Cerebral palsy research news

Monday 25 May 2020

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Interventions and Management

1. Motor Learning in Unilateral Cerebral Palsy and the Influence of Corticospinal Tract Reorganization
Maíra I S Carneiro, Cristina Russo, Riccardo Masson, Davide Rossi Sebastiano, Giovanni Baranello, Chiara Turati, Nadia Bolognini

Eur J Paediatr Neurol. 2020 May 4;S1090-3798(20)30084-2. doi: 10.1016/j.ejpn.2020.04.013. Online ahead of print.

Cerebral Palsy (CP) is a complex neurological disorder, characterized by congenital motor disability associated with behaviour, perception and cognition disorders. The sensorimotor impairments represent the main hallmark of the disease, significantly impacting the quality of life. So far, few studies have investigated motor learning abilities in CP and their association with the plastic reorganization of the motor system remains largely unknown. The present proof-of-principle study explored explicit motor sequence learning in children with unilateral CP and different patterns of motor system reorganization (bilateral, ipsilateral, contralateral). Children with unilateral CP, and a group of age-matched typically developing (TD) children, underwent a sequential finger tapping task, performed with the affected hand by children with CP and with the non-dominant hand by TD children. The pattern of corticospinal tract projections in hemiparetic patients was assessed by single-pulse Transcranial Magnetic Stimulation (TMS). Results showed the presence of finger dexterity impairments in children with unilateral CP presenting with a bilateral or an ipsilateral control of the affected (trained) hand, as compared to TD children. Conversely, motor sequence learning was impaired in unilateral CP with ipsilateral or contralateral corticospinal reorganization, but not in the case of a bilateral control of the paretic hand. These preliminary findings, although referred to small clinical samples, suggest that unilateral control of the paretic upper-limb, from the ipsilateral or the contralateral motor cortex, may not be sufficient to develop typical motor learning with the affected hand, which seems to require a bilateral representation in the motor cortex. This evidence has potential implications for fine motor skills rehabilitation in CP.

PMID: 32417186

2. The Use of Dynamic Weight Support With Principles of Infant Learning in a Child With Cerebral Palsy: A Case Report
Samuel R Pierce, Julie Skorup, Morgan Alcott, Meghan Bochnak, Athylia C Paremski, Laura A Prosser

Phys Occup Ther Pediatr. 2020 May 19;1-10. doi: 10.1080/01942638.2020.1766638. Online ahead of print.

Aims: Typical infant movement is characterized by a high degree of motor exploration, error, and variability. However, children with cerebral palsy (CP) often cannot create these experiences due to their neuromotor impairments. The purpose of this case study is to describe a 6-month course of physical therapy (PT) incorporating principles of infant motor learning using dynamic weight support (DWS) in a child with CP. Methods: The child was a 27-month-old girl with diplegic CP who functioned at Gross Motor Function Classification System Level IV. The child received 68 PT sessions over a six-month period. DWS was used during therapy to encourage motor practice. The therapy area was arranged to encourage active

exploration, motor variability, and error experience. Gross motor function, postural control, parent perception of performance, and parent satisfaction were measured before, during, and after the course of therapy. Results: Gross motor function increased during the treatment beyond the level predicted from natural progression. Postural control fluctuated and demonstrated no appreciable improvement. Parent-perceived performance and satisfaction improved on three of four goals. Conclusions: Using DWS to incorporate principles of infant learning may have facilitated the development of gross motor skills in a child with diplegic CP.

PMID: 32423264

3. Kinect v2 Based System for Gait Assessment of Children With Cerebral Palsy in Rehabilitation Settings
Caue Conterno Barreira, Arturo Forner-Cordero, Patricia Moreno Grangeiro, Rafael Traldi Moura

J Med Eng Technol. 2020 May 18;1-5. doi: 10.1080/03091902.2020.1759709. Online ahead of print.

Cerebral palsy (CP) describes a group of disorders of movement, posture and balance caused by a non-progressive brain injury in the immature brain. It is the most prevalent cause of chronic motor disability in childhood, and although two thirds of CP children are able to walk, they show gait limitations. In this context, rehabilitation therapy can improve muscle balance and gait. Previous studies showed the importance of gait analysis as part of multidisciplinary tools for effective rehabilitation treatment. However, the high cost and the infrastructure required for the implementation of commercial gait analysis systems as well as the time-consuming preparation procedures, limit the access to this service. A low cost, non-restrictive, portable and of simple operation and installation system was developed based on Kinect v2 sensor. This study aims to validate it for capturing and analysing gait parameters in children with cerebral palsy. Several gait parameters from eleven CP patients with different levels of disability classified as a function of the Gross Motor Function Classification System (GMFCS) from II to III were recorded while they walked on a flat surface. The Kinect-based gait analysis system was compared with video-recording that yielded the same results. These results show the potential of Kinect to analyse gait in frail patient populations unobtrusively and with very low cost. More importantly, regarding to spatial parameters, the Kinect system was useful even for the worst case of GMFCS III that show a large gait variability with abnormal patterns.

PMID: 32420771

4. Relationship Between Transverse-plane Kinematic Deviations of Lower Limbs and Gait Performance in Children With Unilateral Cerebral Palsy: A Descriptive Analysis
Ragab K Elnaggar

Gait Posture. 2020 May 11;79:224-228. doi: 10.1016/j.gaitpost.2020.05.003. Online ahead of print.

Background: Transverse-plane kinematic deviations of lower limbs are common in children with unilateral cerebral palsy (UCP), often with detrimental consequences for gait. Research question: To identify the most important factor among rotational anomalies of lower limbs for gait in children with UCP. Methods: In a descriptive observational study, 42 children with UCP (age; 5-8 years) who had the ability of independent walking were included. Comprehensive gait analysis was performed and included assessment of the transverse-plane kinematic deviations of the lower limbs [pelvis, hip, and ankle rotation angles, and foot progression (FP) angle], and spatial-temporal gait features [velocity, step length (SL), single-limb support time (SLSt), temporal gait-symmetry index (T-GSI), and spatial gait-symmetry index (S-GSI)]. Results and significance: The regression analysis indicated that hip rotation was the key determinant of gait velocity ($R2 = 0.75$, $P < .001$) and S-GSI ($R2 = 0.24$, $P = .001$). The FP angle was the most important factor for T-GSI ($R2 = 0.22$, $P = .002$). The ankle rotation explained in part the variance in T-GSI ($R2 = 0.10$, $P = .001$). Conclusion: Gait velocity and spatial gait-symmetry are primarily affected by hip rotation anomalies. The temporal gait-symmetry is generally associated with the FP angle deviation and partly with ankle rotation deviation.

PMID: 32442898

5. Effect of Robot-Assisted Gait Training on Selective Voluntary Motor Control in Ambulatory Children With Cerebral Palsy
Dragana Žarković, Monika Šorfová, James J Tufano, Patrik Kutílek, Slávka Vítečková, Katja Groleger-Sršen, David Ravnik

Indian Pediatr. 2020 May 22;S097475591600186. Online ahead of print.

This pilot study investigated the efficacy of a four week robot-assisted gait training in twelve children with spastic diparesis. Short-term results and a 3-month follow-up showed statistically significantly increased selective motor control, walking farther distances, gross motor score, and decreased joint contractures.

PMID: 32441273

6. Characteristics of Selective Motor Control of the Lower Extremity in Adults With Bilateral Spastic Cerebral Palsy
Takahito Inoue, Yuichiro Yokoi

J Phys Ther Sci. 2020 May;32(5):348-351. doi: 10.1589/jpts.32.348. Epub 2020 May 1.

[Purpose] We aimed to examine the relationship between gross motor function, selective motor control (SMC), range of motion (ROM), and spasticity in the lower extremities of adults with cerebral palsy (CP), as well as the proximal to distal distribution of SMC impairment in lower extremity joints. [Participants and Methods] We recruited 11 adults with bilateral spastic CP, ranging from levels I to III according to the Gross Motor Function Classification System (GMFCS). We evaluated participants according to the Selective Control Assessment of the Lower Extremity (SCALE), ROM, and the Modified Ashworth Scale (MAS). We conducted the Friedman test to assess differences among the SCALE scores of each joint. The relationship between GMFCS level, SCALE scores, ROM, and MAS scores was assessed. [Results] The mean SCALE scores were lower for distal than for proximal joints. The SCALE scores of each leg showed significant inverse correlations with the GMFCS level. [Conclusion] SMC in adults with CP strongly influences gross motor function. SMC did not have a significant relationship with spasticity or ROM. SMC, ROM, and spasticity independently influenced gross motor function in adults with CP. SMC impairment in adults with CP was higher in distal than in proximal joints.

PMID: 32425353

7. Effect of Botulinum Toxin on Equinus Foot Deformity in Cerebral Palsy Patients: A Systematic Review and Network Meta-Analysis
Mohamed Fathi, Ahmed Salah Hussein, Shrouk M Elghazaly, Asmaa Mostafa Al-Kinawy, Ahmed K Abdeltawab, Yasmin M Mansour, Nada Abdallah Elbehbeh, Ahmed Sherif, Ahmed Mohamed Afifi

Meta-Analysis Curr Pharm Des. 2020 May 17. doi: 10.2174/1381612826666200518105633. Online ahead of print.

Background: Cerebral palsy (CP) is a brain disorder that affects the development of movement and posture leading to limitation of Range of Movement (ROM) in the growing children. CP leads to deformities as equinus foot deformity. We aim to investigate the efficacy of different botulinum toxin (BTX) products with or without serial casting in reducing the muscle spasticity in equinus foot deformity in patients with CP. Methods: A systematic review of the literature was performed via searching of the different electronic databases. The following databases were used PubMed, Scopus, Web of Science (WOS), and GHL. We analyzed the extracted data by network meta-analysis method using R software package (version 3.5.0). Results: Regarding Modified Ashworth score (MAS), BTX-A was superior compared to placebo and BTX-A plus immediate casting (MD = -0.39, 95% CI [-0.60; -0.18]) and (MD = -0.50, 95% CI [-0.98; -0.02]) respectively. Concerning growth motor function movement Classification System (GMFM), Neuronox ranked above at 3 months (MD = -1.60, 95% CI [-2.87; -0.33]) and at six months (MD = -1.90, 95% CI [-3.48; -0.32]) compared to BTX-A. Regarding the Modified Tardieu scale (MTS) with knee flexion, BTX-A was superior to BTX-A plus immediate casting (MD = 8.60, 95% CI [1.76; 15.44]). Concerning passive range of movement (PROM) with Knee flexion or extension at 3 months, BTX-A showed a significant improvement compared to BTX-A plus immediate casting. Conclusion: BTX-A ranked best on physician rating scale (PRS), MAS, MTS with knee flexion and PROM (Knee flexion and extension) compared to Neuronox and Botulax. BTX-A alone was also better than BTX-A plus immediate casting.

PMID: 32418518

8. The Effect of a Running Training Intervention on Ankle Power Generation in Children and Adolescents With Cerebral Palsy: A Randomized Controlled Trial
A Chappell, G T Allison, G Williams, N Gibson, S Morris

Clin Biomech (Bristol, Avon). 2020 May 3;76:105024. doi: 10.1016/j.clinbiomech.2020.105024. Online ahead of print.

Background: Children and adolescents with cerebral palsy who are classified as Gross Motor Function Classification Scale level I or II are usually able to run but lack ankle power generation for push-off. The aim of this study was to analyze the efficacy of a running training program in improving ankle power generation in children and adolescents with cerebral palsy. Methods: This randomized controlled trial compared kinematic and spatiotemporal data collected during running from 38 children and adolescents with unilateral or bilateral cerebral palsy before and after a 12-week running program. Normalized speed, stride length, cadence, foot strike pattern, peak ankle power generation, peak hip flexor power generation in swing and propulsion strategy were calculated. Linear mixed models were developed to analyze differences between groups. Findings: At follow-up the intervention group had increased normalized speed of running ($t = -3.68$ $p < .01$) while the control group got slower ($t = 3.17$ $p < .01$). In running, children in Gross Motor Function Classification Scale level II in the intervention group increased ankle power ($t = 2.49$ $p = .01$) while the control group did not change ($t = 0.38$ $p = .71$). In sprinting, children in Gross Motor Function Classification Scale levels I and II in the intervention group maintained ankle power (level I $t = 0.32$ $p = .75$; level II $t = 1.56$ $p = .12$) while those in the control group decreased ankle power (level I $t = 4.69$ $p < .01$; level II $t = 2.52$ $p = .01$). Most within-group differences did not result in significant between-group differences at follow-up. Interpretation: Power generation for running may be responsive to targeted intervention in children with cerebral palsy.

PMID: 32416406

9. Physical Demands by Para-Footballers With Cerebral Palsy in a Small-Sided Game
Matías Henríquez, Sonny Riquelme, Marco Abarca, Felipe Morales, Raúl Reina

J Sports Med Phys Fitness. 2020 May 20. doi: 10.23736/S0022-4707.20.10514-0. Online ahead of print.

Background: Cerebral Palsy (CP) Football is a para-sport performed by individuals with physical impairments of athetosis, ataxia, or hypertonia. However, little is known about the physical demands of para-footballers with CP, and no previous study has analysed those demands in a small-sided game (SSG). This study aims to describe physical parameters using a Global Positioning System device in an SSG played by CP Football players. Methods: Fourteen male international para-footballers with CP took part in this study, which analysed their performance in an SSG of 3 vs. 3 players plus a goalkeeper per team. Also, a group of 12 football players participated as a control group. Results: The total distance covered by the CP footballers during the SSG was 1931.1 ± 213.6 m, and the distance covered per minute was 71.2 ± 9.3 m·min-1, having lower scores than the control group. The maximum speed reached was 20.1 ± 1.8 km·h-1, with a metabolic power of 6.2 ± 0.9 W·kg-1 and lower scores than the control group. Players with the minimal eligible impairment in this para-sport (i.e., sport class FT8) covered a greater distance in high-speed zones compared to players with more severe impairments. Conclusions: This study demonstrated that para-footballers with CP exhibited lower physical performance in an SSG compared to regular football players. Additional studies are necessary to identify the best format of an SSG for football players with CP and its application for training and evidence-based classification.

PMID: 32432446

10. Machine Learning to Quantify Habitual Physical Activity in Children With Cerebral Palsy
Benjamin I Goodlich, Ellen L Armstrong, Sean A Horan, Emmah Baque, Christopher P Carty, Matthew N Ahmadi, Stewart G Trost

Dev Med Child Neurol. 2020 May 18. doi: 10.1111/dmcn.14560. Online ahead of print.

Aim: To investigate whether activity-monitors and machine learning models could provide accurate information about physical

activity performed by children and adolescents with cerebral palsy (CP) who use mobility aids for ambulation. Method: Eleven participants (mean age 11y [SD 3y]; six females, five males) classified in Gross Motor Function Classification System (GMFCS) levels III and IV, completed six physical activity trials wearing a tri-axial accelerometer on the wrist, hip, and thigh. Trials included supine rest, upper-limb task, walking, wheelchair propulsion, and cycling. Three supervised learning algorithms (decision tree, support vector machine [SVM], random forest) were trained on features in the raw-acceleration signal. Model-performance was evaluated using leave-one-subject-out cross-validation accuracy. Results: Cross-validation accuracy for the single-placement models ranged from 59% to 79%, with the best performance achieved by the random forest wrist model (79%). Combining features from two or more accelerometer placements significantly improved classification accuracy. The random forest wrist and hip model achieved an overall accuracy of 92%, while the SVM wrist, hip, and thigh model achieved an overall accuracy of 90%. Interpretation: Models trained on features in the raw-acceleration signal may provide accurate recognition of clinically relevant physical activity behaviours in children and adolescents with CP who use mobility aids for ambulation in a controlled setting.

PMID: 32420632

11. Nutritional Status and Prevalence of Dysphagia in Cerebral Palsy: Usefulness of the Eating and Drinking Ability Classification System Scale and Correlation With the Degree of Motor Impairment According to the Gross Motor Function Classification System [Article in English, Spanish]
A García Ron, R M González Toboso, M Bote Gascón, M T de Santos, R Vecino, A Bodas Pinedo

Neurologia. 2020 May 18;S0213-4853(20)30044-X. doi: 10.1016/j.nrl.2019.12.006. Online ahead of print.

Introduction and objectives: Digestive disorders are one of the most common comorbidities among children with cerebral palsy (CP). The aim of this study is to examine the nutritional status of patients with CP, the prevalence of dysphagia by degree of motor impairment, and the impact of digestive disorders on quality of life. Material and methods: We conducted a descriptive, cross-sectional, open-label study of outpatients with CP from a tertiary hospital in the Region of Madrid using a structured interview, classifying dysphagia using the Eating and Drinking Ability Classification System (EDACS). We gathered demographical and anthropometric data, and analysed the correlation between severity of dysphagia and functional status as measured with the Gross Motor Function Classification System (GMFCS). Results: Our sample included 44 patients (65.9% boys), with a mean (standard deviation) age of 9.34 (5) years and a mean BMI of 18.5 (4.9). Forty-three percent presented safety and efficiency limitations (EDACS level>II). Safety and efficiency limitations were associated with more extensive motor involvement (60% had tetraparesis), more varied clinical manifestations (87% had mixed forms) and poorer functional capacity (100% on GMFCS V). The impact on nutritional status increased with higher EDACS and GMFCS scores. Conclusions: This is the first study into the usefulness of the EDACS scale in a representative sample of Spanish children and adolescents with CP. Our findings underscore the importance of screening for dysphagia in these patients, regardless of the level of motor impairment, and the need for early treatment to prevent the potential consequences: malnutrition (impaired growth, micronutrient deficiencies, osteopaenia, etc.), microaspiration, or recurrent infections that may worsen patients' neurological status.

PMID: 32439150

12. Self-care Performance in Children With Cerebral Palsy: A Longitudinal Study
Andrea Burgess, Roslyn N Boyd, Mark D Chatfield, Jenny Ziviani, Leanne Sakzewski

Dev Med Child Neurol. 2020 May 19. doi: 10.1111/dmcn.14561. Online ahead of print.

Aim: To investigate self-care developmental trajectories in children with cerebral palsy (CP) across all functional ability levels, according to Manual Ability Classification System (MACS) levels. Method: This was a prospective longitudinal population-based study of 71 children aged from 2 years 6 months to 12 years, with CP (47 [66%] males, 24 [34%] females). Pediatric Evaluation of Disability Inventory (PEDI) measures were taken at 2 years 6 months, 3, 4, and 5 years, and the PEDI - Computer Adaptive Test (PEDI-CAT) between 8 and 12 years. At 8 to 12 years, children were classified in MACS levels I (21; 30%), II (22; 31%), III (16; 23%), IV (6; 8%), and V (6; 8%). Longitudinal analysis of the PEDI Functional Skills Scale self-care and PEDI-CAT daily activities domains used the published linking equation, and multilevel mixed-effects regression modelling with interaction between age and MACS. Results: Between 5 and 12 years of age, children classified in MACS levels I to III continued to show progress in self-care development (PEDI-CAT scaled scores estimated change per year: I, 0.72; II, 0.49; III, 0.48). Children classified in MACS level IV showed an upward non-significant trend between 5 and 8 to 12

years (estimated change 0.42; 95% confidence interval [CI] -0.04 to 0.88). Children in MACS level V showed a decline in self-care (estimated change: -0.65; 95% CI -1.16 to -0.14). Interpretation: Self-care development attained by 8 to 12 years of age was related to the severity of manual ability impairment. Application of the linking equation from PEDI to PEDI-CAT is somewhat uncertain at the extreme lower end of the scale. Our study supports recommendations for items to be added to the PEDI-CAT to address floor effect.

PMID: 32430913

13. Authors' Reply Re: Antenatal Magnesium Sulphate for the Prevention of Cerebral Palsy in Infants Born Preterm: A Double-Blind, Randomised, Placebo-Controlled, Multi-Centre Trial: Time Range for Treatment With Magnesium Sulphate
Hanne Trap Wolf, Jesper Brok, Tine Brink Henriksen, Hanne Kristine Hegaard, Gorm Greisen, Tom Weber, Ole Pryds, Jannie Dalby Salvig, Morten Hedegaard, Anja Pinborg, Lene Drasbek Huusom

BJOG. 2020 May 19. doi: 10.1111/1471-0528.16267. Online ahead of print.

PMID: 32427415

Prevention and Cure

14. TRPM7 Mediates Neuronal Cell Death Upstream of Calcium/Calmodulin-Dependent Protein Kinase II and Calcineurin Mechanism in Neonatal Hypoxic-Ischemic Brain Injury
Ekaterina Turlova, Raymond Wong, Baofeng Xu, Feiya Li, Lida Du, Steven Habbous, F David Horgen, Andrea Fleig, Zhong-Ping Feng, Hong-Shuo Sun

Transl Stroke Res. 2020 May 19. doi: 10.1007/s12975-020-00810-3. Online ahead of print.

Transient receptor potential melastatin 7 (TRPM7), a calcium-permeable, ubiquitously expressed ion channel, is critical for axonal development, and mediates hypoxic and ischemic neuronal cell death in vitro and in vivo. However, the downstream mechanisms underlying the TRPM7-mediated processes in physiology and pathophysiology remain unclear. In this study, we employed a mouse model of hypoxic-ischemic brain cell death which mimics the pathophysiology of hypoxic-ischemic encephalopathy (HIE). HIE is a major public health issue and an important cause of neonatal deaths worldwide; however, the available treatments for HIE remain limited. Its survivors face life-long neurological challenges including mental retardation, cerebral palsy, epilepsy and seizure disorders, motor impairments, and visual and auditory impairments. Through a proteomic analysis, we identified calcium/calmodulin-dependent protein kinase II (CaMKII) and phosphatase calcineurin as potential mediators of cell death downstream from TRPM7 activation. Further analysis revealed that TRPM7 mediates cell death through CaMKII, calmodulin, calcineurin, p38, and cofilin cascade. In vivo, we found a significant reduction of brain injury and improvement of short- and long-term functional outcomes after HI after administration of specific TRPM7 blocker waixenicin A. Our data demonstrate a molecular mechanism of TRPM7-mediated cell death and identifies TRPM7 as a promising therapeutic and drug development target for HIE.

PMID: 32430797

15. Neuroprotective Effects of Diabetes Drugs for the Treatment of Neonatal Hypoxia-Ischemia Encephalopathy
Laura Poupon-Bejuit, Eridan Rocha-Ferreira, Claire Thornton, Henrik Hagberg, Ahad A Rahim

Review Front Cell Neurosci. 2020 May 6;14:112. doi: 10.3389/fncel.2020.00112. eCollection 2020.

The perinatal period represents a time of great vulnerability for the developing brain. A variety of injuries can result in death or devastating injury causing profound neurocognitive deficits. Hypoxic-ischemic neonatal encephalopathy (HIE) remains the leading cause of brain injury in term infants during the perinatal period with limited options available to aid in recovery. It can

result in long-term devastating consequences with neurologic complications varying from mild behavioral deficits to severe seizure, intellectual disability, and/or cerebral palsy in the newborn. Despite medical advances, the only viable option is therapeutic hypothermia which is classified as the gold standard but is not used, or may not be as effective in preterm cases, infection-associated cases or low resource settings. Therefore, alternatives or adjunct therapies are urgently needed. Ongoing research continues to advance our understanding of the mechanisms contributing to perinatal brain injury and identify new targets and treatments. Drugs used for the treatment of patients with type 2 diabetes mellitus (T2DM) have demonstrated neuroprotective properties and therapeutic efficacy from neurological sequelae following HIE insults in preclinical models, both alone, or in combination with induced hypothermia. In this short review, we have focused on recent findings on the use of diabetes drugs that provide a neuroprotective effect using in vitro and in vivo models of HIE that could be considered for clinical translation as a promising treatment.

PMID: 32435185