

Cerebral palsy research news

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Interventions and Management

1. Efficacy of integrating a semi-immersive virtual device in the HABIT-ILE intervention for children with unilateral cerebral palsy: a non-inferiority randomized controlled trial

G Saussez, R Bailly, R Araneda, J Paradis, D Ebner-Karestinos, A Klöcker, E S Sogbossi, I Riquelme, S Brochard, Y Bleyenheuft

Randomized Controlled Trial J Neuroeng Rehabil. 2023 Jul 29;20(1):98. doi: 10.1186/s12984-023-01218-4.

Background: The implementation of virtual devices can facilitate the role of therapists (e.g., patient motivation, intensity of practice) to improve the effectiveness of treatment for children with cerebral palsy. Among existing therapeutic devices, none has been specifically designed to promote the application of principles underlying evidence-based motor skill learning interventions. Consequently, evidence is lacking regarding the effectiveness of virtual-based sessions in motor function rehabilitation with respect to promoting the transfer of motor improvements into daily life activities. We tested the effectiveness of implementing a recently developed virtual device (REAtouch®), specifically designed to enable the application of therapeutic motor skill learning principles, during a Hand Arm Bimanual Intensive Therapy Including Lower Extremities (HABIT-ILE) intervention. Methods: Forty children with unilateral cerebral palsy (5-18 years; MACS I-III; GMFCS I-II) were randomly assigned to a control group or a "REAtouch®" experimental group for a 90-h HABIT-ILE daycamp intervention (two weeks). Children in the REAtouch® group spent nearly half of their one-on-one therapeutic time using the REAtouch®. Participants underwent three testing sessions: the week before (T1), after intervention (T2), and at three months follow-up (T3). The primary outcome was the Assisting Hand Assessment (T3-T1; blinded). Secondary outcomes measured uni-bimanual hand function, stereognosis, gait endurance, daily life abilities, and functional goals. Accelerometers and a manual report of daily activities served to document therapeutic dosage and treatment characteristics. We used one-way RMANOVA to compare the efficacies of the two interventions, and non-inferiority analyses to contrast changes in the "REAtouch®" group versus the "HABIT-ILE" control group. Results: We found significant improvements in both groups for most of the outcome measures (p < 0.05). There was significant non-inferiority of changes in the REAtouch® group for upper extremities motor function, functional goals attainment, and abilities in daily life activities (p < 0.05). Conclusions: Use of the REAtouch® device during HABIT-ILE showed non-inferior efficacy compared to the conventional evidence-based HABIT-ILE intervention in children with unilateral cerebral palsy. This study demonstrates the feasibility of using this virtual device in a high dosage camp model, and establishes the possibility of applying the therapeutic principles of motor skill learning during specifically designed virtual-based sessions.

PMID: <u>37516873</u>

2. Safety and efficacy of non-invasive brain stimulation for the upper extremities in children with cerebral palsy: A systematic review

Nicole Metelski, Yu Gu, Lori Quinn, Kathleen M Friel, Andrew M Gordon

Review Dev Med Child Neurol. 2023 Aug 1. doi: 10.1111/dmcn.15720. Online ahead of print.

Aim: To evaluate available evidence examining safety and efficacy of non-invasive brain stimulation (NIBS) on upper

extremity outcomes in children with cerebral palsy (CP). Method: We electronically searched 12 sources up to May 2023 using JBI and Cochrane guidelines. Two reviewers selected articles with predetermined eligibility criteria, conducted data extraction, and assessed risk of bias using the Cochrane Risk of Bias criteria. Results: Nineteen studies were included: eight using repetitive transcranial magnetic stimulation (rTMS) and 11 using transcranial direct current stimulation (tDCS). Moderate certainty evidence supports the safety of rTMS and tDCS for children with CP. Very low to moderate certainty evidence suggests that rTMS and tDCS result in little to no difference in upper extremity outcomes. Interpretation: Evidence indicates that NIBS is a safe and feasible intervention to target upper extremity outcomes in children with CP, although it also indicates little to no significant impact on upper extremity outcomes. These findings are discussed in relation to the heterogeneous participants' characteristics and stimulation parameters. Larger studies of high methodological quality are required to inform future research and protocols for NIBS.

PMID: 37528530

3. Scoliosis in children with severe cerebral palsy: a population-based study of 206 children at GMFCS levels III-V

Svend Vinje, Terje Terjesen, Thomas Kibsgård

Eur Spine J. 2023 Aug 2. doi: 10.1007/s00586-023-07868-1. Online ahead of print.

Purpose: To evaluate the prevalence of scoliosis and the rate of scoliosis progression in children with severe cerebral palsy (CP) at GMFCS levels III-V. Methods: Two hundred and six children (86 girls, 120 boys), born 2002-2008, were recruited from The Norwegian Quality and Surveillance Registry for Cerebral Palsy (NorCP). Inclusion criteria were bilateral CP and GMFCS levels III-V. Scoliosis was evaluated annually by examination of the spine by a physiotherapist. Radiographic examination was performed in children with moderate or severe scoliosis at clinical evaluation. The Cobb angle was used as a measure of curve magnitude. Results: Scoliosis, defined as Cobb angle $\geq 10^{\circ}$, occurred in 121 children (59%). Severe scoliosis (Cobb angle $\geq 40^{\circ}$) developed in 80 of the 206 patients (39%) at a mean age of 10.9 years (range 5-16) and was more prevalent in children at GMFCS level V (62%) than at levels IV (19%) and III (6%). Initial Cobb angle, Cobb angle $\geq 30^{\circ}$ at age 10 years, and GMFCS level V were independent risk factors for severe scoliosis. In children at GMFCS level V, the rate of scoliosis progression decreased with age from a mean of 9.7° per year at age 3-5 years to 2-3° per year in children ≥ 11 years. Conclusions: The prevalence of scoliosis among children with CP increased with decreasing motor functional level. The most important risk factors for progression of scoliosis were high initial Cobb angle $\geq 30^{\circ}$ at age 10 years, and GMFCS level V.

PMID: 37532910

4. Impairments and comorbidities in adults with cerebral palsy and spina bifida: a meta-analysis

Jane N T Sattoe, Sander R Hilberink

Review Front Neurol. 2023 Jul 18;14:1122061. doi: 10.3389/fneur.2023.1122061. eCollection 2023.

Introduction: Aging with a childhood-onset disability, such as cerebral palsy (CP), spina bifida (SB), and muscular diseases (MD), comes along with significant impairments and comorbidities. Despite the increasing evidence an overall picture is lacking. This study aimed to review the literature about adults with CP/SB/MD and impairments and comorbidities to perform a meta-analysis. Materials and methods: Embase, PubMed, Cinahl, and Google Scholar were searched (2000-2020). Search terms included adults with one of the aforementioned disabilities combined with impairments and comorbidities. If specific impairments or comorbidities were reported by at least four studies, these were included in the study. Pooled prevalence (95% Confidence Interval) of impairments/comorbidities were calculated. Results: The search yielded 7,054 studies of which 95 were included in the meta-analysis (64 CP, 31 SB, 0 MD). In total estimates were calculated for 26 (CP) and 11 (SB) outcomes. In adults with CP, pain [56.4% (95%CI 48.8-63.8)], deformities [44.2% (95%CI 12.9-78.4)], intellectual disability [37.2% (95%CI 26.7-48.3)], and fatigue [36.9% (95%CI 24.6-50.1)] were most prevalent; renal disease [3.0% (95%CI 2.1-4.2)] and stroke/rheumatic diseases {4.8% (95%CI 3.4-6.5; 4.8% (95%CI 1.5-9.9)] respectively} were least prevalent. For adults with SB, bladder incontinence [60.0% (95%CI 50.5-69.2)], bowel incontinence [49.2% (95%CI 34.5-64.0)], pain [44.1% (95%CI 27.4-61.5)], and sleeping problems [30.3% (95%CI 4.7-65.8)] were most prevalent; diabetes [4.8% (95%CI 2.8-7.3)] and renal disease [8.7% (95%CI 2.0-19.9)] were least prevalent. The included studies showed large heterogeneity. Conclusions: More research is needed to study health issues in adults with MD. Adults with CP or SB deal with a variety of health issues. More attention for the mental health of these adults is needed. There also is a need for accessible and adequate screening, preventive measures and clinical follow-up.

PMID: 37533474

5. Exosomal Lipid Biomarkers of Oligodendrocyte Pathology to Predict Scoliosis in Children with Cerebral Palsy

Nune Darbinian, Emily C Sparks, Armine Darbinyan, Nana Merabova, Tamara Tatevosian-Geller, Katie Calaku, Sarah Bachman, Huaqing Zhao, Shohreh Amini, Laura Goetzl, Solomon P Samuel, Amer Samdani, Michael E Selzer

Obstet Gynecol Res. 2023;6(2):160-170. doi: 10.26502/ogr0127. Epub 2023 May 22.

Introduction: Cerebral Palsy (CP), the most common cause of disability in children, is phenotypically heterogeneous. Approximately 20% of cases develop severe scoliosis. A pathological hallmark of CP is periventricular leukomalacia (PVL), which is due to dysmyelination, suggesting the possibility of a lipidomic abnormality. Risk factors for CP include perinatal hypoxia, prematurity, multiple gestation, ischemia, infection, and maternal alcohol consumption. There is evidence for low serum levels of omega-3 (ω -3) fatty acids in CP patients, and separately in idiopathic scoliosis. Many effects of free fatty acids (FFAs) are mediated via specific G protein-coupled free fatty acid receptors (FFARs), which play essential roles as nutritional and signaling molecules. FFAs, including ω -3, and their receptors are involved in the development and metabolism of oligodendrocytes (OLs), and are critical to myelination. Thus, the cases of CP that will develop severe scoliosis might be those in which there is a deficiency of ω -3, FFARs, or other lipidomic abnormality that is detectable early in the plasma. If so, we might be able to predict scoliosis and prevent it with dietary supplementation. Methods: Blood samples were collected from four groups of patients at the Philadelphia Shriners Children's Hospital (SCH-P): 1) patients with CP; 2) severe scoliosis (>400); 3) CP plus scoliosis; and 4) non-impaired controls stratified by age (2-18 yrs), gender, and race/ethnicity, under an IRB -approved protocol. Serum proteins and RNA were purified, and OL-derived exosomes (OL-Es) isolated, using myelin basic protein (MBP) as a late OL marker. Protein was used for the detection of MBP and FFAR by enzyme-linked immunosorbent assays (ELISAs), and by flow cytometry. RNA was assayed by digital droplet polymerase chain reaction (ddPCR) for OL markers and FFAR expression. Results: FFAR and MBP proteins were downregulated in each of the three patient groups compared to controls, and this difference was greatest in both patients with CP plus scoliosis. Conclusion: Altogether, MBP and FFAR levels were reduced in OL-Es from both children with CP plus scoliosis. The lipid abnormalities specific to CP with scoliosis were concentrated in OLs. Our data might i) suggest therapeutic targets to reduce dysmyelination and scoliosis in CP, ii) predict which children are at risk for developing scoliosis, iii) lead to therapeutic trials of fatty acids for CP and other dysmyelinating neurological disorders.

PMID: 37538811

6. Hips in cerebral palsy: A clinico-radiological evaluation of hip subluxation in cerebral palsy

Sherashah Kammar, Anand Varma, Sharon Paul, Ijaz Pillai

J Clin Orthop Trauma. 2023 Jul 16;43:102224. doi: 10.1016/j.jcot.2023.102224. eCollection 2023 Aug.

Background: The study was done on children with cerebral palsy in the ages of 2-18 years, with focus on hip subluxation. The objectives of the study were to look at the distribution of different types of CP in the target population; the prevalence of hip subluxation and its association with types and severity of CP. Methods: This is a cross sectional descriptive observational study, done on a hospital out-patient setting. Children with cerebral palsy of ages 2-18 years were recruited and clinically evaluated. Radiological evaluation of the pelvis was done for all subjects. Primary outcome measure was presence of hip subluxation described as Migration Percentage >30% in one or both hips. Prevalence of subluxation and its association with various subtypes of CP were assessed. Results: 203 subjects with cerebral palsy underwent the study. Spastic type of presentation constituted the majority (82.8%). Quadriplegic distribution (53.2%) and functional level of GMFCS 5 (39.4%) were most prevalent. Hip subluxation was noted in 105 of the 203 children with CP (51.7%). 3 patients had complete dislocation of the hip (1.4%). There was an increased prevalence of hip subluxation noted with increasing GMFCS E&R score as well as increasing topographical distribution, which were both statistically significant on univariate analysis (p < 0.005). On multivariate analysis, it was found that neither topographical distribution nor GMFCS E&R score were independent risk factors. Conclusions: Hip subluxation is a significant, debilitating and common treatable complication in children with CP. Subjects with widespread topographical distribution and poor functional ambulatory status are at an increased risk of developing hip subluxation. There also exists a correlation between GMFCS scores and topographical classification and hence, neither are risk factors independent of each other. This study is a first of its kind in the Indian scenario and it hopes to be a step in the direction towards risk stratification, early diagnosis and prompt specific treatment of hip complications in children with cerebral palsy.

PMID: 37538299

7. Radiographic Measurements Associated With Ankle Power Generation During Gait in Patients With Cerebral Palsy

Yoon Hyo Choi, Tae Hun Kwon, Ji Hye Choi, Naun Jeong, Seungbum Koo, Kyoung Min Lee

J Pediatr Orthop. 2023 Jul 31. doi: 10.1097/BPO.00000000002475. Online ahead of print.

Background: Pes planovalgus (PV) deformity accounts for lever arm dysfunction and compromises gait in patients with cerebral palsy (CP). However, the association between ankle power generation and radiographic indices is not yet understood. We aimed to investigate the association between ankle power and radiographic indices during gait in patients with CP concomitant with PV deformity. Methods: Patients older than 14 years with ambulatory CP and PV deformity were included. All the patients underwent 3-dimensional gait analysis and weight-bearing foot radiography. Gait data were collected,

including foot progression angle, tibial rotation, hip rotation, and ankle power generation. Radiographic measurements included anteroposterior (AP) talo-first metatarsal angle, lateral talo-first metatarsal angle, and hindfoot angle. A linear mixed-effects model was performed to identify significant radiographic indices associated with ankle power generation. Results: Thirty-one limbs from 15 patients with spastic diplegia and 6 with spastic hemiplegia were included. Statistical analysis demonstrated that ankle power generation was significantly correlated with the CP type (P=0.0068) and AP talo-1stmetatarsal angle (P=0.0230). Conclusion: Ankle power generation was significantly associated with the AP talo-first metatarsal angle. Surgeons might need to pay attention to correcting forefoot abduction to restore ankle power when planning surgeries for pes PV deformities in patients with CP. Level of evidence: Prognostic Level III.

PMID: 37522472

8. A longitudinal analysis of selective motor control during gait in individuals with cerebral palsy and the relation to gait deviations

Gilad Sorek, Marije Goudriaan, Itai Schurr, Simon-Henri Schless

PLoS One. 2023 Jul 31;18(7):e0289124. doi: 10.1371/journal.pone.0289124. eCollection 2023.

Objective: To investigate longitudinal changes in selective motor control during gait (SMCg) in individuals with cerebral palsy (CP), and to assess if they are related to changes in gait deviations. Method: Twenty-three children/adolescents with spastic CP (mean \pm SD age = 9.0 \pm 2.5 years) and two 3D gait assessments (separated by 590 \pm 202 days) with no interim surgical intervention, were included. SMCg was assessed using muscle synergy analysis to determine the dynamic motor control index (walk-DMC). Gait deviation was assessed using the Gait profile score (GPS) and Gait variable scores (GVS). Results: There were no mean changes in walk-DMC score, GPS or GVS between assessments. However, changes in walk-DMC scores in the more involved leg related to changes in hip flexion-extension and hip internal-external GVS (rp = -0.56; p = 0.017 and rp = 0.65; p = 0.004, respectively). Conclusions: On average, there were no significant longitudinal changes in SMCg. However, there was considerable variability between individuals, which may relate to changes in hip joint kinematics. This suggests that a combination of neural capacity and biomechanical factors influence lower limb muscle co-activation in individuals with CP, with a potential important role for the hip muscles. These findings highlight the importance of taking an individualized approach when evaluating SMCg in individuals with CP.

PMID: 37523363

9. Predicting Gait Patterns of Children With Spasticity by Simulating Hyperreflexia

Kirsten Veerkamp, Christopher P Carty, Niels F J Waterval, Thomas Geijtenbeek, Annemieke I Buizer, David G Lloyd, Jaap Harlaar, Marjolein M van der Krogt

J Appl Biomech. 2023 Aug 2;1-13. doi: 10.1123/jab.2023-0022. Online ahead of print.

Spasticity is a common impairment within pediatric neuromusculoskeletal disorders. How spasticity contributes to gait deviations is important for treatment selection. Our aim was to evaluate the pathophysiological mechanisms underlying gait deviations seen in children with spasticity, using predictive simulations. A cluster analysis was performed to extract distinct gait patterns from experimental gait data of 17 children with spasticity to be used as comparative validation data. A forward dynamic simulation framework was employed to predict gait with either velocity- or force-based hyperreflexia. This framework entailed a generic musculoskeletal model controlled by reflexes and supraspinal drive, governed by a multiobjective cost function. Hyperreflexia values were optimized to enable the simulated gait to best match experimental gait patterns. Three experimental gait patterns were extracted: (1) increased knee flexion, (2) increased ankle plantar flexion, and (3) increased knee flexion and ankle plantar flexion when compared with typical gait. Overall, velocity-based hyperreflexia outperformed force-based hyperreflexia. The first gait pattern could mostly be explained by rectus femoris and hamstrings velocity-based hyperreflexia. This study shows how velocity-based hyperreflexia from specific muscles contributes to different spastic gait patterns, which may help in providing targeted treatment.

PMID: 7532263

10. Consequences of Virtual Reality Experience on Biomechanical Gait Parameters in Children with Cerebral Palsy: A Scoping Review

Regine Lohss, Marco Odorizzi, Morgan Sangeux, Carol-Claudius Hasler, Elke Viehweger

Review Dev Neurorehabil. 2023 Aug 3;1-12. doi: 10.1080/17518423.2023.2242930. Online ahead of print.

Virtual reality (VR), coupled with motion tracking, can investigate walking in a controlled setting while applying various

walking challenges. The purpose of this review was to summarize the evidence on consequences of VR on biomechanical gait parameters in children with cerebral palsy. MEDLINE, Embase and Web of Science were searched. Among 7.574 studies, screened by two independent reviewers, seven studies were included, analyzing treadmill (n = 6) or overground walking (n = 1) under VR. Most frequently reported were the spatiotemporal parameters walking speed, stride length, step width, stance phase, and the kinematic parameters range of knee flexion and peak ankle dorsiflexion. However, methodological approaches and reporting of the results were inconsistent among studies. This review reveals that VR can complement information gained from clinical gait analysis. However, this is still an emerging field of research and there is limited knowledge on the effect of VR on gait parameters, notably during overground walking.

PMID: 37537745

11. The novel Next Step test is a reliable measure of anticipatory postural adjustments made by children with cerebral palsy prior to taking a step

Rachel Rapson, Jos M Latour, Bernie Carter, Vasiliki Pitsouni, Jonathan F Marsden

Gait Posture. 2023 Jul 28;105:110-116. doi: 10.1016/j.gaitpost.2023.07.286. Online ahead of print.

Background: Children with cerebral palsy (CP) make smaller medio-lateral anticipatory postural adjustments (APAs) than typically developing peers when stepping forward to a medial target. They are also less accurate at reaching the stepping target. The Next Step test involves the biomechanical measurement of APAs and foot placement error. These may be useful outcome measures to evaluate dynamic balance in a clinical trial. The reliability of the measures must be assessed to establish their reliability as research tools. Research question: What is the inter-rater and intra-rater reliability of stepping accuracy and measures of APAs made by children prior to taking a step? Methods: Typically developing (TD) (n = 14) or children with CP (n = 16) were recruited from local clinics. Children stepped to electro-luminescent targets placed medially and laterally to each foot. Stepping responses were measured using a force plate and 3D motion analysis of markers placed on the feet and pelvis. The APA was defined as the movement of the centre of pressure (COP) and the centre of mass (COM) estimated via pelvic markers, prior to lifting the lead leg. Stepping accuracy was defined as the absolute distance between the target and end foot position. Participants undertook two data collection sessions separated by at least one week. In session one, the test was measured by rater 1 who repeated this in session two, along with another data collection by a rater 2 or rater 3, after a rest period. Where data were normally distributed, they were assessed for inter-rater and intra-rater reliability using an intra-class correlation coefficient (ICC) and Bland-Altman plots. The standard error of measurement was calculated to determine the minimum difference needed to detect true change. Results: There was no between-group differences in group characteristics (age, weight, height) or in stepping velocity. We found good to excellent reliability when measuring the amplitude and velocity of medio-lateral APAs (ICC range 0.73-0.89). The reliability of antero-posterior APAs was more variable (ICC range 0.08-0.92). The minimum difference to detect a true change for peak medio-lateral motion of COP ranges from 23.7 mm to 29.6 mm and for peak velocity of medio-lateral COM estimate 41-61.9 mm. Stepping accuracy was not normally distributed. Significance: The Next Step test is a reliable measure of dynamic balance. The peak medio-lateral motion of the COP and medio-lateral velocity of the COM estimate are reliable when measured during a constrained stepping task in ambulant children with cerebral palsy.

PMID: <u>37541088</u>

12. Effects of non-immersive virtual reality intervention on children with spastic cerebral palsy: a meta-analysis and systematic review

Nan Wang, Naiquan Liu, Shuqi Liu, Yan Gao

Am J Phys Med Rehabil. 2023 Aug 3. doi: 10.1097/PHM.00000000002321. Online ahead of print.

This review aimed to assess the effectiveness of non-immersive virtual reality intervention compared to traditional rehabilitation in improving the functions of the upper and lower extremities, balance, and social participation among children with spastic cerebral palsy. We used librarian-designed searches of 10 databases to identify research articles on randomized controlled trials that assessed the effectiveness of non-immersive virtual reality in intervening spastic cerebral palsy patients up to 4/15/2023. Independent evaluation was conducted by two trained investigators using the evaluation criteria of RCT quality indicated in the Cochrane Manual of Assessment 'risk- of- bias tool.' The PEDro scale was used to evaluate the method and quality of the literature. 21 research articles involving 779 patients with spastic cerebral palsy were included. Significant differences between the non-immersive virtual reality rehabilitation and traditional rehabilitation groups were observed in all indicators, except for the Jebsen-Taylor Hand Function Test. Non-immersive virtual reality intervention is effective in improving the function of the lower extremity, balance, and social participation in children with spastic cerebral palsy, but its effect on upper limb function is still controversial.

PMID: <u>37535642</u>

13. From 'bench to bedside': Dissolving muscle contractures in cerebral palsy

Henry G Chambers

Dev Med Child Neurol. 2023 Aug 1. doi: 10.1111/dmcn.15724. Online ahead of print.

No abstract available

PMID: 3528540

14. Safety and Efficacy of Plaque Removal Using Manual and Powered Toothbrush in Cerebral Palsy Children by Parents/Caregivers: A Randomized Control Crossover Trial

Ansula N Deshpande, Kishan Naik, Neeraj Deshpande, Neelam Joshi, Vidhi Jaiswal, Rameshwari Y Raol

Int J Clin Pediatr Dent. 2023 Mar-Apr;16(2):344-349. doi: 10.5005/jp-journals-10005-2533.

Aim: The aim of our study was to check the safety and efficacy of plaque removal using manual and powered toothbrush in cerebral palsy children by parents/caregivers. Materials and methods: This was a single blinded, crossover randomized control trial conducted on 60 cerebral palsy children between the age of 6 to 14 years. They were randomly divided using a flip coin method into two groups: group A-manual toothbrush and group B-powered toothbrush. The plaque index (PI), gingival index (GI), and gingival abrasion (GA) score were measured at baseline, then at an interval of 3, 6, 9, and 12 weeks. This was followed by a crossover between two groups with a washout period of 1 week. Results: Both manual and powered toothbrush showed a significant reduction in plaque and gingival score before and after crossover when compared to baseline (p < 0.05). The GA score was reduced to 100% in both groups. However, there was no statistically significant difference between both the groups before and after the crossover. Also, through the questionnaire it was observed that both child (86.6%) and parent (70%) showed positive feedback towards powered toothbrush. Conclusion: It can be concluded from the present study that the efficacy of a powered toothbrush is comparable to that of a manual toothbrush. Parents and caregivers, on the contrary, displayed a favorable attitude towards the use of powered toothbrushes due to their ease of use. Clinical relevance: Cerebral palsy is one of the most common neurological disorders among children. It is associated with poor motor skills and manual dexterity that hampers their ability to brush and thus leads to poor oral hygiene. A powered toothbrush seems more appealing and is specially designed for patients with poor neuromotor coordination.

PMID: 37519975

15. Treatment of oromandibular dystonia with botulinum toxin A improves apnea in a teenager with quadriplegic cerebral palsy: A case report

Jeremy Roberts, Amy Tenaglia, Elisabeth Bellissimo, Heakyung Kim

J Pediatr Rehabil Med. 2023 Jul 27. doi: 10.3233/PRM-220105. Online ahead of print.

This report describes a 15-year-old female with known spastic and dystonic quadriplegic cerebral palsy (CP), Gross Motor Function Classification System IV, and obstructive sleep apnea (OSA). She experienced decreased apneic episodes after receiving onabotulinumtoxin A (BoNT-A) injections for the treatment of oromandibular dystonia (OMD). After her OSA diagnosis, she initially received injections to the bilateral masseter and temporalis muscles with no effect on the frequency of nightly apneic episodes. Subsequently, the bilateral lateral pterygoid muscles were added and she was later noted to have fewer apneic episodes overnight. This case report describes the use of BoNT-A in the muscles of mastication for management of OMD and the ensuing improvement in OSA in a teenager with CP.

PMID: 37522227

16. Characterizing child maltreatment fatalities among child victims with disabilities in the United States, 2010-2019

Devona Samuel, Fiona O'Malley, Farah W Brink, Kristin G Crichton, Bridget Duffy, Megan M Letson, Nichole L Michaels

Child Abuse Negl. 2023 Jul 28;144:106354. doi: 10.1016/j.chiabu.2023.106354. Online ahead of print.

Background: There has been little research on child maltreatment-related fatalities among children with disabilities. Despite being a minority of children in the United States, children with disabilities experience higher rates of victimization. Objective: To characterize fatalities due to child maltreatment among children with disabilities in the United States. Methods: Data from the National Violent Death Reporting System from 2010 to 2019 were analyzed to describe child maltreatment-related deaths among children with disabilities aged birth to 17 years. Results: There were 106 fatalities meeting the study criteria. The average age of the victims was 5.9 years old and 74.6 % were male. The most frequent suspected perpetrators of maltreatment-

related fatalities were biological mothers (35.2 %), and most perpetrators were White (55.7 %). Analyses showed a statistically significant relationship between fatalities caused by neglect and diagnoses of attention deficit hyperactivity disorder, autism spectrum disorder, cerebral palsy, and/or traumatic brain injury. Overall, physical abuse and/or neglect resulting in a fatality among children with disabilities were significantly correlated with the relationship of the perpetrator to the victim. Conclusions: Children with disabilities who died as a result of abuse were more likely to have autism spectrum disorder, a developmental disability, or other physical impairment, with physical abuse being the most prevalent type of abuse that resulted in death. To decrease the likelihood of abuse of disabled children, healthcare practitioners and caseworkers should work together to create strategies to help caregivers cope with the financial, mental, and physical stress that comes with raising children with disabilities.

PMID: 37517210

17. Redefining cerebral palsies as a diverse group of neurodevelopmental disorders with genetic aetiology

Clare L van Eyk, Michael C Fahey, Jozef Gecz

Reiew Nat Rev Neurol. 2023 Aug 3. doi: 10.1038/s41582-023-00847-6. Online ahead of print.

Cerebral palsy is a clinical descriptor covering a diverse group of permanent, non-degenerative disorders of motor function. Around one-third of cases have now been shown to have an underlying genetic aetiology, with the genetic landscape overlapping with those of neurodevelopmental disorders including intellectual disability, epilepsy, speech and language disorders and autism. Here we review the current state of genomic testing in cerebral palsy, highlighting the benefits for personalized medicine and the imperative to consider aetiology during clinical diagnosis. With earlier clinical diagnosis now possible, we emphasize the opportunity for comprehensive and early genomic testing as a crucial component of the routine diagnostic work-up in people with cerebral palsy.

PMID: 37537278

18. Post-neonatally acquired cerebral palsy aetiology: The need for classification and collaboration

Emma Waight

Dev Med Child Neurol. 2023 Aug 1. doi: 10.1111/dmcn.15725. Online ahead of print.

No abstract available

PMID: 37528524

19. Aberrant age-related alterations in spontaneous cortical activity in participants with cerebral palsy

Hannah Bergwell, Michael P Trevarrow, Elizabeth Heinrichs-Graham, Anna Reelfs, Lauren R Ott, Samantha H Penhale, Tony W Wilson, Max J Kurz

Front Neurol. 2023 Jul 13;14:1163964. doi: 10.3389/fneur.2023.1163964. eCollection 2023.

Introduction: Cerebral Palsy (CP) is the most common neurodevelopmental motor disability, resulting in life-long sensory, perception and motor impairments. Moreover, these impairments appear to drastically worsen as the population with CP transitions from adolescents to adulthood, although the underlying neurophysiological mechanisms remain poorly understood. Methods: We began to address this knowledge gap by utilizing magnetoencephalographic (MEG) brain imaging to study how the amplitude of spontaneous cortical activity (i.e., resting state) is altered during this transition period in a cohort of 38 individuals with spastic diplegic CP (Age range = 9.80-47.50 years, 20 females) and 67 neurotypical controls (NT) (Age range = 9.08-49.40 years, Females = 27). MEG data from a five-minute eyes closed resting-state paradigm were source imaged, and the power within the delta (2-4 Hz), theta (5-7 Hz), alpha (8-12 Hz), beta (15-29 Hz), and gamma (30-59 Hz) frequency bands were computed. Results: For both groups, the delta and theta spontaneous power decreased in the bilateral temporoparietal and superior parietal regions with age, while alpha, beta, and gamma band spontaneous power increased in temporoparietal, frontoparietal and premotor regions with age. We also found a significant group x age interaction, such that participants with CP demonstrated significantly less age-related increases in the spontaneous beta activity in the bilateral sensorimotor cortices compared to NT controls. Discussion: Overall, these results demonstrate that the spontaneous neural activity in individuals with CP has an altered trajectory when transitioning from adolescents to adulthood. We suggest that these differences in spontaneous cortical activity may play a critical role in the aberrant motor actions seen in this patient group, and may provide a neurophysiological marker for assessing the effectiveness of current treatment strategies that are directed at improving the mobility and sensorimotor impairments seen in individuals with CP.

PMID: <u>37521295</u>

20. Developing "Adulting for Health": Investigating the Health Needs of Neurodivergent Emerging Adults

Emily Hotez, Julianna A Rava, Lindsay Shea, Alice Kuo

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Introduction: Neurodivergent emerging adults - defined as individuals between the ages of 18 and 30 with intellectual and/or developmental disabilities (e.g., attention-deficit hyperactivity disorder (ADHD), autism, cerebral palsy, learning disabilities, seizures, developmental delays, with or without intellectual impairment) and physical and/or sensory disabilities (e.g., blindness or hearing impairment) - experience poor mental and physical health outcomes. Existing interventions are insufficient because they are not based on the self-reported and developmental needs of this population. Methods: The current study is an exploratory pilot study that features a multidimensional health-based needs assessment of self-identified neurodivergent emerging adults with ADHD, learning disabilities, autism, and other conditions, mean (M) age = 22.8; standard deviation (SD) = 3.4; n = 26). This research used validated measures. The assessment - administered via Qualtrics to the participants in two sites - included the Mental Health Continuum-Short Form, Kessler-6 Psychological Distress Scale, Project EAT (Eating and Activity over Time)-IV (with the intuitive eating, weight-related control, emotional eating, and physical activity subscales), and an original health-focused needs assessment developed by interdisciplinary healthcare professionals and neurodivergent individuals. Results: The sample reported low positive mental health, with only 3% reportedly "flourishing." The sample also reported high psychological distress according to clinical and psychometric cut-off scores; varied intuitive eating and weightcontrol behaviors and attitudes; and distinct needs related to integrating the principles of health promotion into daily life, navigating the healthcare system, and learning from healthcare professionals. Based on these findings, we present an initial conceptualization of "Adulting for Health," a potential virtual education program to promote health-related knowledge and capacities for this population. Conclusions: The results from this exploratory pilot study can be incorporated into existing programs and spur efforts to develop and test new interventions that can ameliorate health disparities for neurodivergent emerging adults.

PMID: 37519609

21. A screening method for visual attention disabilities in cerebral palsy with periventricular leukomalacia

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Purpose: Patients with periventricular leukomalacia (PVL) have been reported to have a variety of complications; however, whether these involve impaired visual attention disabilities remains unclear. Therefore, this study aimed to investigate the presence or absence and degree of visual attention disabilities in patients with PVL and propose a screening test that would allow anyone to check for visual attention disabilities easily. Methods: The study participants were 14 patients with PVL and seven controls with dyskinetic cerebral palsy. All participants performed three types of visual attention tasks: spatial attention tasks, feature-based attention tasks, and object-based attention tasks. The participants also performed counting tasks to determine how many squares of the same size and color could be counted (up to nine). Receiver operating characteristic analysis was used to calculate cutoff values, with disability as the objective variable and the value of the counting task as the explanatory variable. Results: The results revealed that patients with PVL often had visual attention disabilities, as indicated by a significant reduction in tasks requiring divided attention. Visual attention disabilities could be detected by a score of ≤ 8 in the square counting task. Conclusions: These findings suggest that family members and teachers of patients with PVL can easily screen for visual attention disabilities at home and school to improve mobility precautions in patients with this disability.

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22. Intracerebroventricular baclofen therapy improves function and quality of life in a child with severe cerebral palsy

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Limited therapies are available for severe cerebral palsy children (CP) with complex movement disorders, especially when both dystonia and spasticity are present. In this publication, we present the improvement of a child with severe CP after intracerebroventricular baclofen therapy. The treatment can impact not just the movement disorders but also on the quality of life of the child and caregivers. Global functional improvements can be observed on the 6-month follow-up.

PMID: <u>37515719</u>

23. Potential optimized route for mesenchymal stem cell transplantation in a rat model of cerebral palsy

Shiya Huang, Liru Liu, Yuan Huang, Chaoqiong Fu, Tingting Peng, Xubo Yang, Hongyu Zhou, Yiting Zhao, Yi Xu, Xiaoli Zeng, Peishan Zeng, Hongmei Tang, Lu He, Kaishou Xu

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Cerebral palsy (CP) is a movement and posture disorder that affects over 50 million people worldwide. Human umbilical cordderived mesenchymal stem cell (hUC-MSC) transplantation has emerged as an attractive therapeutic strategy for CP. The administration route appears to be crucial for hUC-MSC to provide adequate neuroprotection. Wistar rats were given hypoxiaischemia to make the CP model on postnatal day 5. On postnatal day 21, DiR-labeled hUC-MSC were transplanted into the CP rats by intravenous, intrathecal, and lateral ventricle for cell tracking. Uninfused CP rats served as the negative control. The motor behavioral and pathological alteration was analyzed 11, 25, and 39 days after transplantation to assess motor function, immune inflammation, neurotrophy, and endogenous repair. In vivo imaging tracking techniques revealed that intravenous infusion resulted in fewer transplanted cells in the target brain than intrathecal and lateral ventricle infusion (p<0.05). Three different routes of hUC-MSC infusion improved the motor function of CP rats (p<0.05). At 11 days post-infusion, intrathecal infusion outperformed intravenous with a significant neurotrophic and oligodendrocyte maturation effect (p<0.05). Intrathecal infusion equaled lateral ventricle infusion after 25 days. At 39 days post-infusion, lateral ventricle infusion exceeded intravenous and intrathecal infusion with a significant immunosuppressive effect (p<0.05). Considering the improved effect and less trauma shown early in the intrathecal infusion, repeated intrathecal administration may ultimately lead to the greatest benefit.

PMID: <u>37532123</u>

Prevention and Cure

24. 20-αHydroxycholesterol, an oxysterol in human breast milk, reverses mouse neonatal white matter injury through Gli-dependent oligodendrogenesis

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White matter injuries (WMIs) are the leading cause of neurologic impairment in infants born premature. There are no treatment options available. The most common forms of WMIs in infants occur prior to the onset of normal myelination, making its pathophysiology distinctive, thus requiring a tailored approach to treatment. Neonates present a unique opportunity to repair WMIs due to a transient abundance of neural stem/progenitor cells (NSPCs) present in the germinal matrix with oligodendrogenic potential. We identified an endogenous oxysterol, 20-aHydroxycholesterol (20HC), in human maternal breast milk that induces oligodendrogenesis through a sonic hedgehog (shh), Gli-dependent mechanism. Following WMI in neonatal mice, injection of 20HC induced subventricular zone-derived oligodendrogenesis and improved myelination in the periventricular white matter, resulting in improved motor outcomes. Targeting the oligodendrogenic potential of postnatal NSPCs in neonates with WMIs may be further developed into a novel approach to mitigate this devastating complication of preterm birth.

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