Cerebral palsy research news

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Interventions and Management

1. Effectiveness of the home-based training program Tele-UPCAT (Tele-monitored UPper Limb Children Action Observation Training) in unilateral cerebral palsy: a randomized controlled trial

Elena Beani, Valentina Menici, Elisa Sicola, Adriano Ferrari, Hilde Feys, Katrijn Klingels, Lisa Mailleux, Roslyn Boyd, Giovanni Cioni, Giuseppina Sgandurra

Eur J Phys Rehabil Med. 2023 Jul 18. doi: 10.23736/S1973-9087.23.07945-5. Online ahead of print.

Background: The effects of unilateral cerebral palsy (UCP) are largely observed in the upper limb (UL), which represents the main focus of rehabilitation for this disorder. Thanks to an increment in home training and progress in technology innovative systems have been created. The Tele-UPCAT (Tele-monitored UPper Limb Children Action Observation Training) platform is dedicated to the delivery at home of a program for UL rehabilitation, based on action observation therapy (AOT). Aim: This study aimed to investigate the immediate effectiveness of Tele-UPCAT for promoting UL skills in children with UCP and to determine if immediate effects were retained in the medium and long term. Design: Tele-UPCAT was conducted on an intention-to-treat basis and was proposed as a randomized, allocation concealed (waitlist controlled) and evaluator-blinded clinical trial with two investigative arms: intensive in-home AOT program and standard care (SC). Setting: This is a home-based AOT program delivered with a customized ICT platform. Population: Thirty children (mean age 11.61±3.55 years) with confirmed diagnosis of spastic UCP with predominant UL involvement and cognitive level within or at normal limits were enrolled in this study. Orthopedic surgery or an intramuscular botulinum toxin A injection in the UL within 6 months prior to enrolment represented an exclusion criteria. Methods: Participants were randomized using concealed random allocation. They were assessed according to the study design with the Assisting Hand Assessment (AHA), the Box and Block Test (BBT) and the Melbourne Assessment 2 (MA2). Linear mixed models were used for statistical analysis. Results: A significant difference between the AOT and SC groups was identified immediately after the training on the AHA (6.406 [2.73] P=0.021) with an effect size (ES) of 1.99, and for the BBT of the less affected hand (9.826 [4.535] P=0.032) with an ES of 1.44. These effects were sustained at medium and long term. Conclusions: This study supports the effectiveness of AOT home training in promoting UL skills in children with UCP, with immediate effects lasting for 6 months.

PMID: 37462399

2. Botox injection in treatment of sialorrhea in children with cerebral palsy

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Am J Neurodegener Dis. 2023 Jun 15;12(3):97-102. eCollection 2023.

Background: The occurrence of sialorrhea (drooling) in children with cerebral palsy is one of the important complications of this disease, which is associated with the impaired quality of life of patients and also the dissatisfaction of their parents. Botox injection in the salivary glands is one of the treatment methods that has recently received special attention in these patients, but there are still many challenges regarding its effectiveness and safety. We aimed to test the effectiveness and safety of botulinum toxin type A in reducing sialorrhea in children with cerebral palsy. Methods: This semi-experimental before-after study was performed on 12 children who suffering from sialorrhea. The ethics code of this project is

IR.MUI.MED.REC.1400.774 and the clinical trial registry code is IRCT20220516054868N1 (https://www.irct.ir/trial/64393). In each of the parotid and submandibular glands, an amount of 0.5 U/kg of botulinum toxin type A was injected by ultrasound guidance under general anesthesia. Before and 6 months after the intervention, the severity and frequency of drooling were tested by Drooling Frequency and Severity Scale. Results: We found a decreasing trend in the severity and frequency scores for drooling within one month; however, after that time, until the end of the 24th week, we saw an increasing trend in the intensity and frequency of this complication. Only two-thirds of parents were satisfied with the therapeutic protocol. Side effects related to botox injection were revealed in 25.0% mostly as dysphagia. Conclusion: Botox injection in salivary glands is not a definitive and stable treatment in the treatment of sialorrhea in children with cerebral palsy.

PMID: 37457841

3. Identifying Effective Treatments for Dystonia in Patients with Cerebral Palsy: A Precision Therapeutics Approach

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Neurology. 2023 Jul 18;10.1212/WNL.0000000000207593. doi: 10.1212/WNL.0000000000207593. Online ahead of print.

Recent focus on improving the recognition of dystonia in cerebral palsy (DCP) has highlighted the need for more effective treatments. Evidence supports improved functional outcomes with early interventions for patients with cerebral palsy, but it is not known which interventions are most effective for DCP. Current pharmacologic recommendations for DCP are based largely on anecdotal evidence, with medications demonstrating minimal to moderate improvements in dystonia and variable efficacy between patients. Patients, families, and clinicians have identified the need for new and improved treatments in DCP, naming this as the top research theme in a recent Neurology publication. Precision therapeutics focuses on providing early, effective interventions that are individualized to every patient and can guide research priorities to improve treatments for DCP. This commentary outlines current obstacles to improving treatment of DCP and addresses how precision therapeutics can address each of these obstacles through four key components: (1) identification of predictive biomarkers to select patients likely to develop DCP in the future and for whom early intervention may be appropriate to delay or prevent full manifestation of dystonia, (2) stratification of patients with DCP into subgroups according to shared features (clinical, functional, biochemical, etc) to provide a targeted intervention based on those shared features, (3) administration of an individualized dose of an effective intervention to ensure adequate concentrations of the therapeutic entity at the site of action, and (4) monitoring of objective biomarkers of response to intervention. With implementation of each of these components of precision therapeutics, new and more effective treatments for every person with DCP can be realized.

PMID: 37463749

4. Transcranial electric motor evoked potential monitoring during scoliosis surgery in children with cerebral palsy and active seizure disorder: is it feasible and safe?

M Wade Shrader, Sabina DiCindio, Katherine G Kenny, Alier J Franco, Ran Zhang, Mary C Theroux, Kenneth J Rogers, Suken A Shah

Spine Deform. 2023 Jul 17. doi: 10.1007/s43390-023-00730-w. Online ahead of print.

Purpose: Use of spinal cord monitoring in children with cerebral palsy (CP) and neuromuscular scoliosis is challenging. The previous reports suggest low success rates in the setting of CP, and it is unclear if transcranial electric motor evoked potentials (TcMEP) monitoring is contraindicated in patients with an active seizure disorder. The purpose of this study was to determine (1) are patients with CP able to be appropriately monitored with TcMEP? and (2) does TcMEP cause an increase in seizure activity? Methods: This was an institutional review board-approved retrospective cohort study observing 304 patients from 2011 to 2020. Inclusion criteria included all patients with CP undergoing posterior spinal fusion during this time. Intraoperative data were examined for the ability to obtain monitoring and any intraoperative events. Patients were followed for 3 months postoperatively to determine any increase in seizure activity that could have been attributed to the TcMEP monitoring. Results: Of the 304 patients who were observed, 21% (20.8%) were unable to be monitored due to lacking baseline signals from the extremities. Seventy-seven percent (77.5%) were successfully monitored with TcMEP. For these patients, no increased seizure activity was documented either intra- or postoperatively. Conclusion: A high percentage of children (77.5%) with CP were able to be successfully monitored with TcMEP during posterior spinal fusion. Furthermore, the concerns about increased seizure activity after TcMEP were not supported by the data from this cohort. Technical details of successful neuromonitoring in these patients are important and included increased stimulation voltage requirements and latency times.

PMID: 37458896

5. Proteomic changes of the bilateral M1 and spinal cord in hemiplegic cerebral palsy mouse: Effects of constraint-induced movement therapy (CIMT)

Yuan Huang, Zhaofang Chen, Yunxian Xu, Liru Liu, Hongmei Tang, Lu He, Jingbo Zhang, Hongyu Zhou, Yi Xu, Jingyi Zhao, Lilan Wu, Kaishou Xu

Behav Brain Res. 2023 Jul 15;452:114583. doi: 10.1016/j.bbr.2023.114583. Online ahead of print.

Hemiplegic cerebral palsy (HCP) is a non-progressive movement and posture disorder that affects one side of the body. Constraint-induced movement therapy (CIMT) can improve the hand function of children with HCP. We used label-free proteomic quantification technology to evaluate proteomic changes in the bilateral M1 and spinal cord in HCP mouse induced by hypoxia/ischemia and CIMT. Nissl staining showed reduced neuron density in the HCP mice's lesioned and contralesional M1. The rotarod test and grip strength test showed motor dysfunction in mice with HCP and improved motor ability after CIMT. A total of 5147 proteins were identified. Fifty-one, five, and sixty common differentially expressed proteins (DEPs), which were co-regulated by HCP and CIMT, were found in the lesioned M1, the contralesional M1 and the spinal cord respectively. The significant proteins included alpha-centractin, metaxin complex, PKC, septin 11, choline transporter-like proteins, protein 4.1, teneurin-4, and so on, which mainly related to synapse stability, neuronal development and maintenance, axon development, and myelin formation. The KEGG pathways of HCP-induced DEPs mainly related to lipid metabolism, synaptic remodeling, SNARE interactions in vesicular transport and axon formation. The CIMT-induced DEPs were mainly related to synaptic remodeling and axon formation in the lesioned M1 and spinal cord. This study investigated the proteomic changes of the bilateral M1 and spinal cord as well as the CIMT-induced proteomic changes in HCP mice, which might provide new insights into the therapy of HCP.

PMID: 37454934

6. Improving dynamic balance by self-controlled feedback in children with cerebral palsy

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Hum Mov Sci. 2023 Jul 19;90:103123. doi: 10.1016/j.humov.2023.103123. Online ahead of print.

Aims: Maintaining balance is an important topic for participation of children with Cerebral Palsy (CP) in their own activities. Purpose of the present study was to investigate the effect of self-controlled and yoked-group feedback on dynamic balance of children with Spastic Hemiplegic Cerebral Palsy (SHCP). Methods: Using Convenience Sampling Method, twenty students with Cerebral Palsy, aged 8-10 years old, were selected from special schools and divided into the Self-Controlled (SC) and Yoked feedback groups. Children in SC group requested feedback when necessary during the acquisition phase; in contrast, participants in yoked group replicated the feedback schedule of their counterparts in SC group without any choice. Modified Star Excursion Balance Test (SEBT) was used for both dynamic balance intervention and assessment. To analyze the data, Multivariate Analysis of Covariance (MANCOVA) and Analysis of Covariance (ANCOVA) Tests were performed at $p < 0.05$. Results: Based on MANCOVA test results, a significant difference were found between SC and Yoked groups after controlling for pretest at least in one balance variables (anterior, posterolateral, and posteromedial). Results of ANCOVA test showed a significant difference between the balance variables in the anterior, Posterolateral, and posteromedial directions in children with cerebral palsy. Conclusions: Findings of our study support the idea that requested feedback in SC conditions could have more benefits for motor learning since it is adjusted with the needs and preferences of children.

PMID: 37478681

7. Botulinum toxin type A for spasticity in cerebral palsy patients: Which impact on popliteal angle to hamstring length? A proof-of-concept study

Massimiliano Murgia, Alessandro de Sire, Pierangela Ruiu, Francesco Agostini, Arianna Valeria Bai, Giovanni Pintabona, Teresa Paolucci, Jonathan Bemporad, Marco Paoloni, Andrea Bernetti

J Back Musculoskelet Rehabil. 2023 Jul 6. doi: 10.3233/BMR-220381. Online ahead of print.

Background: Cerebral palsy (CP) is the most common physical disability in childhood. It is a heterogeneous condition in terms of etiology, motor type and severity of impairments. Clinical impairments, such as increased muscle tone (spasticity), muscle weakness and joint stiffness contribute to the abnormal development of functional activities, including gait. Objective: The objective of this study was to investigate the popliteal angle to hamstring length after ultrasound guided Incobotulinum toxin A injections for spasticity in CP patients. Methods: In this proof-of-concept study, we included outpatients with CP and crouch gait correlated to hamstrings spasticity referred to the Pediatric Rehabilitation outpatient clinic of Umberto I University Hospital, Sapienza University of Rome, in the period between February and October 2018. Methods: Modified Ashworth Scale (MAS) of hamstring muscles, Popliteal Angle and Modified Popliteal Angle, Passive Knee Extension and 10 Meter Walk Test (10MWT) were assessed at baseline (T0) and three weeks after ultrasound guided injection (T1) of Incobotulinum Toxin A (dose weight and site dependent). Results: Thirteen patients (5 male and 8 female), mean aged 9.91 ± 3.59, were included. The clinical evaluation at T0 showed hamstring muscles spasticity, with MAS of 2.4 ± 0.6, popliteal angle -51.7∘± 11.0∘, modified popliteal angle of -39.5∘± 11.0∘, passive knee extension of -14.0∘± 8.7∘ and 10MWT of 14.3 ± 4.6 seconds. At T1, hamstring muscles MAS mean value was 1.7 ± 0.6 ($p< 0.01$), popliteal angle 41.3∘± 7.0∘ ($p< 0.001$), modified popliteal angle -32.9∘± 10.4∘ ($p< 0.001$), passive knee extension -4.0∘± 4.2∘ ($p< 0.05$) and 10MWT 12.6 ± 4.8 seconds ($p< 0.05$). None of the treated patients reported any adverse event related to Incobotulinum Toxin A injection. Conclusion: Incobotulinum toxin A treatment

has been proven to be safe and effective for hamstring muscles spasticity management in CP patients. Further studies with larger samples and longer follow-up are warranted to assess the efficacy of this treatment on the popliteal angle.

PMID: 37458025

8. Gait velocity control using projection mapping for children with spastic diplegia cerebral palsy

Minoru Kimoto, Kyoji Okada, Kazutaka Mitobe, Masachika Saito, Hitoshi Sakamoto

Clin Biomech (Bristol, Avon). 2023 Jul 13;108:106043. doi: 10.1016/j.clinbiomech.2023.106043. Online ahead of print.

Background: Gait characteristics in children with cerebral palsy vary according to their individual walking speed. As such, establishing methods to maintain a consistent gait velocity are necessary to evaluate specific intervention effects in this clinical population. Our study aim was to validate the accuracy of projection mapping for guiding gait velocity to a control gait velocity. Methods: This was a cross-sectional study of 13 children with cerebral palsy (mean age [standard deviation] of 12.42 [2.31] years). The target velocity was calculated from the average speed obtained across three trials of self-selected walking speed. A virtual reality system with four projectors was used to project an image onto the floor to guide children to match two gait conditions: 100% and 125% velocity of the average speed. Participants completed three gait trials at each velocity under image guidance. Gait velocity was quantified using a 3-dimensional motion capture system. Bland-Altman plots were used to analyze systematic errors and the limits of agreement calculated. Findings: The results indicated the limits of agreement were acceptable for 0.10 m/s for 100% velocity and 0.12 m/s for 125% velocity. Therefore, projection mapping was effective in guiding children to adjust their gait to the intended velocity. Interpretation: Projection mapping is a novel method for guiding children with cerebral palsy to walk at a controlled target velocity that may improve the reliability of gait analysis.

PMID: 37473607

9. Muscle co-contraction and co-activation in cerebral palsy during gait: A scoping review

S Mohammadyari Gharehbolagh, C Dussault-Picard, D Arvisais, P C Dixon

Review Gait Posture. 2023 Jul 9;105:6-16. doi: 10.1016/j.gaitpost.2023.07.002. Online ahead of print.

Background: Cerebral palsy (CP) results from an injury to a developing brain. Muscle activation patterns during walking are disrupted in individuals with CP. Indeed, excessive muscle co-contraction or co-activation (MCo/MCa) is one of the characteristics of pathological gait. Although some researchers have studied MCo/MCa in individuals with CP during gait, inconsistent results limit our understanding of this literature. Increased knowledge of MCo/MCa patterns in individuals with CP may help the development of improved gait management approaches. Research question: This review aims to summarize MCo/MCa patterns while walking in individuals with CP across the existing literature and compare them with their healthy peers. Methods: This study follows the Joanna Briggs Institute (JBI) guidelines and the recommendations presented in PRISMA Extension for Scoping Reviews (PRISMA-ScR). The recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Extension for scoping Reviews statement were respected. The following databases were searched: MEDLINE (Ovid), EMBASE (Ovid), CINAHL Plus with Full Text (Ebsco), SPORTDiscus with Full Text (Ebsco), and Web of Science. Results: Among 2545 identified studies, 21 studies remained after screening. In total, 337 participants with CP and 249 healthy participants were included. Both MCo and MCa terminologies are used for describing simultaneous muscle activation; however, when it is measured by electromyography (EMG), MCa terminology should be preferred to facilitate interpretation. A wide range of MCo/MCa patterns has been found across studies using different methodologies (e.g., gait protocol, computation methods). Finally, most of the included studies confirm that MCo/MCa is increased in individuals with CP during walking compared to controls. Significance: This review identified missing concepts and common limitations in the literature which could be addressed in future research such as the association between MCo/MCa and gait deviations, and the most appropriate MCo/MCa computation method.

PMID: 37453339

10. Retracted: Efficacy of Rehabilitation Therapy and Pharmacotherapy on Children with Cerebral Palsy: A Meta-Analysis

Computational And Mathematical Methods In Medicine

Retraction of Publication Comput Math Methods Med. 2023 Jul 12;2023:9781092. doi: 10.1155/2023/9781092. eCollection 2023.

[This retracts the article DOI: 10.1155/2022/6465060.].

PMID: 37475916

11. The age-related association between serum creatinine and cardiorespiratory morbidity and mortality and fractures among adults with cerebral palsy

Daniel G Whitney, Edward A Hurvitz

Adv Med Sci. 2023 Jul 18;68(2):249-257. doi: 10.1016/j.advms.2023.07.001. Online ahead of print.

Purpose: Serum creatinine may be an objective biomarker of salient health issues in adults with cerebral palsy (CP). The objective was to assess the age-related association between serum creatinine with 3-year risk of cardiorespiratory morbidity/mortality and fracture among adults with CP. Patients and methods: This retrospective cohort study used medical records between Jan. 1, 2012 and Oct. 2, 2022 from adults ≥18 years old with CP. The association between baseline serum creatinine with the 3-year risk of all-cause mortality, respiratory/cardiovascular morbidity/mortality, and fracture was assessed by age and sex using logistic regression. The discriminative ability of serum creatinine alone and in conjunction with other variables was assessed. Results: Over the 3-year follow-up, 8.3% of 1368 adults with CP had all-cause mortality, 25.6% had respiratory morbidity/mortality, 12.4% had cardiovascular morbidity/mortality, and 8.9% sustained a fracture. The association between serum creatinine with outcomes was dependent on age. For younger adults, lower creatinine had a higher odds ratio (OR) for all-cause mortality, respiratory morbidity/mortality, and fracture. For 51-60 year olds, higher creatinine had a higher OR for cardiovascular morbidity/mortality. Serum creatinine alone had modest prediction of outcomes, and generally improved prediction when added to models that included sex and co-occurring intellectual disabilities and epilepsy (c-statistic range, 0.54 -0.84). Conclusions: Lower serum creatinine may reflect frailty while higher levels may reflect kidney dysfunction, helping to explain the differential associations by age. Serum creatinine may be a useful biomarker as part of risk prediction models for these salient health issues for adults with CP.

PMID: 37473639

12. Direct speech reconstruction from sensorimotor brain activity with optimized deep learning models

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J Neural Eng. 2023 Jul 19. doi: 10.1088/1741-2552/ace8be. Online ahead of print.

Development of brain-computer interface (BCI) technology is key for enabling communication in individuals who have lost the faculty of speech due to severe motor paralysis. A BCI control strategy that is gaining attention employs speech decoding from neural data. Recent studies have shown that a combination of direct neural recordings and advanced computational models can provide promising results. Understanding which decoding strategies deliver best and directly applicable results is crucial for advancing the field. In this paper, we optimized and validated a decoding approach based on speech reconstruction directly from high-density electrocorticography recordings from sensorimotor cortex during a speech production task. We show that 1) dedicated machine learning optimization of reconstruction models is key for achieving the best reconstruction performance; 2) individual word decoding in reconstructed speech achieves 92-100% accuracy (chance level is 8%); 3) direct reconstruction from sensorimotor brain activity produces intelligible speech. These results underline the need for model optimization in achieving best speech decoding results and highlight the potential that reconstruction-based speech decoding from sensorimotor cortex can offer for development of next-generation BCI technology for communication.

PMID: 37467739

13. A brain-computer typing interface using finger movements

Nishal P Shah, Matthew S Willsey, Nick Hahn, Foram Kamdar, Donald T Avansino, Leigh R Hochberg, Krishna V Shenoy, Jaimie M Henderson

Int IEEE EMBS Conf Neural Eng. 2023 Apr;2023:10.1109/ner52421.2023.10123912. doi: 10.1109/ner52421.2023.10123912. Epub 2023 May 19.

Intracortical brain computer interfaces (iBCIs) decode neural activity from the cortex and enable motor and communication prostheses, such as cursor control, handwriting and speech, for people with paralysis. This paper introduces a new iBCI communication prosthesis using a 3D keyboard interface for typing using continuous, closed loop movement of multiple fingers. A participant-specific BCI keyboard prototype was developed for a BrainGate2 clinical trial participant (T5) using neural recordings from the hand-knob area of the left premotor cortex. We assessed the relative decoding accuracy of flexion/extension movements of individual single fingers (5 degrees of freedom (DOF)) vs. three groups of fingers (thumb, index-middle, and ring-small fingers, 3 DOF). Neural decoding using 3 independent DOF was more accurate (95%) than that using 5 DOF (76%). A virtual keyboard was then developed where each finger group moved along a flexion-extension arc to acquire targets that corresponded to English letters and symbols. The locations of these letter/symbols were optimized using natural language statistics, resulting in an approximately a 2× reduction in distance traveled by fingers on average compared to a random keyboard layout. This keyboard was tested using a simple real-time closed loop decoder enabling T5 to type with 31 symbols at 90% accuracy and approximately 2.3 sec/symbol (excluding a 2 second hold time) on average.

PMID: 37465143

14. Turkish validity and reliability of the level of sitting scale in children with cerebral palsy

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Turk J Med Sci. 2023 Apr;53(2):603-609. doi: 10.55730/1300-0144.5621. Epub 2023 Apr 19.

Background: The Level of Sitting Scale (LSS) is a valid and reliable classification index that categorizes sitting ability. The aim of this study is to establish the Turkish validity and reliability of the LSS in children with cerebral palsy (CP). Methods: In total, 165 children (75 girls and 90 boys) between the ages of 4 and 18 years who were diagnosed with CP were included in the study. All children were evaluated by two independent physiotherapists for the interrater reliability analysis of the LSS and were reevaluated 1 week later by the same physiotherapist for the intrarater reliability analysis. The Gross Motor Function Classification System (GMFCS) was used for validity analysis. Results: The intrarater reliability analyses of the LSS showed an intraclass correlation coefficient of 0.999 (ICC 95% CI [0.999-1]),and the interrater reliability analyses showed an intraclass correlation coefficient of 0.998 (ICC 95% CI [0.998-0.999]). A statistically significant, negative, and strong correlation was found between the GMFCS and the LSS ($p < 0.001$, $r = -0.770$). Discussion: The Turkish version of the LSS in children with CP is a valid and reliable scale. The Turkish LSS can be used by researchersand clinicians in research and to determine the sitting level of children with CP.

PMID: 37476883

15. Retracted: Investigation on Quality of Life and Economic Burden of Children with Cerebral Palsy in Changzhou

Journal Of Healthcare Engineering

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[This retracts the article DOI: 10.1155/2022/1519689.].

PMID: 37476812

16. Out-of-pocket costs for families and people living with cerebral palsy in Australia

Georgina Henry, Annabel Webb, Claire Galea, Alison Pearce, Isabelle Balde, Fiona Garrity, Sophie Marmont, James Espie, Nadia Badawi, Sarah McIntyre

PLoS One. 2023 Jul 20;18(7):e0288865. doi: 10.1371/journal.pone.0288865. eCollection 2023.

The most recent cost estimates of cerebral palsy (CP) in Australia did not include out-of-pocket costs for families. This study aimed to: 1) describe and estimate out-of-pocket costs for people with CP and their families by age and gross motor function classification system (GMFCS) level; 2) measure financial distress. A cross-sectional quantitative survey design was used with qualitative approaches to analyse open-ended questions. A CP-specific out-of-pocket costs survey was co-designed with people with lived experience. Adults with CP and carers were recruited from Australian population-based CP Registers and via social media. Sociodemographic variables were analysed descriptively and median (IQR) expenses for health, assistive technology, personal care, housing, occupation, transport, leisure, respite and holidays, by age (0-6; 7-17; 18 years +) and gross motor function [GMFCS level I-II vs III-V] were calculated. The In Charge Financial Distress/Financial Wellbeing Scale measured financial distress. Regression analyses were conducted to investigate costs and financial distress. Additional out-of-pocket costs itemised in open-ended questions were charted. Comments were thematically analysed using the framework approach. 271 surveys were completed for children 0-6 years (n = 47), children/adolescents 7-17 years (n = 124) and adults (n = 100). 94% of participants had out-of-pocket costs associated with CP, with an overall annual median of $4,460 Australian dollars (IQR $11,955). After controlling for income, private insurance and disability funding, the GMFCS III-V group had costs two times higher than the GMFCS I-II group (2.01; 95% CI 1.15-3.51). Age was not significantly associated with costs. 36% of participants had high to overwhelming financial distress; this was not associated with age or GMFCS level after controlling for financial factors. Families had several additional disability costs. Open-ended responses revealed experiences of financial concern were influenced by funding scheme experiences, reduced income, uncertainty, access to support networks and an inability to afford CP-related costs. Cost estimates and financial distress indicators should inform policy, funding and clinical decisions when planning interventions to support people with CP and their families.

PMID: 37471345

17. The association of maternal overweight on long-term neurodevelopmental outcomes in premature infants (< 29 weeks) at 18-24 months corrected age

Marina Journault, Prashanth Murthy, Neha Bansal, Selphee Tang, Essa Al Awad, Dianne Creighton, Jill Newman, Abhay Lodha

J Perinatol. 2023 Jul 21. doi: 10.1038/s41372-023-01733-1. Online ahead of print.

Objective: To determine the association of maternal pre-pregnancy body mass index (BMI) and neurodevelopmental impairment (NDI) at 18-24 months corrected age (CA) in infants born < 29 weeks gestation. Study design: Infants born between 2005 and 2015 at < 29 weeks gestation were included. BMI was categorized into BMI1 [18.5-24.9 kg/m2], BMI2 [25-29.9 kg/m2], BMI3 [≥ 30 kg/m2]. Primary outcome was death or NDI (Bayley-III scores < 85, cerebral palsy, hearing or visual impairment). Univariate and multivariate analysis were used. Results: There were 315 infants in BMI1, 235 in BMI2, and 147 in BMI3 groups. Adjusted odds ratio (aOR) of death or NDI in BMI2 vs. BMI1 and BMI3 vs BMI1 groups were 1.33 (95% CI 0.86-2.06) and 0.76 (95% CI 0.47-1.22). Adjusted odds ratio of Bayley-III language composite < 85 was 2.06 (95% CI 1.28-3.32). Conclusion: Pre-pregnancy BMI was not associated with death or NDI in extremely preterm infants. Infants born to overweight mothers had higher odds of low language scores.

PMID: 37479886

18. Prescription Opioid Use for Adolescents With Neurocognitive Disability Undergoing Surgery: A Pilot Study

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J Surg Res. 2023 Jul 19;291:237-244. doi: 10.1016/j.jss.2023.06.007. Online ahead of print.

Introduction: Parents frequently report retaining unused opioid pills following their child's surgery due to fear of untreated postoperative pain. Assessment of pain in adolescents with neurocognitive disability is challenging. We hypothesized that parents of adolescents with neurocognitive disability may report less opioid use and higher opioid pill retention. Methods: Adolescents (13-20 y) undergoing elective surgery (posterior spinal fusion, hip reconstruction, arthroscopy, tonsillectomy) were prospectively enrolled from a tertiary children's hospital from 2019 to 2020. Only adolescents prescribed opioids at discharge were included. Parents completed a preoperative survey collecting sociodemographic characteristics and two postoperative surveys at 30- and 90-d. Neurocognitive disability was determined at time of enrollment by caregiver report, and included adolescents with cerebral palsy, severe autism spectrum disorder, and discrete syndromes with severe neurocognitive disability. Results: Of 125 parent-adolescent dyads enrolled, 14 had neurocognitive disability. The median number of opioid pills prescribed at discharge did not differ by neurocognitive disability (29, interquartile range {IQR}: 20.0-33.3 versus 30, IQR: 25.0-40.0, P = 0.180). Parents of both groups reported similar cumulative days of opioid use (7.0, IQR: 3.0-21.0 versus 6.0, IQR:3.0-10.0, P = 0.515) and similar number of opioid pills used (4, IQR: 2.0-4.5 versus 12, IQR: 3.5-22.5, P = 0.083). Parents of both groups reported similar numbers of unused opioid pills (17, IQR: 12.5-22.5 versus 19, IQR: 8.0-29.0, P = 0.905) and rates of retention of unused opioids (15.4% versus 23.8%, P = 0.730). Conclusions: The number of opioid pills prescribed did not differ by neurocognitive disability and parents reported similar opioid use and retention of unused opioid pills. Larger studies are needed to identify opportunities to improve postoperative pain control for children with neurocognitive disability.

PMID: 37478647

19. Exposure to per- and polyfluoroalkyl substances in early pregnancy and risk of cerebral palsy in children

Andreas Vilhelmsson, Lars Rylander, Anna Jöud, Christian H Lindh, Kristina Mattsson, Zeyan Liew, Pengfei Guo, Beate Ritz, Karin Källén, Jesse D Thacher

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Background: Most cerebral palsy (CP) cases have an unexplained etiology, but a role for environmental exposures has been suggested. One purported environmental risk factor is exposure to endocrine-disrupting pollutants specifically per- and polyfluoroalkyl substances (PFAS). Objectives: We investigated the association between prenatal PFAS exposures and CP in Swedish children. Methods: In this case-control study, 322 CP cases, 343 population controls, and 258 preterm controls were identified from a birth registry in combination with a CP follow-up program from 1995 to 2014 and linked to a biobank which contains serum samples from week 10-14 of pregnancy. Maternal serum concentrations of four PFAS compounds: perfluorohexane sulfonate (PFHxS), perfluorooctanoic acid (PFOA), perfluorononanoic acid (PFNA), and perfluorooctane sulfonate (PFOS) were analyzed using liquid chromatography-tandem-mass-spectrometry. We estimated odds ratios (ORs) and 95 % confidence intervals (CIs) for CP and each PFAS in quartiles and as continuous variables controlling for various sociodemographic and lifestyle factors. Results: In crude and adjusted analyses, we did not find consistent evidence of associations between serum PFHxS, PFOA, PFNA, PFOS and concentrations in early pregnancy and CP, except in preterm

infants. The ORs comparing the highest PFAS quartiles to the lowest were 1.05 (95 % CI: 0.63-1.76), 0.96 (95 % CI: 0.55-1.68), 0.71 (95 % CI: 0.41-1.25), and 1.17 (95 % CI: 0.61-2.26), for PFHxS, PFOA, PFNA, and PFOS, respectively. Some positive associations were observed for preterm infants, but the results were imprecise. Similar patterns were observed in analyses treating PFAS as continuous variables. Conclusions: In this study, we found little evidence that early pregnancy prenatal exposure to PFHxS, PFOA, PFNA, or PFOS increases the risk of CP. However, some positive associations were observed for preterm cases and warrant further investigation.

PMID: 37474063

20. Severe Congenital Heart Defects and Cerebral palsy

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Objective: To report the prevalence of cerebral palsy (CP) in children with severe congenital heart defects (CHD) and the outcome/severity of the CP. Methods: Population-based, data-linkage study between cerebral palsy and congenital anomaly registers in Europe and Australia. The EUROCAT definition of severe CHD (sCHD) was used. Linked data from four regions in Europe and two in Australia were included. All children born in the regions from 1991 through 2009 diagnosed with CP and/or sCHD were included. Linkage was completed locally. De-identified linked data were pooled for analysis. Results: The study sample included 4989 children with CP and 3684 children with sCHD. The total number of livebirths in the population was 1,734,612. The prevalence of CP was 2.9 per 1000 births (95% CI 2.8-3.0) and the prevalence of sCHD was 2.1 per 1000 births (95% CI 2.1-2.2). Of the children with sCHD, 1.5% (n=57) had a diagnosis of CP of which 35 (61%) children had pre/perinatally acquired CP (resulting from a brain injury up to 28 days of life) and 22 (39%) children had a post-neonatal cause (a brain injury between 28 days and 2 years). Children with CP and sCHD more often had unilateral spastic cerebral palsy and more intellectual impairments than children with CP without congenital anomalies. Conclusions: In high-income countries, the proportion of children with CP is much higher in children with sCHD than in the background population. The severity of children with CP and sCHD is milder compared with children with CP without congenital anomalies.

PMID: 37473991

21. AGAP1-associated endolysosomal trafficking abnormalities link gene-environment interactions in a neurodevelopmental disorder

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AGAP1 is an Arf1 GAP that regulates endolysosomal trafficking. Damaging variants have been linked to cerebral palsy and autism. We report three new individuals with microdeletion variants in AGAP1. Affected individuals have intellectual disability (3/3), autism (3/3), dystonia with axial hypotonia (1/3), abnormalities of brain maturation (1/3), growth impairment (2/3) and facial dysmorphism (2/3). We investigated mechanisms potentially underlying AGAP1 neurodevelopmental impairments using the Drosophila ortholog, CenG1a. We discovered reduced axon terminal size, increased neuronal endosome abundance, and elevated autophagy at baseline. Given potential incomplete penetrance, we assessed gene-environment interactions. We found basal elevation in phosphorylation of the integrated stress-response protein eIF2α and inability to further increase eIF2α-P with subsequent cytotoxic stressors. CenG1a-mutant flies have increased lethality from exposure to environmental insults. We propose a model wherein disruption of AGAP1 function impairs endolysosomal trafficking, chronically activating the integrated stress response, and leaving AGAP1-deficient cells susceptible to a variety of second hit cytotoxic stressors. This model may have broader applicability beyond AGAP1 in instances where both genetic and environmental insults co-occur in individuals with neurodevelopmental disorders.

PMID: 37470098

22. Neurodevelopmental outcomes in congenital and perinatal infections

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Purpose of review: Congenital infections are a major cause of childhood multidomain neurodevelopmental disabilities. They contribute to a range of structural brain abnormalities that can cause severe neurodevelopmental impairment, cerebral palsy,

epilepsy, and neurosensory impairments. New congenital infections and global viral pandemics have emerged, with some affecting the developing brain and causing neurodevelopmental concerns. This review aims to provide current understanding of fetal infections and their impact on neurodevelopment. Recent findings: There are a growing list of congenital infections causing neurodevelopmental issues, including cytomegalovirus, Zika virus, syphilis, rubella, lymphocytic choriomeningitis virus, and toxoplasmosis. Fetal exposure to maternal SARS-CoV-2 may also pose risk to the developing brain and impact neurodevelopmental outcomes, although studies have conflicting results. As Zika virus was a recently identified congenital infection, there are several new reports on child neurodevelopment in the Caribbean and Central and South America. For many congenital infections, children with in-utero exposure, even if asymptomatic at birth, may have neurodevelopmental concerns manifest over time. Summary: Congenital infections should be considered in the differential diagnosis of a child with neurodevelopmental impairments. Detailed pregnancy history, exposure risk, and testing should guide diagnosis and multidisciplinary evaluation. Children with congenital infections should have long-term follow-up to assess for neurodevelopmental delays and other neurosensory impairments. Children with confirmed delays or high-risk should be referred for rehabilitation therapies.

PMID: 37466092

23. A randomized controlled trial of a home-based computerized executive function intervention for children with cerebral palsy

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Children with cerebral palsy (CP) often show executive function (EF) impairments that are key to quality of life. The aim of this study was to assess whether a home-based computerized intervention program improves executive functions (EFs) compared to usual care. Sixty participants (30 females) with CP (8-12 years old) were paired by age, sex, motor ability, and intelligence quotient score and then randomized to intervention and waitlist control groups. The intervention group received a 12-week home-based computerized EF intervention (5 days/week, 30 min/day, total dose 30 h). Core and higher-order EFs were assessed before, immediately after, and 9 months after completing the intervention. The intervention group performed better than the waitlist control group in the three core EFs (immediately and 9 months after the intervention): inhibitory control ($F = 7.58$, $p = 0.13$ and $F = 7.85$, $p = 0.12$), working memory ($F = 8.34$, $p = 0.14$ and $F = 7.55$, $p = 0.13$), and cognitive flexibility ($F = 4.87$, $p = 0.09$ and $F = 4.19$, $p = 0.08$). No differences were found between the groups in higher-order EFs or EF manifestations in daily life. Conclusions: A home-based computerized EF intervention improved core EFs in children with CP, but further research is needed to identify strategies that allow the transfer of these improvements to everyday life.

PMID: 37462799

24. Uncertainties regarding cerebral palsy diagnosis: opportunities to operationalize the consensus definition

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Background and objectives: Cerebral palsy (CP), the most common motor disability of childhood, is variably diagnosed. We hypothesized that child neurologists and neurodevelopmentalists, often on the frontlines of CP diagnosis in North America, harbor uncertainties regarding the practical application of the most recent CP consensus definition from 2006. Methods: We conducted a cross-sectional survey of child neurologists and neurodevelopmentalists at the 2022 Child Neurology Society Annual Meeting. Attendees were provided the 2006 CP consensus definition and asked whether they had any uncertainties about the practical application of the definition across four hypothetical clinical vignettes. Results: Of 230 attendees, 164 responded to the closing survey questions (71%). 145/164 (88%) expressed at least one uncertainty regarding the clinical application of the 2006 definition. Overwhelmingly, these areas of uncertainty focused on: 1) Age, both with regards to the minimum age of diagnosis and the maximum age of brain disturbance or motor symptom onset, (67/164, 41%), and 2) Interpretation of the term "non-progressive" (48/164, 29%). The vast majority of respondents (157/164, 96%) answered 'Yes' to the question: Do you think we should revise the 2006 consensus definition of CP? Discussion: We propose that the uncertainties we identified could be addressed by operationalizing the 2006 consensus definition to support a more uniform CP diagnosis. To address the most common CP diagnostic uncertainties we identified, we propose 3 points of clarification based on the available literature: 1) Motor symptoms/signs should be present by 2 years old; 2) CP can and should be diagnosed as early as possible, even if activity limitation is not yet present, if motor symptoms/signs can be reasonably predicted to yield activity limitation (e.g. by using standardized examination instruments, Brain MRI, and a suggestive clinical history); and 3) The clinical motor disability phenotype should be non-progressive through 5 years old. We anticipate that operationalizing the 2006 definition of CP in this manner could clarify the uncertainties we identified among child neurologists and neurodevelopmentalists and reduce the diagnostic variability that currently exists.

PMID: 37461618

25. Serotonin syndrome from combination hydrocodone and cyclobenzaprine in a patient with cerebral palsy

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Aim: Serotonin syndrome (SS) is a life-threatening syndrome that occurs with the use of serotonergic drugs, most commonly due to two or more agents. Cerebral palsy is associated with mood disorders, and more commonly pain, with a prevalence of up to 50-80%. Case presentation: A 58-year-old female with cerebral palsy, metastatic malignancy and mood disorder who presented to the emergency department with acute-on-chronic pain, and signs of SS. She was initiated on iv. dilaudid, titrated off oral medications and scheduled for a left-sided sacroiliac joint injection. Results: It was suspected that due to additional doses of hydrocodone and cyclobenzaprine, she developed moderate-SS. Conclusion: Physicians need to be cognizant of comorbidities and uncommon pain medications that can predispose patients to SS.

PMID: 37458236