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Cerebral palsy research news

Monday 18 July 2022

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Interventions and Management

1. Feasibility of family-directed home-based bimanual intensive therapy combined with modified constraint induced movement therapy (h-BITmCI) in very low and low bimanual functional level: A brief report
Rocío Palomo-Carrión, Helena Romay-Barrero, Cristina Lirio-Romero, Rubén Arroyo-Fernádez, Marta M-Guijarro-Herraiz, Asunción Ferri-Morales

Dev Neurorehabil. 2022 Jul 14;1-8. doi: 10.1080/17518423.2022.2099993. Online ahead of print.

Objective: To examine the feasibility of a home-based hybrid Bimanual-Intensive-Therapy combined with modified Constraint-Induced-Movement-Therapy (h-BITmCI) in children with spastic unilateral cerebral palsy (SUCP) with low and very low bimanual functional level. Methods: A single-group of 10 children aged 5-8 years old, performed the hybrid home Bimanual-Intensive-Therapy (BIT, 80 hours) combined with modified Constraint-Induced-Movement-Therapy (mCIMT, 20 hours): h-BITmCI. Thus, Bimanual Functional Performance (BFP), Quality of Life (QoL) and expectations from families were measured through the Assisting Hand Assessment, (AHA), Pediatric Quality of Life Inventory, for Cerebral Palsy, (PedsQLTM v. 3.0, CP) and a specific questionnaire for families for baseline period (week 0), during the treatment phase (week 4 and week 8) and after the intervention (week 10). Repeated measures ANOVA analysis (with post hoc test correction) was used for the BFP and QoL, with a confidence interval (CI) of 95% and with p value <.008 considered statistically significant. Results: Ten children completed the study with an average of 77-hours-BIT and 17-hours-mCIMT. None of the participants dropped out of the study during the follow-up process, and the parents' expectations were fulfilled, indicating high caregiver compliance. During the first 80 hours of BIT, a mean increase of 3.7 AHA units was obtained for the BFP ($p = 1.00$) and 1.64 points in the QoL ($p = 1.00$). Clinically relevant changes were observed in the last two weeks (20 hours mCIMT) with a mean increase of 10.6 AHA units in BFP and 6.29 points in QoL ($p < .001$). Conclusions: h-BITmCI protocol is feasible to be performed at home with the family's involvement, obtaining the greatest improvements after 100 hours of both therapies. Thus, mCIMT would be a relevant condition to increase the affected upper limb functionality, rather than the dosage used to obtain clinically relevant changes.

PMID: 35833864

2. Functional Splinting efficacy in a Specific Task Home Program for Children with Cerebral Palsy. A Randomized Controlled Trial
Patricia Roldán-Pérez, Vanesa Abuín-Porras, Almudena Buesa-Estéllez, María Ortiz-Lucas

Dev Neurorehabil. 2022 Jul 13;1-10. doi: 10.1080/17518423.2022.2099027. Online ahead of print.

Background: The purpose of this study is to investigate whether wearing a functional hand splint adds benefit to carrying out a task-specific home program. Methods: Thirty-three children were randomly assigned to the Specific Task and Splint Group or

to a comparison group. Participants were evaluated before and after 6 weeks of intervention and at 14 weeks of follow-up. Results: Both groups improved on the Assisting Hand Assessment and the Children's Hand-use Experience Questionnaire (AHA Units p = .000; CHEQ bimanual tasks p = .000; CHEQ grasp efficacy p = .000 and CHEQ time utilization p = .018). No differences were found between the groups after the intervention or after the follow-up. Conclusions: Hand skills improved in both groups who received a task-specific home program. Wearing a functional hand splint did not appear to improve effectiveness in addition to the home program. This study is registered in ClinicalTrials.gov (NCT03282422).

PMID: 35822931

3. Electromyographic Response of the Abdominal Muscles and Stabilizers of the Trunk to Reflex Locomotion Therapy (RLT). A Preliminary Study
Fátima Pérez-Robledo, Juan Luis Sánchez-González, Beatriz María Bermejo-Gil, Rocío Llamas-Ramos, Inés Llamas-Ramos, Antonio de la Fuente, Ana María Martín-Nogueras

J Clin Med. 2022 Jul 3;11(13):3866. doi: 10.3390/jcm11133866.

Reflex locomotion therapy (RLT) was developed by Vaclav Vojta in 1954 as a diagnostic and treatment tool. This therapy is mainly used to rehabilitate children with motor disorders and risk of cerebral palsy. It is also used for adults with neurological and motor impairment. RLT is based on specific postures and regular stimulation points through which a series of reflex responses are triggered. The neurophysiological mechanisms of this therapy have recently been discovered. This study aims to objectively evaluate muscular responses at the abdominal level after stimulation in the first phase of reflex rolling by showing, with surface electromyography analysis (sEMG), the muscular activity in trunk stabilizing muscles (rectus abdominis, external oblique, internal oblique, and serratus anterior) before, during, and after the application of RLT. A total sample of 27 healthy subjects over 18 years of age was recruited. An experimental study on a cohort was conducted. Two experimental conditions were considered: stimuli according to the Vojta protocol, and a control non-STI condition. Regarding muscular electrical activity, statistically significant differences were determined in all muscles during right-sided stimulation in the VSTI condition (p < 0.001), but not in the non-STI condition. The mean increase in muscle activity in the VSTI condition during the first stimulation ranged from 7% to 20% in the different abdominal muscles. In conclusion, an sEMG response was observed in the abdominal muscles during stimulation of the pectoral area as described in RLT, compared to stimulation of non-described areas.

PMID: 35807151

4. Fate of hips complicated by avascular necrosis of the femoral head following reconstructive surgery in nonambulatory patients with cerebral palsy
Byoung Kyu Park, Hoon Park, Kun Bo Park, Isaac Rhee, Sungmin Kim, Hyun Woo Kim

Sci Rep. 2022 Jul 11;12(1):11767. doi: 10.1038/s41598-022-16023-7.

The purpose of this study was to evaluate the influence of avascular necrosis of the femoral head (AVN) following hip reconstructions on the future hip development of cerebral palsy (CP) patients. A retrospective study of 394 hips in 205 nonambulatory patients with spastic CP who underwent reconstructive hip surgery was performed. The mean age at surgery was 7.3 ± 2.4 years. The mean follow-up duration was 5.6 ± 2.7 years, and the mean age at the latest follow-up was 12.8 ± 3.4 years. AVN was classified in terms of its severity and location. Femoral head remodelling was assessed by the spherical index and the Mose circle. An unsatisfactory radiological outcome was defined as having a migration percentage of more than 30% at the final follow-up. AVN was observed in 169 (42.9%) hips. Older age at the time of surgery, higher preoperative migration percentage, and open reduction procedures were predictors for the development of AVN. Hips with AVN confined to the lateral epiphysis, and AVN involving the entire epiphysis with preserved height experienced successful remodelling. 27 (65.9%) of the 41 hips with unsatisfactory outcomes experienced AVN. Younger age, higher postoperative migration percentage, and occurrence of AVN were related to unsatisfactory outcomes. The highest incidence of failed remodelling and unsatisfactory outcomes were observed in hips with entire epiphyseal involvement and more than 50% loss of its height. AVN following hip reconstructions is not necessarily associated with poor hip development, however, depending on the severity and location, it is a prognostic factor for unsatisfactory radiological outcomes.

PMID: 35817817

5. "That's frustrating": Perceptions of ankle foot orthosis provision, use, and needs among people with cerebral palsy and caregivers
Nicole L Zaino, Momona Yamagami, Deborah J Gaebler-Spira, Katherine M Steele, Kristie F Bjornson, Heather A Feldner

Prosthet Orthot Int. 2022 Jul 8. doi: 10.1097/PXR.0000000000000165. Online ahead of print.

Background: Cerebral palsy (CP) affects roughly 3 per 1000 births in the United States and is the most common pediatric developmental motor disability. Ankle foot orthoses (AFOs) are commonly prescribed to provide support and improve function for individuals with CP. Objectives: The study objective was to evaluate the lived experiences of individuals with CP and their caregivers regarding AFO access, use, and priorities. We examined experiences around the perceived purpose of AFOs, provision process, current barriers to use, and ideas for future AFO design. Study design: Secondary qualitative data analysis. Methods: Secondary data analysis was performed on semistructured focus groups that included 68 individuals with CP and 74 caregivers. Of the focus group participants, 66 mentioned AFOs (16 individuals with CP and 50 caregivers). Deidentified transcripts were analyzed using inductive coding, and the codes were consolidated into themes. Results: Four themes emerged: 1) AFO provision is a confusing and lengthy process, 2) participants want more information during AFO provision, 3) AFOs are uncomfortable and difficult to use, and 4) AFOs can benefit mobility and independence. Caregivers and individuals with CP recommended ideas such as 3D printing orthoses and education for caregivers on design choices to improve AFO design and provision. Conclusions: Individuals with CP and their caregivers found the AFO provision process frustrating but highlight that AFOs support mobility and participation. Further opportunities exist to support function and participation of people with CP by streamlining AFO provision processes, creating educational materials, and improving AFO design for comfort and ease of use.

PMID: 35833742

6. Not all Forms of Muscle Hypertonia Worsen With Fatigue: A Pilot Study in Para Swimmers
Luca Puce, Nicola Luigi Bragazzi, Antonio Currà, Lucio Marinelli, Laura Mori, Filippo Cotellessa, Karim Chamari, Marta Ponzano, Mohammad Hossein Samanipour, Pantelis T Nikolaidis, Carlo Biz, Pietro Ruggieri, Carlo Trompetto

Front Physiol. 2022 Jun 22;13:902663. doi: 10.3389/fphys.2022.902663. eCollection 2022.

In hypertonic muscles of patients with upper motor neuron syndrome (UMNS), investigation with surface electromyography (EMG) with the muscle in a shortened position and during passive muscle stretch allows to identify two patterns underlying hypertonia: spasticity and spastic dystonia. We recently observed in Para swimmers that the effect of fatigue on hypertonia can be different from subject to subject. Our goal was, therefore, to understand whether this divergent behavior may depend on the specific EMG pattern underlying hypertonia. We investigated eight UMNS Para swimmers (five men, mean age 23.25 ± 3.28 years), affected by cerebral palsy, who presented muscle hypertonia of knee flexors and extensors. Muscle tone was rated using the Modified Ashworth Scale (MAS). EMG patterns were investigated in rectus femoris (RF) and biceps femoris (BF) before and after two fatiguing motor tasks of increasing intensity. Before the fatiguing tasks, two subjects (#2 and 7) had spasticity and one subject (#5) had spastic dystonia in both RF and BF. Two subjects (#3 and 4) showed spasticity in RF and spastic dystonia in BF, whereas one subject (#1) had spasticity in RF and no EMG activity in BF. The remaining two subjects (#6 and 8) had spastic dystonia in RF and no EMG activity in BF. In all the 16 examined muscles, these EMG patterns persisted after the fatiguing tasks. Spastic dystonia increased ($p < 0.05$), while spasticity did not change ($p > 0.05$). MAS scores increased only in the muscles affected by spastic dystonia. Among the phenomena possibly underlying hypertonia, only spastic dystonia is fatigue-dependent. Technical staff and medical classifiers should be aware of this specificity, because, in athletes with spastic dystonia, intense and prolonged motor activity could negatively affect competitive performance, creating a situation of unfairness among Para athletes belonging to the same sports class.

PMID: 35812331

7. Accelerometer-measured physical activity, sedentary behavior, and sleep in children with cerebral palsy and their adherence to the 24-hour activity guidelines
Raquel Y Hulst, Jan Willem Gorter, Joyce Obeid, Jeanine M Voorman, Ilse M van Rijssen, Anke Gerritsen, Johanna M A Visser-Meily, Sigrid Pillen, Olaf Verschuren

Dev Med Child Neurol. 2022 Jul 14. doi: 10.1111/dmcn.15338. Online ahead of print.

Aim: To measure and describe the 24-hour activities (i.e. physical activity, sedentary behavior, and sleep) and to examine adherence to the 24-hour activity guidelines among children with cerebral palsy (CP) using actigraphy. Method: Children's 24-hour activities were recorded over 7 days using hip- and wrist-worn ActiGraph wGT3X-BT accelerometers. Results: In total, 362 days and 340 nights from 54 children with CP (Gross Motor Function Classification System [GMFCS] levels I-III; 44% females; median age [range] 6 years 6 months [3-12 years]) were included. Mean (SD) daily wear time was 746.2 (48.9) minutes, of which children spent on average 33.8% in light physical activity (251.6 [58.7] minutes per day), 5.2% in moderate-to-vigorous physical activity (38.5 [20.1] minutes per day), and the remaining 61.1% being sedentary (456.1 [80.4] minutes per day). Physical activity decreased while sedentary behavior increased with increasing GMFCS level. In total, 13% of all children met the physical activity recommendations, and 35% met the age-appropriate sleep duration recommendation. The proportion of children meeting the combined 24-hour guidelines for physical activity and sleep was low (5.9%), especially in those classified in GMFCS level III (0%). Interpretation: The observed low 24-hour guideline adherence rates emphasize the importance of considering the entire continuum of movement behaviors in the care of children with CP, in efforts to promote healthy lifestyle behaviors and prevent negative health outcomes.

PMID: 35833425

8. Use of accelerometry to investigate standing and dynamic body balance in people with cerebral palsy: A systematic review

Paola Janeiro Valenciano, Núbia Ribeiro Conceição, Alexandre Jehan Marcori, Luis Augusto Teixeira

Review Gait Posture. 2022 Jul 7;96:357-364. doi: 10.1016/j.gaitpost.2022.06.017. Online ahead of print.

Background: People with cerebral palsy (CP) often have difficulties related to maintaining body balance in their daily living activities. Accelerometers are low-cost wearable devices with potential use to objectively assess balance. Research question: What are the main characteristics and findings from protocols used in research aiming to investigate standing or dynamic body balance stability through trunk accelerometry in people with CP? Method: We searched in December 2021 seven databases, Pubmed, Embase, Cochrane, Science Direct, Scopus, PEDro, and Lilacs, with descriptors related to cerebral palsy, accelerometer, and balance. Results: Ten studies were included, with a total of 197 evaluated people with CP. These studies were classified as moderate or high methodological quality. We found convergence on the use of the sensor at the lumbar region (L3), with sampling frequency at 100 Hz. For balance assessment, 60 % of the reviewed studies used the 10-m walk test, while the other studies used different walking distances, or the quiet standing test. For data processing, the low-pass filter at 20 Hz has been used predominantly, and the most commonly used variable to evaluate balance stability has been root mean square of trunk acceleration. Children and adolescents with CP had higher acceleration values and greater gait complexity than typically developing children. Individuals with bilateral impairment had greater anteroposterior and mediolateral trunk accelerations than those with unilateral impairment. Trunk acceleration was shown to be sensitive to improvement in gait stability from interventions, and acceleration-based measures have been found to correlate with qualitative balance assessment tools. Significance: Trunk accelerometry in quiet posture and dynamic tasks was shown to be a valid and sensitive measurement to evaluate balance stability in children and adolescents with CP. It is a small, light, low-cost and easy-to-handle tool that is effective for measuring body balance on different tasks in this population.

PMID: 35820240

9. Exercise intensity of active video gaming in cerebral palsy: hip- versus wrist-worn accelerometer data

Pınar Kaya Ciddi, Öznur Yilmaz

Dev Neurorehabil. 2022 Jul 11;1-6. doi: 10.1080/17518423.2022.2099028. Online ahead of print.

Objective: The aim of this study was to compare exercise intensity of active video games (AVGs) between hip- and wrist-worn accelerometer data in cerebral palsy (CP). Methods: Twenty children and adolescents (9.35 ± 3.71 years) with CP performed two exercise sessions, completing a standardized series of AVGs. Exercise intensity was collected, while one accelerometer was fitted to wrist and hip in separate, counterbalanced sessions. Results: Accelerometer counts per minute and cut-points determined were significantly different between the wrist- and hip-worn outputs ($p < .001$). Metabolic equivalents (METs) of performing AVGs exceeded the three METs moderate intensity threshold in wrist-worn (3.12 ± 0.86) accelerometer and hip-worn data tend to underestimate intensity (1.16 ± 0.08). Conclusions: Previous studies showed METs required to perform

AVGs were related to moderate intensity (3-6 METs) in CP with mild deficits. Wrist-worn accelerometer, exceeding 3 METs, seem to have higher accuracy in measuring exercise intensity of AVGs than hip-worn.

PMID: 35815544

10. Electro-suit treatment of children with unilateral cerebral palsy alters nonlinear dynamics of walking
Peter C Raffalt, Jesper Bencke, Kristian Mortensen, Tina P Torabi, Christian Wong, Merete B Speedtsberg

Clin Biomech (Bristol, Avon). 2022 Jul 8;98:105714. doi: 10.1016/j.clinbiomech.2022.105714. Online ahead of print.

Background: Cerebral palsy (CP) is characterized by spasticity and muscle contracture development and associated with mild to severe motor impairments including reduced gait function. Treatment with the Exopulse® suit has been shown to reduce spasticity of the affected muscles and constitutes a non-invasive alternative to pharmaceutical agents and surgical denervation. The present study investigated the effect of systematic treatment with the Exopulse® suit on the nonlinear dynamics and variability of trunk accelerations during walking in children with unilateral CP. Methods: Twelve patients (mean age: 12 years, range 7-17 years) with unilateral CP (GMFCS level 1 and 2) received 24 weeks Exopulse® suit treatment with patient-specific muscle stimulation. Before and after the treatment, the patients completed 4 min treadmill walking while trunk accelerometry was obtained. The nonlinear dynamics was quantified by the largest Lyapunov exponent and the complexity index from the multiscale entropy and movement variability was quantified by the root mean square ratio. Pre- vs post-treatment differences were evaluated by a paired Student's t-test. Findings: The largest Lyapunov exponent (p-value = 0.041) and the complexity index (p-value = 0.030) of the acceleration in the anterior-posterior direction was significantly lower post-treatment. No other between-trial differences were observed. Interpretation: The present study suggests that 24 weeks of Exopulse® suit treatment alters the nonlinear dynamics but not the variability of the trunk accelerations during walking in children with unilateral CP. The temporal structure of the trunk acceleration in the anterior-posterior direction was altered towards that of healthy individuals.

PMID: 35839741

11. Active Virtual Reality for Chronic Primary Pain: Mixed Methods Randomized Pilot Study
Natalie Tuck, Catherine Pollard, Clinton Good, Caitlin Williams, Gwyn Lewis, Murray Hames, Tipu Aamir, Debbie Bean

JMIR Form Res. 2022 Jul 13;6(7):e38366. doi: 10.2196/38366.

Background: The modern management of chronic pain is largely focused on improving functional capacity (often despite ongoing pain) by using graded activation and exposure paradigms. However, many people with chronic pain find functional activation programs aversive, and dropout rates are high. Modern technologies such as virtual reality (VR) could provide a more enjoyable and less threatening way for people with chronic pain to engage in physical activity. Although VR has been successfully used for pain relief in acute and chronic pain settings, as well as to facilitate rehabilitation in conditions such as stroke and cerebral palsy, it is not known whether VR can also be used to improve functional outcomes in people with chronic pain. Objective: This study aimed to assess the feasibility of conducting an adequately powered randomized controlled trial (RCT) to test the efficacy of VR in a chronic pain treatment center and assess the acceptability of an active VR treatment program for patients in this setting. Methods: For this mixed methods pilot study, which was designed to test the feasibility and acceptability of the proposed study methods, 29 people seeking treatment for chronic pain were randomized to an active VR intervention or physiotherapy treatment as usual (TAU). The TAU group completed a 6-week waitlist before receiving standard treatment to act as a no-treatment control group. The VR intervention comprised twice-weekly immersive and embodied VR sessions using commercially available gaming software, which was selected to encourage movement. A total of 7 VR participants completed semistructured interviews to assess their perception of the intervention. Results: Of the 99 patients referred to physiotherapy, 53 (54%) were eligible, 29 (29%) enrolled, and 17 (17%) completed the trial, indicating that running an adequately powered RCT in this setting would not be feasible. Despite this, those in the VR group showed greater improvements in activity levels, pain intensity, and pain interference and reported greater treatment satisfaction and perceived improvement than both the waitlist and TAU groups. Relative effect sizes were larger when VR was compared with the waitlist (range small to very large) and smaller when VR was compared with TAU (range none to medium). The qualitative analysis produced the following three themes: VR is an enjoyable alternative to traditional physiotherapy, VR has functional and psychological benefits despite continued pain, and a well-designed VR setup is important. Conclusions: The active VR intervention in this study was highly acceptable to participants, produced favorable effects when compared with the waitlist, and showed similar outcomes as those of TAU. These findings suggest that a confirmatory RCT is warranted; however,

substantial barriers to recruitment indicate that incentivizing participation and using a different treatment setting or running a multicenter trial are needed.

PMID: 35830224

12. Clinician perspectives on the implementation of inpatient cycling-based exergames for children with cerebral palsy: A qualitative study
Analyssa Cardenas, Marina Petrevska, Elaine Biddiss, Darcy Fehlings

Objective: To understand the perspectives of key stakeholder clinicians in implementing inpatient cycling-based exergames for children with cerebral palsy (CP) into pediatric rehabilitation. Methods: Sixteen clinicians (nurses, physiotherapists, recreational therapists) that participated in a study exploring the feasibility of implementing cycling-based exergames for inpatient children with CP were interviewed. Clinicians' responses were coded using the Theoretical Domains Framework (TDF). Beliefs were generated from each response and relevant domains were identified. Results: Ten domains from the TDF were identified as relevant. Key enablers to clinician participation in future implementation included revision of clinician roles and responsibilities, the belief that children with CP will benefit from exergames, and the belief in potential applicability to other pediatric populations. Barriers included clinician limited time and exergame responsibilities not aligning with perceived clinician roles. Conclusions: This study identifies key barriers and enablers that future inpatient pediatric rehabilitation settings should consider when incorporating exergames into rehabilitation practice.

PMID: 35815548

13. Risk Factors for Dental Caries Experience in Children and Adolescents with Cerebral Palsy-A Scoping Review
Sarah Cui, Rahena Akhter, Daniel Yao, Xin-Yun Peng, Mary-Anne Feghali, Winnie Chen, Emily Blackburn, Elizabeth Fieldja Martin, Gulam Khandaker

Review Int J Environ Res Public Health. 2022 Jun 30;19(13):8024. doi: 10.3390/ijerph19138024.

Cerebral palsy is a developmental motor disorder which has far-reaching impacts on oral health. This scoping review examined the extent of research undertaken regarding the risk factors affecting dental caries experience in children and adolescents with cerebral palsy. Data were obtained from the electronic databases Web of Science and PubMed, using 10 search strings, for studies published between 1983 and 2018. Eligible studies were required to have investigated caries in children under 18 with cerebral palsy, as well as be written in English. 30 papers published were identified for inclusion in the review. These included 23 cross-sectional, 6 case-control, and 1 longitudinal study. Studies were categorized into six domains of risk factors: socioeconomic status (SE); cerebral palsy subtype (CPS); demographics (D); condition of oral cavity (OC); dental habits (DH); nutrition and diet (ND). This review was conducted and reported in accordance with Preferred Reporting Items for Systematic reviews and Meta-Analyses Extension for Scoping Reviews (PRISMA-ScR) guidelines. The most significant risk factors were caregiver-related education levels, oral health literacy, and sugar intake; this underlines the important role of special education and dental awareness in reducing dental caries incidence in CP children. Other factors showed divergent findings, highlighting the need for standardization and culturally specific studies in future literature.

PMID: 35805684

14. Comparison of Malocclusion Prevalence, Type and Severity between Cerebral Palsy and Healthy Subjects: A Prospective Case-Control Study
Victoria Martínez-Mihi, Vanessa Paredes-Gallardo, Francisco-Javier Silvestre, Javier Silvestre-Rangil

Background: To analyze the prevalence, type and severity of malocclusions in a group of patients with cerebral palsy (CP) using a facial and occlusal analysis and the Dental Aesthetic Index (DAI). Methods: A prospective, case-control study was made of two groups, a cerebral palsy and a control group, with the determination of the facial and occlusion analysis in the three spatial planes. The Dental Aesthetic Index (DAI) was used to assess the severity of malocclusion. Results: The patients with CP presented a higher prevalence of increased facial lower third height and a greater tendency towards right-side canine and molar class II malocclusion, narrower transverse relationship and crossbite. The DAI scores were statistically significantly

higher in the CP group. Increased physical impairment in the CP group was associated to greater DAI scores. Conclusions: The prevalence and severity of malocclusion were significantly greater in the CP group. The type of malocclusion predominantly found in these patients was molar class II, with open bite, increased overjet and a narrow arch. The CP group also presented mixed breathing with higher DAI scores and decreased facial lower third height.

PMID: 35806996

15. Associations of Circulating Insulin-Growth Factor-1 With Cognitive Functions and Quality of Life Domains in Ambulatory Young Adults With Cerebral Palsy: A Pilot Study
Ted Kheng Siang Ng, Patricia C Heyn, Alex Tagawa, Christina Coughlan, James J Carollo

Front Neurol. 2022 Jun 27;13:748015. doi: 10.3389/fneur.2022.748015. eCollection 2022.

Objective: Adults with cerebral palsy (CP) often have impaired cognitive functions. CP also has deteriorations in multiple quality-of-life (QoL) domains. The bio-psycho-social health psychology model posits that biological factor interacts with social and psychological functions. However, the biological determinant of psycho-social and functional outcomes in CP has been scarcely examined. Circulating Insulin-like growth factor-1 (IGF-1) is associated with cognitive deficits in older adults, we thus aimed to examine the associations of circulating IGF-1 with: (1) objectively measured cognitive functions, (2) self-reported cognitive functions, and (3) QoL measures in adults diagnosed with CP. Methods: Seventy-two adults with CP and varying degrees of cognitive functions were recruited from an accredited clinical motion analysis laboratory at a regional Children's Hospital. Circulating IGF-1 was measured using post-fasting serum. The Wechsler Adult Intelligence Scale (WAIS) tests were administered to assess multiple cognitive functions, whereas the Patient-Reported Outcomes Measurement Information System (PROMIS) was used to measure multiple domains of self-reported health, including cognitive complaints and eight QoL domains. Results: Sixty-eight participants had complete data [mean age = 25 (SD = 5.3), female = 52.8%]. Controlling for covariates, circulating IGF-1 was associated with multiple cognitive domains, including positively with declarative memory and executive function and inversely with visual-spatial and motor skills, and processing speed, while no association with subjective memory complaint was detected. Circulating IGF-1 was also inversely associated with four QoL domains, including depressive symptoms, executive function, physical function, and social roles and activities. Conclusions: In CP, circulating IGF -1 might be a useful biological determinant of objective cognitive functions and several quality-of-life domains commonly impaired in CP.

PMID: 35832183

16. Epilepsy and proxy-reported health-related quality of life in children and young people with non-ambulatory cerebral palsy
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Dev Med Child Neurol. 2022 Jul 12. doi: 10.1111/dmcn.15336. Online ahead of print.

Aim: To assess the association between epilepsy characteristics and proxy-reported health-related quality of life (HRQoL) in children and young people with non-ambulatory cerebral palsy (CP) and seizures. Method: This was a cross-sectional study of 164 children and young people (74 females, 90 males; mean age 10 years 6 months, range 2-21 years, SD 5 years 5 months). Caregivers completed the Child Health Index of Life with Disabilities (CPCHILD) in an outpatient setting. We utilized univariable linear regression and multivariable modeling to study relationships between variables and CPCHILD scores. Results: Gross Motor Function Classification System levels were 37% IV and 63% V. Sociodemographic factors included the Child Opportunity Index (median 51, interquartile range [IQR] 25-80). A median of 2 (IQR 1-3) antiseizure medications (ASMs) were used, and days with seizures ranged from 0 (30%) to 28 (20%) days in the previous 4 weeks. Total CPCHILD scores decreased 2.3 points for each ASM (95% confidence interval [CI] -4.1 to -0.42). Compared to persons with focal epilepsy, those with generalized epilepsy had lower total CPCHILD scores (-5.7; 95% CI -11 to -0.55). Number of days with seizures was not associated with total CPCHILD scores. Interpretation: Proxy-reported HRQoL was affected by epilepsy-specific features in children and young people with severe CP.

PMID: 35820144

17. Profile of children with cerebral palsy at a tertiary hospital in eastern Nepal
Shipra Chaudhary, Nisha Keshary Bhatta, Prakash Poudel, Jyoti Agrawal, Rosan Prasad Shah Kalawar, Jitendra Prasad Jayswal

BMC Pediatr. 2022 Jul 13;22(1):415. doi: 10.1186/s12887-022-03477-x.

Background: The clinical spectrum of Cerebral palsy (CP) can differ in various places depending upon knowledge of the people and resources for prevention, diagnosis and management. Although studied extensively in high-resource countries, adequate data related to CP from resource-constraint settings are lacking. This study aims to describe the profile of children with CP at a tertiary care center in eastern Nepal. Methods: This was a hospital-based cross-sectional descriptive study done from 2017 to 2018. Children 6 months to 15 years who presented with CP were enrolled and their clinical details recorded and described. Results: Amongst 110 children with CP, 74.54% were male. Majority (76.36%) were 5 years or below with the median age being 3(2.00-4.75) years. Children with spastic quadriplegia (44.44%) and Gross Motor Function Classification System level III (41.81%) were most common. Etiologically, perinatal factors (64.54%) like perinatal asphyxia (35.45%) and prematurity (20.90%) and postnatal infections (25.45%) were common. The common comorbidities were intellectual disability (71.81%) and epilepsy (66.36%). The main treatment modalities were: antiepileptics (59.09%) and centre-based physiotherapy sessions (35.45%). School education was provided in 23.07% with special education in 11.53%. Conclusions: This study describes the profile of CP at our centre in eastern Nepal. Predominance of perinatal complications and postnatal infections points towards the urgent need to further improve the perinatal and neonatal health care delivery system and practices.

PMID: 35831826

18. Development and Validation of a Deep Learning Method to Predict Cerebral Palsy From Spontaneous Movements in Infants at High Risk
Daniel Groos, Lars Adde, Sindre Aubert, Lynn Boswell, Raye-Ann de Regnier, Toril Fjørtoft, Deborah Gaebler-Spira, Andreas Haukeland, Marianne Loennecken, Michael Msall, Unn Inger Möinichen, Aurelie Pascal, Colleen Peyton, Heri Ramampiaro, Michael D Schreiber, Inger Elisabeth Silberg, Nils Thomas Songstad, Niranjan Thomas, Christine Van den Broeck, Gunn Kristin Øberg, Espen A F Ihlen, Ragnhild Støen

Randomized Controlled Trial JAMA Netw Open. 2022 Jul 1;5(7):e2221325. doi: 10.1001/jamanetworkopen.2022.21325.

Importance: Early identification of cerebral palsy (CP) is important for early intervention, yet expert-based assessments do not permit widespread use, and conventional machine learning alternatives lack validity. Objective: To develop and assess the external validity of a novel deep learning-based method to predict CP based on videos of infants' spontaneous movements at 9 to 18 weeks' corrected age. Design, setting, and participants: This prognostic study of a deep learning-based method to predict CP at a corrected age of 12 to 89 months involved 557 infants with a high risk of perinatal brain injury who were enrolled in previous studies conducted at 13 hospitals in Belgium, India, Norway, and the US between September 10, 2001, and October 25, 2018. Analysis was performed between February 11, 2020, and September 23, 2021. Included infants had available video recorded during the fidgety movement period from 9 to 18 weeks' corrected age, available classifications of fidgety movements ascertained by the general movement assessment (GMA) tool, and available data on CP status at 12 months' corrected age or older. A total of 418 infants (75.0%) were randomly assigned to the model development (training and internal validation) sample, and 139 (25.0%) were randomly assigned to the external validation sample (1 test set). Exposure: Video recording of spontaneous movements. Main outcomes and measures: The primary outcome was prediction of CP. Deep learning-based prediction of CP was performed automatically from a single video. Secondary outcomes included prediction of associated functional level and CP subtype. Sensitivity, specificity, positive and negative predictive values, and accuracy were assessed. Results: Among 557 infants (310 [55.7%] male), the median (IQR) corrected age was 12 (11-13) weeks at assessment, and 84 infants (15.1%) were diagnosed with CP at a mean (SD) age of 3.4 (1.7) years. Data on race and ethnicity were not reported because previous studies (from which the infant samples were derived) used different study protocols with inconsistent collection of these data. On external validation, the deep learning-based CP prediction method had sensitivity of 71.4% (95% CI, 47.8%-88.7%), specificity of 94.1% (95% CI, 88.2%-97.6%), positive predictive value of 68.2% (95% CI, 45.1%-86.1%), and negative predictive value of 94.9% (95% CI, 89.2%-98.1%). In comparison, the GMA tool had sensitivity of 70.0% (95% CI, 45.7%-88.1%), specificity of 88.7% (95% CI, 81.5%-93.8%), positive predictive value of 51.9% (95% CI, 32.0%-71.3%), and negative predictive value of 94.4% (95% CI, 88.3%-97.9%). The deep learning method achieved higher accuracy than the conventional machine learning method (90.6% [95% CI, 84.5%-94.9%] vs 72.7% [95% CI, 64.5%-79.9%]; P < .001), but no significant improvement in accuracy was observed compared with the GMA tool (85.9%; 95% CI, 78.9%-91.3%; P = .11). The deep learning prediction model had higher sensitivity among infants with nonambulatory CP (100%; 95% CI, 63.1%-100%) vs ambulatory CP (58.3%; 95% CI, 27.7%-84.8%; P = .02) and spastic bilateral CP (92.3%; 95% CI, 64.0%-99.8%) vs spastic unilateral CP (42.9%; 95% CI, 9.9%-81.6%; P < .001). Conclusions and relevance: In this prognostic study, a deep learning-based method for predicting CP at 9 to 18 weeks' corrected age had predictive accuracy on external validation, which suggests possible avenues for using deep learning-based software to provide objective early detection of CP in clinical settings.

PMID: 35816301

19. Brain lesion type, corticospinal tract organization, and task demands may be predictive of mirror movements and motor outcomes in children with unilateral cerebral palsy
Deborah Dewey

Dev Med Child Neurol. 2022 Jul 9. doi: 10.1111/dmcn.15343. Online ahead of print.

PMID: 35809248

20. Enhanced nociceptive behavior and expansion of associated primary afferents in a rabbit model of cerebral palsy
Emily J Reedich, Landon T Genry, Meredith A Singer, Clarissa Fantin Cavarsan, Elvia Mena Avila, Daphne M Boudreau, Michael C Brennan, Alyssa M Garrett, Lisa Dowaliby, Megan R Detloff, Katharina A Quinlan

J Neurosci Res. 2022 Jul 15. doi: 10.1002/jnr.25108. Online ahead of print.

Spastic cerebral palsy (CP) is a movement disorder marked by hypertonia and hyperreflexia; the most prevalent comorbidity is pain. Since spinal nociceptive afferents contribute to both the sensation of painful stimuli as well as reflex circuits involved in movement, we investigated the relationship between prenatal hypoxia-ischemia (HI) injury which can cause CP, and possible changes in spinal nociceptive circuitry. To do this, we examined nociceptive afferents and mechanical and thermal sensitivity of New Zealand White rabbit kits after prenatal HI or a sham surgical procedure. As described previously, a range of motor deficits similar to spastic CP was observed in kits born naturally after HI (40 min at ~70%-80% gestation). We found that HI caused an expansion of peptidergic afferents (marked by expression of calcitonin gene-related peptide) in both the superficial and deep dorsal horn at postnatal day (P)5. Non-peptidergic nociceptive afferent arborization (labeled by isolectin B4) was unaltered in HI kits, but overlap of the two populations (peptidergic and non-peptidergic nociceptors) was increased by HI. Density of glial fibrillary acidic protein was unchanged within spinal cord white matter regions important in nociceptive transmission at P5. We found that mechanical and thermal nociception was enhanced in HI kits even in the absence of motor deficits. These findings suggest that prenatal HI injury impacts spinal sensory pathways in addition to the more well-established disruptions to descending motor circuits. In conclusion, changes to spinal nociceptive circuitry could disrupt spinal reflexes and contribute to pain experienced by individuals with CP.

PMID: 35839339

Prevention and Cure

21. Trial of Erythropoietin for Hypoxic-Ischemic Encephalopathy in Newborns
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Randomized Controlled Trial N Engl J Med. 2022 Jul 14;387(2):148-159. doi: 10.1056/NEJMoa2119660.

Background: Neonatal hypoxic-ischemic encephalopathy is an important cause of death as well as long-term disability in survivors. Erythropoietin has been hypothesized to have neuroprotective effects in infants with hypoxic-ischemic encephalopathy, but its effects on neurodevelopmental outcomes when given in conjunction with therapeutic hypothermia are unknown. Methods: In a multicenter, double-blind, randomized, placebo-controlled trial, we assigned 501 infants born at 36 weeks or more of gestation with moderate or severe hypoxic-ischemic encephalopathy to receive erythropoietin or placebo, in conjunction with standard therapeutic hypothermia. Erythropoietin (1000 U per kilogram of body weight) or saline placebo was

administered intravenously within 26 hours after birth, as well as at 2, 3, 4, and 7 days of age. The primary outcome was death or neurodevelopmental impairment at 22 to 36 months of age. Neurodevelopmental impairment was defined as cerebral palsy, a Gross Motor Function Classification System level of at least 1 (on a scale of 0 [normal] to 5 [most impaired]), or a cognitive score of less than 90 (which corresponds to 0.67 SD below the mean, with higher scores indicating better performance) on the Bayley Scales of Infant and Toddler Development, third edition. Results: Of 500 infants in the modified intention-to-treat analysis, 257 received erythropoietin and 243 received placebo. The incidence of death or neurodevelopmental impairment was 52.5% in the erythropoietin group and 49.5% in the placebo group (relative risk, 1.03; 95% confidence interval [CI], 0.86 to 1.24; P = 0.74). The mean number of serious adverse events per child was higher in the erythropoietin group than in the placebo group (0.86 vs. 0.67; relative risk, 1.26; 95% CI, 1.01 to 1.57). Conclusions: The administration of erythropoietin to newborns undergoing therapeutic hypothermia for hypoxic-ischemic encephalopathy did not result in a lower risk of death or neurodevelopmental impairment than placebo and was associated with a higher rate of serious adverse events. (Funded by the National Institute of Neurological Disorders and Stroke; ClinicalTrials.gov number, NCT02811263.).

PMID: 35830641

22. Motor function and safety after allogeneic cord blood and cord tissue-derived mesenchymal stromal cells in cerebral palsy: An open-label, randomized trial
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Dev Med Child Neurol. 2022 Jul 10. doi: 10.1111/dmcn.15325. Online ahead of print.

Aim: To evaluate safety and motor function after treatment with allogeneic umbilical cord blood (AlloCB) or umbilical cord tissue-derived mesenchymal stromal cells (hCT-MSC) in children with cerebral palsy (CP). Method: Ninety-one children (52 males, 39 females; median age 3 years 7 months [range 2-5 years]) with CP due to hypoxic-ischemic encephalopathy, stroke, or periventricular leukomalacia were randomized to three arms: (1) the AlloCB group received 10 × 107 AlloCB total nucleated cells (TNC) per kilogram at baseline (n = 31); (2) the hCT-MSC group received 2 × 106 hCT-MSC at baseline, 3 months, and 6 months (n = 28); (3) the natural history control group received 10 × 107 AlloCB TNC per kilogram at 12 months (n = 31). Motor function was assessed with the Gross Motor Function Measure-66 (GMFM-66) and Peabody Developmental Motor Scale, Second Edition. Results: Infusions (n = 143) were well tolerated, with eight infusion reactions (three in the AlloCB group, five in hCT-MSC) and no other safety concerns. At 12 months, the mean differences (95% confidence intervals [CI]) between actual and expected changes in GMFM-66 score were AlloCB 5.8 points (3.4-8.2), hCT-MSC 4.3 (2.2-6.4), and natural history 3.1 (1.4-5.0). In exploratory, post hoc analysis, the mean GMFM-66 score (95% CI) of the hCT-MSC group was 1.4 points higher than natural history (-1.1 to 4.0; p = 0.27), and the AlloCB group was 3.3 points higher than natural history (0.59-5.93; p = 0.02) after adjustment for baseline Gross Motor Function Classification System level, GMFM-66 score, and etiology. Interpretation: High-dose AlloCB is a potential cell therapy for CP and should be further tested in a randomized, blinded, placebo-controlled trial.

PMID: 35811372

23. Stem cell therapy for cerebral palsy: Proceeding with caution
Gavin Clowry

Dev Med Child Neurol. 2022 Jul 12. doi: 10.1111/dmcn.15344. Online ahead of print.

PMID: 35822233