the proposed protocols. What This Article Adds: The core therapeutic principle of CIMT (i.e., remind the child to use the more affected hand) may be more easily duplicated by parents. Parents may have overestimated their child's engagement and given relatively higher scores; therefore, occupational therapists should also consider the opinions of the children themselves.

PMID: 37611319

3. Design and Use of a 3D-Printed Dynamic Upper Extremity Orthosis for Children With Cerebral Palsy and Severe Upper Extremity Involvement: A Pilot Study

Lori B Ragni, Stacy Kirsch Dlugacz, Cali Sadowsky, Gabriella Cammarata, Debra A Sala, Victoria Bill, Renat Sukhov, Alice Chu

Am J Occup Ther. 2023 Jul 1;77(4):7704205060. doi: 10.5014/ajot.2023.050095.

Importance: Children with cerebral palsy (CP) and severe hand impairment have limited options for upper extremity (UE) orthoses. Objective: To (1) design and fabricate a customized low-cost, functional, three-dimensional (3D) printed dynamic upper extremity orthosis (DUEO) and (2) examine, using a comprehensive evaluation, the effect of the orthosis on the UE function of children with unilateral UE CP, Manual Ability Classification System (MACS) Levels III to V. Design: Pilot study. Assessments were performed pretreatment and immediately posttreatment. Setting: Hospital-based outpatient occupational therapy department. Participants: Five patients, ages 13 to 17 yr, with CP and unilateral UE involvement MACS Levels III to V. Intervention: Custom forearm thumb opponens orthosis and the DUEO were designed and fabricated by a multidisciplinary team for use during eight 1-hr occupational therapy sessions targeting bimanual UE training. Outcomes and measures: Pretreatment and posttreatment assessments included the Assisting Hand Assessment (AHA), Melbourne Assessment 2 (MA-2), Pediatric Motor Activity Log-Revised (PMAL-R), and the Pediatric Quality of Life Inventory: CP Module (PedsQL:CP). Results: All participants had higher posttreatment scores on at least one measure. Four had minimal clinically important differences (MCID) on the AHA. Three met MCID criteria on MA-2 subtests (one negative change). Four demonstrated improvement on the PMAL-R (one participant achieved an MCID score), and three reported improvements in more than one PedsQL:CP domain. Conclusions and relevance: This novel 3D-printed device, in combination with occupational therapy, shows promising evidence that children who score in lower MACS levels can show gains in UE function. What This Article Adds: This study demonstrates that a customized, 3D-printed dynamic orthosis, in combination with occupational therapy intervention, can facilitate UE function in children with severe hand impairment.

PMID: 37611318

4. Intrailiac Osteotomy With Superior Lateral Outcropping Bone: A Previously Undescribed Procedure for Hip Subluxation in Cerebral Palsy

Benjamin Sketchler, David A Yngve

Cureus. 2023 Jul 18;15(7):e42065. doi: 10.7759/cureus.42065. eCollection 2023 Jul.

Background: Surgical treatment of hip subluxation in cerebral palsy typically involves proximal femoral osteotomy with or without concurrent supra-acetabular pelvic osteotomy. The literature lacks data on isolated pelvic osteotomy for this condition. We present superior lateral outcropping bone as a novel procedure for augmenting pelvic osteotomies for additional femoral coverage. Methods: In this retrospective case series, all patients were included for whom a single surgeon at a single institution performed pelvic osteotomy with adjunctive superior lateral outcropping bone for the treatment of hip subluxation in cerebral palsy over a 12-year period. Patients with less than two years of X-ray follow-up were excluded, as were patients with frank dislocation preoperatively. Regarding each case, multiple variables were collected, including X-ray measurements of migration percentage and acetabular index preoperatively, immediately postoperatively, and at last available X-ray. Paired t tests were performed to confirm a significant difference between preoperative and postoperative measurements. Surgical failure was defined as either any subsequent hip or pelvic procedure other than myotendinous lengthening or alcohol nerve blocks, or final migration percentage of greater than 50%. Results: Thirty-three hips (23 patients, 13 males) were included. Mean age at surgery was seven years. Mean time to follow-up was 49 months. Migration percentage of the hips improved from an average 44% preoperatively to 25% at first postoperative measurement and 22% at final follow-up ($p < 0.001$). Acetabular index improved from an average 27 degrees preoperatively to 15 degrees at first postoperative measurement and 17 degrees at final follow-up ($p < 0.001$). No hips met failure criteria of repeat surgery other than myotendinous lengthening or nerve blocks, but two presented with a migration percentage of greater than 50% at final follow-up, giving us a failure rate of 6%. Conclusions: We present a novel procedure that appears to provide safe and successful outcomes for hip subluxation in cerebral palsy. Our clinical results compare favorably to those in the literature for isolated proximal femoral osteotomy for similar patient populations, yet there is no need for implanted hardware.

PMID: 37602084

5. Study Confirms Safety and Effectiveness of Intra-Articular Glucocorticoids for Painful Hip Dislocation in Children and Young Adults with Neurologic Impairment

Simone Benvenuto, Egidio Barbi, Silvia Boaretto, Matteo Landolfo, Francesco Rispoli, Giorgio Cozzi, Marco Carbone

Children (Basel). 2023 Aug 6;10(8):1353. doi: 10.3390/children10081353.

Background: Hip dislocation is a common source of pain in children with neurologic impairment. When medical interventions fail, orthopedic surgery does not guarantee a definitive result as the displacement may continue postoperatively and a second operation is often required. Methods: Retrospective analysis of data regarding the safety and effectiveness of an intra-articular corticosteroid injection (IACI) in 11 patients, aged 15 ± 5 years old, collected through a telephonic questionnaire administered to parents. Results: 21 IACIs were performed, a mean number of 1.9 ± 1.5 times for each patient, at a mean age (of the first IACI) of 13.5 ± 5 years. According to the parents, the IACI significantly lowered the number of participants experiencing pain (82% reduction) and using analgesics (60% reduction). There was also a significant improvement in the children's hip mobility (63% reduction in patients experiencing stiffness), decubitus (90% reduction in obligated positioning), behavior (80% reduction in lamenting or crying patients), sleep quality (87.5% reduction in patients awakening every night), and caregivers' quality of life (91% reduction in worried parents). The mean reported duration of the IACIs' benefit was 5.4 ± 2.4 months (range 1-9), with a positive correlation with the number of IACIs ($r = 0.48$; p-value = 0.04) and a negative correlation with the age at the first injection ($r = -0.71$; p-value = 0.02). The only reported adverse event was mild local swelling in one child. Conclusions: the IACI could represent a safe and effective intervention for painful hip dislocation, both before and after surgery, with a long-lasting benefit which seems to increase as multiple IACIs are performed.

PMID: 37628352

6. A prospective assessment of gait kinematics and related clinical examination measures in cerebral palsy crouch gait

Rory O'Sullivan, Helen French, Frances Horgan

HRB Open Res. 2023 Aug 7;5:81. doi: 10.12688/hrbopenres.13647.2. eCollection 2022.

Background While prospectively assessed crouch gait in cerebral palsy (CP) does not necessarily progress, prospective changes in clinical examination measures have not been reported. This study prospectively examined the association between selected clinical examination variables and change in crouch gait in a cohort with bilateral CP. Methods Inclusion criteria were a diagnosis of ambulant bilateral CP, knee flexion at mid-stance >19 0 and a minimum of two-years between gait analyses. The change in kinematic variables was assessed using Statistical Parameter Mapping (SPM) and changes in clinical measures using appropriate paired tests. Linear regression examined the association between progression of crouch and clinical examination variables. Results There was no mean change in crouch in 27 participants over 3.29 years. However, there was significant variability within this group. Clinical hamstring tightness (60.00 0 to 70.48 0, $p<0.01$) and external knee rotation during stance (SPM analysis, $p<0.001$) increased but there was no association between changes in clinical examination variables and changes in crouch (p-values 0.06 - 0.89). Conclusions This prospective study found no association between the changes in clinical examination variables and changes in crouch highlighting the likely multi-factorial aetiology of this gait pattern and the need for larger prospective studies. The variability crouch gait progression among the 27 participants highlights the pitfall of group mean values in such a heterogeneous population.

PMID: 37601116

7. Pilot Translational Precision Biobehavioral Assays for Early Detection of Motor Impairments in a Rat Model of Cerebral Palsy

Gwendolyn Gerner, Vera Joanna Burton, Yuma Kitase, Shenandoah Robinson, Lauren L Jantzie

Life (Basel). 2023 Aug 14;13(8):1746. doi: 10.3390/life13081746.

Background: Cutting-edge neonatal programs diagnose cerebral palsy (CP) or "high risk of CP" using validated neurobehavioral exams in combination with risk history and neuroimaging. In rat models, digital gait analyses are the gold standard adult assessment, but tools in infant rats are limited. Refinement of infant rat neurobehavioral correlates of CP will establish translational behavioral biomarkers to delineate early mechanisms of CP in both humans and rodent models of CP. Objective: To facilitate precision medicine approaches of neurodevelopmental health and integrate basic and clinical research approaches for CP, we developed and piloted a new assay of neonatal rat neurobehavior to mimic human neonate exams. Methods: Our established rat model of CP secondary to chorioamnionitis (CHORIO) that induces bilateral motor impairment reminiscent of spastic CP was used. On postnatal day 10 (P10), 5 min videos were recorded of 26 (6 sham and 20 CHORIO) animals moving freely in a cage were reviewed by an evaluator trained in the human General Movements Assessment (GMA).

Non-blinded observation revealed two behaviors that differed between rat pups in each group (time spent rearing; multi-dimensional nose sweeping; and sniffing). Each video was re-coded for these criteria by an evaluator blind to group status. Differences between sham and CP groups were analyzed using a Mann-Whitney U-test or Student's t-test ($p < 0.05$ level of significance). Results: Neonatal rats with CP exhibited sensorimotor impairment and decreased spatial exploration. CP rats spent significantly less time rearing (17.85 ± 1.60 s vs. 34.8 ± 2.89 s, $p = 0.007$) and engaged in multi-dimensional nose sweeping and sniffing (2.2 ± 0.58 episodes vs. 5.5 ± 0.96 episodes, $p = 0.03$) than sham controls. Conclusions: These pilot findings of harmonized translational and precision biobehavioral assays provide an opportunity for increased expediency of clinical trials at the earliest stages of brain development.

PMID: 37629603

8. Leg Cycling Leads to Improvement of Spasticity by Enhancement of Presynaptic Inhibition in Patients with Cerebral Palsy

Senshu Abe, Yuichiro Yokoi, Naoki Kozuka

Phys Ther Res. 2023;26(2):65-70. doi: 10.1298/ptr.E10228. Epub 2023 Jun 20.

Objective: The purpose of this study was to investigate if leg cycling could reduce lower extremity spasticity in patients with cerebral palsy (CP). In addition, we investigated whether the intervention could cause changes in the modulation of presynaptic inhibition. Methods: This study was a quasi-experimental study, with pretest-posttest for 1 group. Participants in this experiment were eight adult patients with CP with lower extremity spasticity. Spasticity parameters assessed were the amplitude of soleus maximum Hoffmann's reflex (Hmax) and maximum angular velocity (MAV) of knee flexion measured using the pendulum test. D1 inhibition, which seems to be related to the presynaptic inhibition, was recorded by measuring soleus Hoffmann's reflex (H-reflex) with conditioned electric stimuli to the common peroneal nerve. Results: D1 inhibition was significantly enhanced immediately by the cycling intervention. The amplitude of the soleus Hmax was significantly depressed, and there was significant difference in Hmax/maximum M-wave. The MAV was increased due to inhibition of the stretch reflex. Conclusion: Leg cycling suppressed stretch reflex and H-reflex, and caused plasticity of inhibitory circuits in patients with CP with lower extremity spasticity. These findings strongly suggest that lower extremity spasticity can be improved by cycling movements.

PMID: 37621569

9. Altered corpus callosum structure in adolescents with cerebral palsy: connection to gait and balance

Julia Jaatela, Timo Nurmi, Jaakko Vallinoja, Helena Mäenpää, Viljami Sairanen, Harri Piitulainen

Brain Struct Funct. 2023 Aug 24. doi: 10.1007/s00429-023-02692-1. Online ahead of print.

Cerebral palsy (CP) is the most common motor disorder in childhood. Recent studies in children with CP have associated weakened sensorimotor performance with impairments in the major brain white-matter (WM) structure, corpus callosum (CC). However, the relationship between CC structure and lower extremity performance, specifically gait and balance, remains unknown. This study investigated the transcallosal WM structure and lower limb motor stability performance in adolescents aged 10-18 years with spastic hemiplegic ($n = 18$) or diplegic ($n = 13$) CP and in their age-matched controls ($n = 34$). The modern diffusion-weighted MRI analysis included the diffusivity properties of seven CC subparts and the transcallosal lower limb sensorimotor tract of the dominant hemisphere. Children with CP had comprehensive impairments in the cross-sectional area, fractional anisotropy, and mean diffusivity of the CC and sensorimotor tract. Additionally, the extent of WM alterations varied between hemiplegic and diplegic subgroups, which was seen especially in the fractional anisotropy values along the sensorimotor tract. The diffusion properties of transcallosal WM were further associated with static stability in all groups, and with dynamic stability in healthy controls. Our novel results clarify the mechanistic role of the corpus callosum in adolescents with and without CP offering valuable insight into the complex interplay between the brain's WM organization and motor performance. A better understanding of the brain basis of weakened stability performance could, in addition, improve the specificity of clinical diagnosis and targeted rehabilitation in CP.

PMID: 37615759

10. Examining the Role of Sublingual Atropine for the Treatment of Sialorrhea in Patients with Neurodevelopmental Disabilities: A Retrospective Review

Kayla Durkin Petkus, Garey Noritz, Laurie Glader

J Clin Med. 2023 Aug 11;12(16):5238. doi: 10.3390/jcm12165238.

Sialorrhea is common in children with neurodevelopmental disabilities (NDD) and is reported in >40% of children with cerebral palsy (CP). It causes a range of complications, including significant respiratory morbidity. This single-center

retrospective chart review aims to document sublingual atropine (SLA) utilization to guide further study in establishing its role in secretion management for children with NDD. A chart review was completed for patients with NDD ≤ 22 years of age treated with SLA at a free-standing children's hospital between 1 January 2016 and 1 June 2021. Descriptive statistics were generated to summarize findings. In total, 190 patients were identified, of which 178 met inclusion criteria. The average starting dose for SLA was 1.5 mg/day, or 0.09 mg/kg/day when adjusted for patient weight. Eighty-nine (50%) patients were prescribed SLA first line for secretion management while 85 (48%) patients tried glycopyrrolate prior to SLA. SLA was used after salivary Botox, ablation, and/or surgery in 16 (9%) patients. This study investigates SLA as a potential pharmacologic agent to treat sialorrhea in children with NDD. We identify a range of prescribing patterns regarding dosing, schedule, and place in therapy, highlighting the need for further evidence to support and guide its safe and efficacious use.

PMID: 37629280

11. Assessment for Tactile Perception in Children With Cerebral Palsy

Kai-Jie Liang, Hao-Ling Chen, Kuo-Lun Huang, Ting-Ming Wang, Jeng-Yi Shieh, Tien-Ni Wang

Observational Study Am J Occup Ther. 2023 Jul 1;77(4):7704205050. doi: 10.5014/ajot.2023.050106.

Importance: Impaired tactile perception frequently accompanies motor deficits in children with cerebral palsy (CP). Assessing tactile perception precisely for children with CP remains challenging because of a lack of assessments with robust psychometric evidence or standard procedures. Objective: To develop a standardized assessment tool, the Tactile Perceptual Test (TPT), for measuring tactile perception in children with CP and to examine its psychometric properties. Design: Observational study design. Setting: University research laboratory and medical center. Participants: Children with CP (n = 100) and typical development (TD; n = 50). Outcomes and measures: The TPT includes four subtests measuring stereognosis, roughness, hardness, and heaviness. Three comparator instruments, Semmes-Weinstein monofilaments, Two-Point Discrimination, and the stereognosis subtest of the Revised Nottingham Sensory Assessment, were used for convergent validity. Results: Good test-retest reliability was confirmed for all of the TPT subtests. The values of minimal detectable change were acceptable. Moderate correlations between the TPT and comparator instruments were found, as expected. For known-groups validity, the significant difference was confirmed between children with CP and those with TD. Conclusions and relevance: The TPT is a reliable and valid measure for multiple subdomains of tactile perception in children with CP. This tactile assessment may help clarify tactile performance to provide appropriate, precise interventions. What This Article Adds: The TPT measures tactile perception in children with CP. It has four subdomains of tactile perception that could facilitate prioritization of tactile treatment of specific subdomains and thereby aid in the provision of appropriate interventions.

PMID: 37624995

12. Prevalence of orofacial injuries resulting from trauma in individuals with cerebral palsy: A systematic review and meta-analysis

Giovanna Santeli Heiden, Raphael Victor Silva Andrade, Bianca Marques de Mattos de Araujo, Ulisses Xavier da Silva-Neto, Flares Baratto-Filho, Bianca Simone Zeigelboim, Camila de Castro Corrêa, Karinna Veríssimo Meira Taveira, Cristiano Miranda de Araujo

Review Dent Traumatol. 2023 Aug 21. doi: 10.1111/edt.12879. Online ahead of print.

Individuals with cerebral palsy (CP) may have cognitive, sensitive, behavioral, communicative, and convulsive disorders. Because defensive reflexes are reduced by CP, the risk of orofacial trauma is greater in these individuals. This study aimed to evaluate the prevalence of orofacial injuries resulting from trauma in patients with CP. This review was reported according to preferred reporting items for systematic reviews and meta-analyses (PRISMA) and registered in the International Prospective Register of Systematic Reviews (PROSPERO-CRD42022293570). The search was performed for articles published until January 2023 in Embase, Latin American and Caribbean Literature on Health Sciences (LILACS), PubMed/Medline, Scopus, and Web of Science databases. Gray literature was also consulted through Google Scholar, OpenGrey, ProQuest Dissertations, and Theses. Studies in which orofacial injuries due to trauma were prevalent in individuals with CP were included. The risk of bias was assessed using the Joanna Briggs Institute Critical Appraisal Tool. Additionally, a random-effects meta-analysis was conducted. Twelve studies were included in the synthesis, of which nine presented a low risk of bias and three presented a moderate risk. When considering the general prevalence of orofacial injuries in patients with CP, a prevalence of 34% [95% CI = 18%-52%; I2 = 98%] was observed, with enamel and dentin fractures being the most common orofacial injuries. Approximately one in three patients with CP showed at least one type of orofacial injury involving dental trauma. There is a lack of literature assessing the prevalence of these traumas in soft tissues and the evidence for this outcome remains uncertain.

PMID: 37605544

13. Usability of the dynamic scaffolding system: an adaptive mobility device in children with special needs

Turgay Altunalan, Beyzanur Dikmen Hoşbaş, Melek Vatansever

Disabil Rehabil Assist Technol. 2023 Aug 23;1-8. doi: 10.1080/17483107.2023.2248185. Online ahead of print.

Purpose: Maintaining vertical position and moving are essential to healthy development. Children with motor difficulties may need assistive devices to stand upright or move. The Dynamic Scaffolding System (DSS) device was developed to support these skills. This study aims to explain the DSS's developmental stages, compare the device's usage times based on diagnoses and motor impairment, and investigate the degree of satisfaction among parents of children using the device. Materials and methods: The study included children with difficulty standing or stepping and their parents. We compared usage times of DSS depending on diagnosis (cerebral palsy (CP) or other diagnoses) and motor impairment levels. We assessed parental satisfaction by using the Quebec User Evaluation of Satisfaction with Assistive Technology (QUEST 2.0) and recorded adverse events. Results: The ages of the participants (n:100) were between 9 and 108 months (44.94 ± 17.59), and 60% of the children had CP, and 40% had other diagnoses (genetic, metabolic, neuromuscular diseases). The duration of daily use of DSS ranged from 44.17 (±26.16) to 110 (±97.98) minutes, and the duration was similar among children at different levels of motor impairment ($p = 0.262$). The parents were most satisfied with the size, simplicity of use, and effectiveness, and they were least satisfied with the ease of adjustment, safety, and durability. They did not report any adverse events during the study. Conclusions: DSS can be considered a useable assistive device option for children with CP and other diagnoses with difficulty standing or stepping and a satisfactory device for parents of such children.

PMID: 37610156

14. Cerebral palsy in children born after assisted reproductive technology in Norway: Risk, prevalence, and clinical characteristics

Henriette Carlsen, Torstein Vik, Guro L Andersen, Kristine Stangenes, Solveig Bjellmo, Kjersti Westvik-Johari, Sandra Julsen Hollung

Acta Obstet Gynecol Scand. 2023 Aug 21. doi: 10.1111/aogs.14663. Online ahead of print.

Introduction: The aim was to investigate the risk, prevalence, and clinical characteristics of cerebral palsy among children born after assisted reproductive technology (ART) in Norway. Material and methods: All liveborn children from 2002 to 2015 were included. Information was collected from the Medical Birth Registry of Norway, linked to the Norwegian Quality and Surveillance Registry for Cerebral Palsy as of December 31, 2022. Logistic regression analyses were used to calculate the prevalence of cerebral palsy per 1000 live births after ART and natural conception with birth year as covariate, crude odds ratios (OR) for cerebral palsy among children born after ART using children born after natural conception as reference, and OR adjusted for potential confounders, with 95% confidence intervals (CI). Potential mediators of the association were studied in stratified analyses. Descriptive statistics were used to compare proportions in clinical characteristics among children with cerebral palsy born after ART and natural conception. Results: Among 833 645 livebirths, 23 645 children were born after ART and of the latter 97 were diagnosed with cerebral palsy. The overall prevalence of cerebral palsy after ART was 4.10 per 1000 live births (95% CI 3.36-5.00), decreasing from 7.79 per 1000 in 2002 to 3.55 in 2015. Compared with children born after natural conception, the OR for cerebral palsy was 2.01 (95% CI 1.63-2.47) adjusted for mother's age at birth, parity, and pre-pregnancy health. When restricted to singletons born at term, the adjusted OR for cerebral palsy was 1.13 (95% CI 0.76-1.69). The distribution of cerebral palsy subtypes and the severity of gross and fine motor function and associated impairments did not differ significantly between children with cerebral palsy born after ART and natural conception. Conclusions: Children born after ART had a risk of cerebral palsy that was twice that of children born after natural conception. The increased risk of cerebral palsy after ART is likely attributed to multiple pregnancies and preterm births. The prevalence of cerebral palsy after ART decreased significantly during the study period, despite an increased use of ART in the population. The distribution of clinical characteristics did not differ between children with cerebral palsy born after ART and those born after a natural conception, suggesting that the risk factors for, and causes of cerebral palsy were similar.

PMID: 37602751

15. Validity and reliability of the Turkish version of the hand-use-at-home questionnaire for children with unilateral cerebral palsy and neonatal brachial plexus palsy

Ayca Evkaya-Acar, Evrim Karadag-Saygi, Ayse Simsek, Duygu Karali-Bingul, Bulent Elbasan

Disabil Rehabil. 2023 Aug 24;1-7. doi: 10.1080/09638288.2023.2248885. Online ahead of print.

Purpose: To translate the Hand-Use-at-Home questionnaire (HUH), assesses the amount of spontaneous use of the affected hand in children with 18 bimanual activities, into Turkish and examine its validity and reliability on children with neonatal brachial plexus palsy (NBPP) or unilateral cerebral palsy (UCP). Materials and methods: The HUH was translated and cross-

culturally adapted to Turkish and administered to children with NBPP (n = 25) and UCP (n = 42) between 3 and 10 years. The psychometric analyses included reliability by internal consistency (Cronbach's alpha) and test/retest reliability (intraclass correlation coefficient, ICC) structural validity was evaluated with exploratory factor analysis, and construct validity was investigated by matching the HUH with the Pediatric Outcome Data Collection Instrument Upper Extremity Scale (PODCI) (NBPP only), and Children's Hand-Use Experience Questionnaire (CHEQ) (UCP only). Results: HUH showed excellent test-retest reliability (ICC2,1 = 0.988 Cl (0.977-0.992)), excellent internal consistency (Cronbach's-α = 0.989), and moderate correlation with CHEQ (rs = 0.558) in UCP and high correlation with PODCI Scale (rs = 0.789) in NBPP group. The HUH had low and moderate correlation respectively lesion-extent levels (r=-0.457) in NBPP and 5 Manual Ability Classification System levels (r=-0.688) in the UCP group. Conclusion: The HUH is a valid and reliable tool to assess the amount of spontaneous use of the affected hand in Turkish children with NBPP and UCP.

PMID: 37615356

16. Neurodevelopmental Outcome of Very Low Birth Weight Infants in the Northern District of Israel: A Cross-Sectional Study

Michal Molad, Ayala Gover, Zaki Marai, Karen Lavie-Nevo, Irina Kessel, Lilach Shemer-Meiri, Marina Soloveichik

Children (Basel). 2023 Jul 31;10(8):1320. doi: 10.3390/children10081320.

Background: Currently, no local database in Israel collects neurodevelopmental outcomes of very low birth weight (VLBW) preterm infants. We investigated neurodevelopmental outcomes in one district of the largest healthcare organization in Israel. Methods: A cross-sectional study including all VLBW (<1500 g) preterm infants born between 1 January 2006 and 31 December 2016 who were followed in any of seven child development centers in Israel's Northern District. Data were retrospectively collected from the computerized medical record database. Results: Out of 436 participants, 55.1% had normal developmental outcomes. A total of 8.9% had cerebral palsy (CP), 12.2% had a global developmental delay (GDD), and 33.4% had a language delay. Out of the extremely preterm infants (n = 109), 20.2% had CP, 22.0% had GDD, and 44.9% had language delay. We found a statistically significant higher rate of abnormal neurodevelopment outcomes in non-Jews compared to Jews (57% vs. 37.8%, respectively, $p < 0.0001$). Conclusions: We found a relatively high overall rate of CP in our local population and a significant difference in neurodevelopmental outcomes between Jews and non-Jews. This study emphasizes the need for an expanded and detailed national database collecting post-discharge outcomes, as well as an assessment of national healthcare resource allocation and inequalities in preterm infants' post-discharge care.

PMID: 37628319

17. Family Needs Assessment of Patients with Cerebral Palsy Attending Two Hospitals in Accra, Ghana

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Children (Basel). 2023 Jul 29;10(8):1313. doi: 10.3390/children10081313.

Background: The family represents the most essential and supportive environment for children with cerebral palsy (CP). To improve children's outcomes, it is crucial to consider the needs of families in order to offer family-centered care, which tailors services to these needs. Objective: We conducted a needs assessment to identify the family needs of patients with CP attending two hospitals in Accra. Methods: The study was a cross-sectional study involving primary caregivers of children with CP attending neurodevelopmental clinics. Structured questionnaires were used to collect data spanning an 8-month period. The data were summarized, and statistical inference was made. Results: Service needs identified were childcare, counseling, support groups, financial assistance, and recreational facilities. Information needs included adult education, job training/employment opportunities, education, health and social programs, knowledge about child development, and management of behavioral and feeding/nutrition problems. Reducing extensive travel time was desirable to improve access to healthcare. With the increasing severity of symptoms came the need for improved accessibility in the home to reduce the child's hardship, as well as assistive devices, recreational facilities, and respite for the caregiver(s). Conclusion: Families of children with CP have information, service, and access needs related to their disease severity and family context.

PMID: 37628312

18. Editorial Highlights from the Comorbidities and Complications of Cerebral Palsy Special Issue

Monica S Cooper, Christine Imms

Editorial J Clin Med. 2023 Aug 16;12(16):5329. doi: 10.3390/jcm12165329.

Cerebral palsy is a life-long condition and the most common cause of physical disability in childhood [...].

PMID: 37629371

19. Comorbidities Affecting Children with Autism Spectrum Disorder: A Retrospective Chart Review

Jessy Burns, Ryan Phung, Shayna McNeill, Ana Hanlon-Dearman, M Florencia Ricci

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Autism spectrum disorder (ASD) is a developmental disorder characterized by deficits in social interaction/communication, restricted interests, and repetitive behaviors. Recent discussions have emerged worldwide regarding the heterogeneity around presentation/etiology and comorbidities. This study aimed to determine the frequency and characteristics of comorbidities among children diagnosed with ASD in Manitoba and to evaluate differences in presentation between those with and without medical comorbidities. We conducted a retrospective chart review of >1900 electronic charts at the only publicly funded referral site for children ≤6 years requiring evaluation for ASD in Manitoba. All children aged 0-6 years diagnosed with ASD at this site between May 2016 and September 2021 were identified. $\chi 2$ and t-tests were used to compare groups. Of the total of 1858 children identified, 1452 (78.1%) were boys, 251 (13.5%) were prematurely born, and 539 (29.0%) had ≥1 medical comorbidity. Global developmental delay (GDD) was diagnosed in 428 (23.0%). The age of referral and diagnosis did not differ between groups. Comorbidities were more common among premature children (16.0% vs. 12.5%, p: 0.005) and children with comorbid GDD (34.9% vs. 18.2%, $p < 0.001$). Neurological comorbidities were most common (37.1%). No sex difference in the overall presence of comorbidities was found (boys = 77.1% vs. 78.5%, p: 0.518); however, girls had a higher incidence of neurological comorbidities, e.g., cerebral palsy, seizures, hypotonia (14.8% vs. 9.64%, p: 0.009), as well as genetic comorbidities (4.92% vs. 2.75%, p: 0.04). The high rates of associated neurological conditions, GDD, and prematurity add heterogeneity to this group leading to potential difficulties with prognosis and service allocation. Primary vs. secondary ASD can be a way of separating individuals based on relevant medical comorbidities.

PMID: 37628413

20. Botulinum Toxin Treatment of Adult Muscle Stem Cells from Children with Cerebral Palsy and hiPSC-Derived Neuromuscular Junctions

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Botulinum neurotoxin type-A (BoNT) injections are commonly used as spasticity treatment in cerebral palsy (CP). Despite improved clinical outcomes, concerns regarding harmful effects on muscle morphology have been raised, and the BoNT effect on muscle stem cells remains not well defined. This study aims at clarifying the impact of BoNT on growing muscles (1) by analyzing the in vitro effect of BoNT on satellite cell (SC)-derived myoblasts and fibroblasts obtained from medial gastrocnemius microbiopsies collected in young BoNT-naïve children (t0) compared to age ranged typically developing children; (2) by following the effect of in vivo BoNT administration on these cells obtained from the same children with CP at 3 (t1) and 6 (t2) months post BoNT; (3) by determining the direct effect of a single and repeated in vitro BoNT treatment on neuromuscular junctions (NMJs) differentiated from hiPSCs. In vitro BoNT did not affect myogenic differentiation or collagen production. The fusion index significantly decreased in CP at t2 compared to t0. In NMJ cocultures, BoNT treatment caused axonal swelling and fragmentation. Repeated treatments impaired the autophagic-lysosomal system. Further studies are warranted to understand the long-term and collateral effects of BoNT in the muscles of children with CP.

PMID: 37626881

21. Divergent neurodevelopmental profiles of very-low-birth-weight infants

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Background: Advanced perinatal medicine has decreased the mortality rate of preterm infants. Long-term neurodevelopmental outcomes of very-low-birth-weight infants (VLBWIs) remain to be investigated. Methods: Participants were 124 VLBWIs who had in-hospital birth from 2007 to 2015. Perinatal information, developmental or intelligence quotient (DQ/IQ), and neurological comorbidities at ages 3 and 6 years were analyzed. Results: Fifty-eight (47%) VLBWIs received neurodevelopmental assessments at ages 3 and 6 years. Among them, 15 (26%) showed DQ/IQ <75 at age 6 years. From age 3 to 6 years, 21 (36%) patients showed a decrease (≤-10), while 5 (9%) showed an increase (≥+10) in DQ/IQ scores. Eight (17%) with autism spectrum disorder or attention-deficit hyperactivity disorder (ASD/ADHD) showed split courses of DQ/IQ,

including two with ≤-10 and one with +31 to their scores. On the other hand, all 7 VLBWIs with cerebral palsy showed DQ ≤35 at these ages. Magnetic resonance imaging detected severe brain lesions in 7 (47%) of those with DQ <75 and 1 (18%) with ASD/ADHD. Conclusions: VLBWIs show a broad spectrum of neurodevelopmental outcomes after 6 years. These divergent profiles also indicate that different risks contribute to the development of ASD/ADHD from those of cerebral palsy and epilepsy in VLBWIs. Impact: Very-low-birth-weight infants (VLBWIs) show divergent neurodevelopmental outcomes from age 3 to 6 years. A deep longitudinal study depicts the dynamic change in neurodevelopmental profiles of VLBWIs from age 3 to 6 years. Perinatal brain injury is associated with developmental delay, cerebral palsy and epilepsy, but not with ASD or ADHD at age 6 years.

PMID: 37626120

22. Acquired Brain Injuries Across the Perinatal Spectrum: Pathophysiology and Emerging Therapies

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The development of the central nervous system can be directly disrupted by a variety of acquired factors, including infectious, inflammatory, hypoxic-ischemic, and toxic insults. Influences external to the fetus also impact neurodevelopment, including placental health, maternal comorbidities, adverse experiences, environmental exposures, and social determinants of health. Acquired perinatal brain insults tend to affect the developing brain in a stage-specific manner that reflects the susceptible cell types, developmental processes, and risk factors present at the time of the insult. In this review, we discuss the pathophysiology, neurodevelopmental outcomes, and management of common acquired perinatal brain conditions. In the fetal brain, we divide insults based on trimester, and in the postnatal brain, we focus on common pathologies that have a presentation dependent on gestational age at birth: white matter injury and germinal matrix hemorrhage/intraventricular hemorrhage in preterm infants and hypoxic-ischemic encephalopathy in term infants. Although specific treatments for fetal and newborn brain disorders are currently limited, we emphasize therapies in preclinical or early clinical phases of the development pipeline. The growing number of novel cell type- and stage-specific emerging therapies suggests that in the near future we may have a dramatically improved ability to treat acquired perinatal brain disorders and to mitigate the associated neurodevelopmental consequences.

PMID: 37625929

23. Sentence Length Effects on Intelligibility in Two Groups of Older Children With Neurodevelopmental Disorders

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Am J Speech Lang Pathol. 2023 Aug 25;1-14. doi: 10.1044/2023_AJSLP-23-00093. Online ahead of print.

Purpose: The purpose of this study was to examine the impact of sentence length on intelligibility in two groups of older children with neurodevelopmental disabilities. Method: Nine children diagnosed with cerebral palsy (CP) and eight children diagnosed with Down syndrome (DS), between the ages of 8 and 17 years, repeated sentences varying in length from two to seven words. Three hundred forty adult listeners (20 listeners per child) provided orthographic transcriptions of children's speech, which were used to calculate intelligibility scores. Results: There was a significant main effect of sentence length on intelligibility for children with CP. Intelligibility significantly increased from two- and three-word sentences to four-, five-, and six-word sentences, then significantly decreased from four-, five-, and six-word sentences to seven-word sentences. There was a main effect of sentence length on intelligibility for children with DS. Intelligibility significantly increased from two-word sentences to four-, five-, and six-word sentences. Conclusions: The primary findings of this study include the following: (a) Unlike in typically developing children, sentence length continues to influence intelligibility well into adolescence for children with neurodevelopmental disorders, and (b) sentence length may influence intelligibility differently in children with CP than in children with DS; however, other factors besides the type of neurodevelopmental disorder (e.g., severity of speech motor involvement and/or cognitive-linguistic impairment) could play a role in the relationship between sentence length and intelligibility and must be investigated in future studies.

PMID: 37625147

24. The hereditary spastic paraplegias

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Review Handb Clin Neurol. 2023;196:59-88. doi: 10.1016/B978-0-323-98817-9.00022-3.

The hereditary spastic paraplegias (HSPs) are a group of more than 90 genetic disorders in which lower extremity spasticity and weakness are either the primary neurologic impairments ("uncomplicated HSP") or when accompanied by other neurologic

deficits ("complicated HSP"), important features of the clinical syndrome. Various genetic types of HSP are inherited such as autosomal dominant, autosomal recessive, X-linked, and maternal (mitochondrial) traits. Symptoms that begin in early childhood may be nonprogressive and resemble spastic diplegic cerebral palsy. Symptoms that begin later, typically progress insidiously over a number of years. Genetic testing is able to confirm the diagnosis for many subjects. Insights from gene discovery indicate that abnormalities in diverse molecular processes underlie various forms of HSP, including disturbance in axon transport, endoplasmic reticulum morphogenesis, vesicle transport, lipid metabolism, and mitochondrial function. Pathologic studies in "uncomplicated" HSP have shown axon degeneration particularly involving the distal ends of corticospinal tracts and dorsal column fibers. Treatment is limited to symptom reduction including amelioration of spasticity, reducing urinary urgency, proactive physical therapy including strengthening, stretching, balance, and agility exercise.

PMID: 37620092

25. Chronic Neurological Disorders and Predisposition to Severe COVID-19 in Pediatric Patients in the United States

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Pediatr Neurol. 2023 Jul 22;147:130-138. doi: 10.1016/j.pediatrneurol.2023.07.012. Online ahead of print.

Background: We investigated the association between chronic pediatric neurological conditions and the severity of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Methods: This matched retrospective case-control study includes patients (n = 71,656) with chronic complex neurological disorders under 18 years of age, with laboratory-confirmed diagnosis of COVID-19 or a diagnostic code indicating infection or exposure to SARS-CoV-2, from 103 health systems in the United States. The primary outcome was the severity of coronavirus disease 2019 (COVID-19), which was classified as severe (invasive oxygen therapy or death), moderate (noninvasive oxygen therapy), or mild/asymptomatic (no oxygen therapy). A cumulative link mixed effects model was used for this study. Results: In this study, a cumulative link mixed effects model (random intercepts for health systems and patients) showed that the following classes of chronic neurological disorders were associated with higher odds of severe COVID-19: muscular dystrophies and myopathies (OR = 3.22; 95% confidence interval [CI]: 2.73 to 3.84), chronic central nervous system disorders (OR = 2.82; 95% CI: 2.67 to 2.97), cerebral palsy (OR = 1.97; 95% CI: 1.85 to 2.10), congenital neurological disorders (OR = 1.86; 95% CI: 1.75 to 1.96), epilepsy (OR = 1.35; 95% CI: 1.26 to 1.44), and intellectual developmental disorders (OR = 1.09; 95% CI: 1.003 to 1.19). Movement disorders were associated with lower odds of severe COVID-19 (OR = 0.90; 95% CI: 0.81 to 0.99). Conclusions: Pediatric patients with chronic neurological disorders are at higher odds of severe COVID-19. Movement disorders were associated with lower odds of severe COVID-19.

PMID: 37611407

26. Mechanisms of Tertiary Neurodegeneration after Neonatal Hypoxic-Ischemic Brain Damage

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Neonatal encephalopathy linked to hypoxia-ischemia (H-I) which is regarded as the most important neurological problem of the newborn, can lead to a spectrum of adverse neurodevelopmental outcomes such as cerebral palsy, epilepsy, hyperactivity, cognitive impairment and learning difficulties. There have been numerous reviews that have focused on the epidemiology, diagnosis and treatment of neonatal H-I; however, a topic that is less often considered is the extent to which the injury might worsen over time, which is the focus of this review. Similarly, there have been numerous reviews that have focused on mechanisms that contribute to the acute or subacute injury; however, there is a tertiary phase of recovery that can be defined by cellular and molecular changes that occur many weeks and months after brain injury and this topic has not been the focus of any review for over a decade. Therefore, in this article we review both the clinical and pre-clinical data that show that tertiary neurodegeneration is a significant contributor to the final outcome, especially after mild to moderate injuries. We discuss the contributing roles of apoptosis, necroptosis, autophagy, protein homeostasis, inflammation, microgliosis and astrogliosis. We also review the limited number of studies that have shown that significant neuroprotection and preservation of neurological function can be achieved administering drugs during the period of tertiary neurodegeneration. As the tertiary phase of neurodegeneration is a stage when interventions are eminently feasible, it is our hope that this review will stimulate a new focus on this stage of recovery towards the goal of producing new treatment options for neonatal hypoxic-ischemic encephalopathy.

PMID: 37601279

27. Precision medicine in neurosurgery: The evolving role of theranostics

Drashti Patel, Andrew Nguyen, Chance Fleeting, Anjali B Patel, Mohammed Mumtaz, Brandon Lucke-Wold

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Theranostics in neurosurgery is a rapidly advancing field of precision medicine that combines diagnostic and therapeutic modalities to optimize patient outcomes. This approach has the potential to provide real-time feedback during therapy and diagnose a condition while simultaneously providing treatment. One such form of theranostics is focused ultrasound, which has been found to be effective in inducing neuroablation and neuromodulation and improving the efficacy of chemotherapy drugs by disrupting the blood-brain barrier. Targeted radionuclide therapy, which pairs positron emission tomography tracers with therapeutic effects and imaging modalities, is another promising form of theranostics for neurosurgery. Automated pathology analysis is yet another form of theranostics that can provide real-time feedback during the surgical resection of tumors. Electrical stimulation has also shown promise in optimizing therapies for patients with cerebral palsy. Overall, theranostics is a cost-effective way to optimize medical care for patients in neurosurgery. It is a relatively new field, but the advancements made so far show great promise for improving patient outcomes.

PMID: 37601162

Prevention and Cure

28. School-Age Outcomes of Antenatal Magnesium Sulphate in Preterm Infants

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Review Children (Basel). 2023 Jul 31;10(8):1324. doi: 10.3390/children10081324.

Background: Antenatal magnesium sulphate (MgSO4) therapy given to women at risk of preterm birth reduced the risk of cerebral palsy in early childhood. However, its effect on longer-term neurological outcomes remains uncertain. This study aimed to assess the effects of antenatal MgSO4 therapy on school-age outcomes of preterm infants. Methods: We conducted a systematic review and meta-analysis. We searched MEDLINE, EMBASE, CENTRAL, and CINAHL for randomized controlled trials (RCTs). Two reviewers independently evaluated the eligibility for inclusion and extracted data. Results: Ten RCTs were included. Only two of them were on school-age outcomes. Antenatal MgSO4 therapy had no impact on cerebral palsy, hearing impairment, neurosensory disability, and death at school-age. Meta-analysis on mental retardation and visual impairment was not able to be performed due to different methods of evaluation. In the analysis of short-term outcomes conducted as secondary outcomes, antenatal MgSO4 therapy increased the risk of maternal adverse events with any symptom (3 RCTs; risk ratio 2.79; 95% confidence interval 1.10 to 7.05, low certainty of evidence) but was not associated with any neonatal symptoms. Conclusions: The number of cases was insufficient to determine the impact of antenatal MgSO4 therapy on school-age outcomes. Further accumulation of long-term data is required.

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