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NEWS
Cerebral Palsy Research

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Interventions and Management

1. Upper limb and hand patterns in cerebral palsy: Reliability of two new classifications.

Chaleat-Valayer E, Bard-Pondarre R, Bernard JC, Roumenoff F, Lucet A, Denis A, Occelli P, Touzet S.

Eur J Paediatr Neurol. 2017 May 10. pii: S1090-3798(17)31603-3. doi: 10.1016/j.ejpn.2017.04.1332. [Epub ahead of print]

AIM: To evaluate the inter- and intra-rater reliability of two previously developed classifications of upper limb and hand patterns. METHOD: Two hundred and twelve films of patients with CP (118 of UL postures and 94 of hand tasks; median age 14, 3-46 years) were viewed by 18 examiners from 2 different rehabilitation centers, and one expert who had participated in the design of the classifications. They classed upper limb (3 patterns with sub-types) and hand patterns (2 patterns with subtypes) twice, at 2 months' interval. Inter- and intra-rater reliability were analysed. RESULTS: Intra-rater and inter-rater reliability were very high for upper limb and hand patterns ($0.87 < k < 0.92$), and high for the subtypes ($0.58 < k < 0.68$). Examiners stated that both classifications were useful and feasible in clinical practice. INTERPRETATION: Despite the single, short training session on use of the classifications, agreement between the examiners and the expert examiner was good to high, confirming that these classifications are easy to use and reliable. The classifications proposed here provide homogenous terminology for use in both clinical practice and research, to describe, evaluate and follow-up changes in upper limb and hand patterns in patients with cerebral palsy, particularly those with dyskinesia.

PMID: 28532985

2. Use of active video gaming in children with neuromotor dysfunction: a systematic review.

Hickman R, Popescu L, Manzanares R, Morris B, Lee SP, Dufek JS.

Dev Med Child Neurol. 2017 May 19. doi: 10.1111/dmcn.13464. [Epub ahead of print]

AIM: To examine current evidence on use of active video gaming (AVG) to improve motor function in children with movement disorders including cerebral palsy, developmental coordination disorder, and Down syndrome. METHOD: Scopus, MEDLINE, Cochrane Library, EMBASE, and CINAHL were searched. Included papers studied the use of AVG for improving movement-related outcomes in these populations. Parameters studied included health condition, strength of evidence, AVG delivery methods, capacity for individualizing play, outcomes addressed, effectiveness for achieving outcomes, and challenges/limitations. RESULTS: The 20 extracted articles varied in quality. Studies involved children with six different conditions using AVG in clinical, home, or school settings for 49 different motor outcomes. Dosage varied in frequency and duration. Choice of games played and difficulty level were therapist determined (n=6) or child controlled (n=14). The most common study limitations were small sample sizes and difficulty individualizing treatment. All articles showed improvement in outcomes with AVG, although differences were not consistently significant compared with conventional therapy. INTERPRETATION: Heterogeneity of measurement tools and target outcomes prevented meta-analysis

or development of formal recommendations. However, AVG is feasible and shows potential for improving outcomes in this population. Additional investigations of dosing variables, utility as a home supplement to clinical care, and outcomes with larger sample sizes are merited.

PMID: 28542867

3. The Effectiveness of a Computer Game-Based Rehabilitation Platform for Children With Cerebral Palsy: Protocol for a Randomized Clinical Trial.

Kanitkar A, Szturm T, Parmar S, Gandhi DB, Rempel GR, Restall G, Sharma M, Narayan A, Pandian J, Naik N, Savadatti RR, Kamate MA.

JMIR Res Protoc. 2017 May 18;6(5):e93. doi: 10.2196/resprot.6846.

BACKGROUND: It is difficult to engage young children with cerebral palsy (CP) in repetitive, tedious therapy. As such, there is a need for innovative approaches and tools to motivate these children. We developed the low-cost, computer game-based rehabilitation platform CGR that combines fine manipulation and gross movement exercises with attention and planning game activities appropriate for young children with CP. OBJECTIVE: The objective of this study is to provide evidence of the therapeutic value of CGR to improve upper extremity (UE) motor function for children with CP. METHODS: This randomized controlled, single-blind, clinical trial with an active control arm will be conducted at 4 sites. Children diagnosed with CP between the ages of 4 and 10 years old with moderate UE impairments and fine motor control abnormalities will be recruited. RESULTS: We will test the difference between experimental and control groups using the Quality of Upper Extremity Skills Test (QUEST) and Peabody Developmental Motor Scales, Second Edition (PDMS-2) outcome measures. The parents of the children and the therapist experiences with the interventions and tools will be explored using semi-structured interviews using the qualitative description approach. CONCLUSIONS: This research protocol, if effective, will provide evidence for the therapeutic value and feasibility of CGR in the pediatric rehabilitation of UE function.

PMID: 28526673

4. Changes in gait parameters after femoral derotational osteotomy in cerebral palsy patients with medial femoral torsion.

Kim HY, Cha YH, Byun JY, Chun YS, Choy WS.

J Pediatr Orthop B. 2017 May 19. doi: 10.1097/BPB.0000000000000467. [Epub ahead of print]

Medial femoral torsion (MFT) is a common pathologic gait in cerebral palsy (CP) children that can be corrected by femoral derotational osteotomy (FDO). It is not clearly known as to how much various gait parameters change after FDO. The aim of this study was to quantify changes in gait parameters after FDO. The study group included 19 young CP patients (28 limbs, age<20 years, average age: 13.2 years) with symptomatic MFT, treated with distal FDO. The study group was divided into two groups: the unilateral FDO group (UG) and the bilateral FDO group (BG). The mean degree of derotation was 24.6° (25.0° for UG, 24.4° for BG). Pre-FDO and post-FDO values of Staheli's rotational profiles and kinematic data were compared. A paired t -test and Pearson's correlation were used for statistical analysis. The mean internal hip rotation was 71.4±6.9° before surgery and 48.6±10.7° after surgery in the UG (P<0.05) and it was 63.8±15.8° before surgery and 40.9±9.2° after FDO in the BG (P<0.05). The change in the foot progression angle (FPA) was 12.9° in the UG group (P<0.05) and 12.6° in the BG group (P<0.05). The degree of FPA had changed by about a half of the surgical derotation angle. Changes in the mean hip rotation during gait were 14.8° in the UG (P<0.05) and 6.7° in the BG (P<0.05) groups. The overall pelvic rotation was not changed after surgery. However, in patients with preoperative compensatory pelvic rotation of more than 5°, there was a change of 5.3±4.8° in the UG and 6.6±1.54° in the BG after surgery (P<0.05). There was also a trend showing that the younger the patient, the more the pelvic rotation changed (P=0.069). In-toeing gait because of MFT improved with FDO in CP patients. The expected degree of postoperative correction of FPA and hip rotation is about a half of the FDO degree. The degree of compensatory pelvic rotation should be considered to determine the correction angle of FDO, especially in young patients with preoperative pelvic rotation of more than 5°.

PMID: 28537994

5. The effects of neck and trunk stabilization exercises on cerebral palsy children's static and dynamic trunk balance: case series.

Shin JW, Song GB, Ko J.

J Phys Ther Sci. 2017 Apr;29(4):771-774. doi: 10.1589/jpts.29.771. Epub 2017 Apr 20.

[Purpose] The purpose of this case series was to examination the effects of trunk and neck stabilization exercise on the static, dynamic trunk balance abilities of children with cerebral palsy. [Subjects and Methods] The study included 11 school aged children diagnosed with paraplegia due to a premature birth. Each child engaged in exercise treatments twice per week for eight weeks; each treatment lasted for 45 minutes. After conducting a preliminary assessment, exercise treatments were designed based on each child's level of functioning. Another assessment was conducted after the eight weeks of treatment. [Results] The Trunk Control Measurement Scale evaluation showed that the exercise treatments had a significant effect on static sitting balance, selective movement control, dynamic reaching, and total Trunk Control Measurement Scale scores. [Conclusion] The results indicate that neck and trunk stabilization exercises that require children's active participation are helpful for improving static and dynamic balance ability among children diagnosed with cerebral palsy.

PMID: 28533628

6. The effects of a multisensory dynamic balance training on the thickness of lower limb muscles in ultrasonography in children with spastic diplegic cerebral palsy.

Nam SM, Kim WH, Yun CK.

J Phys Ther Sci. 2017 Apr;29(4):775-778. doi: 10.1589/jpts.29.775. Epub 2017 Apr 20.

[Purpose] This study aimed to investigate the effects of multisensory dynamic balance training on muscles thickness such as rectus femoris, anterior tibialis, medial gastrocnemius, lateral gastrocnemius in children with spastic diplegic cerebral palsy by using ultrasonography. [Subjects and Methods] Fifteen children diagnosed with spastic diplegic cerebral palsy were divided randomly into the balance training group and control group. The experimental group only received a multisensory dynamic balance training, while the control group performed general physiotherapy focused balance and muscle strengthening exercise based Neurodevelopmental treatment. Both groups had a therapy session for 30 minutes per day, three times a week for six weeks. The ultrasonographic muscle thickness were obtained in order to compare and analyze muscle thickness before and after in each group. [Result] The experimental group had significant increases in muscle thickness in the rectus femoris, tibialis anterior, medial gastrocnemius and lateral gastrocnemius muscles. The control group had significant increases in muscle thickness in the tibialis anterior. The test results of the rectus femoris, medial gastrocnemius and lateral gastrocnemius muscle thickness values between the groups showed significant differences. [Conclusion] In conclusion, a multisensory dynamic balance training can be recommended as a treatment method for patients with spastic diplegic cerebral palsy.

PMID: 28533629

7. Risk factors for daytime or combined incontinence in children with cerebral palsy.

Samijn B, Van den Broeck C, Deschepper E, Renson C, Hoebeke P, Plasschaert F, Vande Walle J, Van Laecke E.

J Urol. 2017 May 19. pii: S0022-5347(17)71380-8. doi: 10.1016/j.juro.2017.05.067. [Epub ahead of print]

PURPOSE: To identify risk factors for daytime or combined urinary incontinence (UI) in children with cerebral palsy (CP). MATERIALS AND METHODS: A cross-sectional case-control study was conducted including children with CP with or without UI from the CP-Reference Centre at *** (blinded for review) and two associated special education schools. Factors were subdivided in three clusters, namely demographic and general medical data, CP classification and bladder and bowel dysfunction. Data was obtained using uroflowmetry with EMG testing, a non-validated questionnaire and bladder diaries. Univariate and multivariate analysis was performed for variables and clusters respectively. A final associative logistic model including all clusters was developed. RESULTS: The study included 34 incontinent children and 45 continent children. UI was associated with intellectual disability (OR 7.69), swallowing problems (OR 15.11), the use of external aids (OR 27.50) and the use of laxatives (OR 13.31). UI was positively associated with dyskinesia (OR 5.67) or combined spasticity and dystonia (OR 4.78), bilateral involvement (OR 4.25), gross motor function classification system level IV (OR 10.63) and V (OR 34.00) and

severe impairment in manual (OR 24.27) or communication skills (OR 14.38). Lower maximum voided volume (OR 0.97) and oral fluid intake (OR 0.96) influenced UI negatively. Pathological uroflow curves were not significantly associated with incontinence. The final model defined functional impairment, intellectual disability and oral fluid intake as predictive factors for UI. CONCLUSIONS: Risk analysis revealed functional impairment, intellectual disability and fluid intake as important factors influencing continence in a child with CP.

PMID: 28533005

8. Efficacy of photobiomodulation therapy on masseter thickness and oral health-related quality of life in children with spastic cerebral palsy.

Santos MTBR, Nascimento KS, Carazzato S, Barros AO, Mendes FM, Diniz MB.

Lasers Med Sci. 2017 May 23. doi: 10.1007/s10103-017-2236-4. [Epub ahead of print]

The study aimed to evaluate the efficacy of photobiomodulation therapy (PBMT) on bilateral masseter muscle thickness and amplitude of mouth opening in children with spastic cerebral palsy (CP), and the impact on their oral health-related quality of life (OHRQOL). Three groups were included: experimental CP group (EG: n = 26 with oral complaints), positive control CP group (PCG: n = 26 without complaints), and negative control group (NCG: n = 26 without CP). In the EG, the masseter muscles on both sides were irradiated with an infrared low-level Ga-Al-As laser (λ = 808 ± 3 nm, 120 mW) using a 3 J/cm2 energy dose per site, with a 20 s exposure time per site (spot area: 4 mm2; irradiance: 3 W/cm2; energy delivery per point: 2.4 J) six times over six consecutive weeks. Masseter thickness, assessed through ultrasonography, and the amplitude of mouth opening were measured in the EG before and after six applications of PBMT and once in the PCG and NCG. The Parental-Caregiver Perception Questionnaire (P-CPQ) was used to evaluate OHRQOL. ANOVA, chi-square, t tests, and multilevel linear regression were used for statistical analysis. In the EG, the study results revealed average increments of 0.77 (0.08) millimeter in masseter thickness ($P < 0.05$) and 7.39 (0.58) millimeter for mouth opening ($P < 0.05$) and reduction in all P-CPQ domains ($P < 0.001$), except for social well-being. The six applications of PBMT increased masseter thickness and mouth opening amplitude and reduced the impact of spastic CP on OHRQOL.

PMID: 28536904

9. Folie à Deux in Monozygotic Twins with Cerebral Palsy.

Francois D, Bander E, D'Agostino M, Swinburne A, Broderick L, Grody MB, Salajegheh A.

Clin Schizophr Relat Psychoses. 2017 Spring;11(1):61-64. doi: 10.3371/1935-1232-11.1.61.

PMID: 28548577

Prevention and Cure

10. A review of the emerging potential therapy for neurological disorders: human embryonic stem cell therapy.

Shroff G, Dhanda Titus J, Shroff R.

Am J Stem Cells. 2017 Apr 15;6(1):1-12. eCollection 2017.

The first human embryonic stem cell (hESC) line was developed in the late nineties. hESCs are capable of proliferating indefinitely and differentiate into all the three embryonic germ layers. Further, the differentiation of hESC lines into neural precursor cells and neurons, astrocytes and oligodendrocytes showed their potential in treating several incurable neurological disorders such as spinal cord injury (SCI), cerebral palsy (CP), Parkinson's disease (PD). In this review, we will discuss the global scenario of research and therapeutic use of hESCs in the treatment of neurological disorders. Following this, we will

discuss the development of a unique hESC line, how it differs from the other available hESC lines and its use in the treatment of neurological disorders. hESCs were isolated from mixture of neuronal and non-neuronal progenitor cells in their pre progenitor state in a Good Laboratory Practices, Good Tissue Practices and Good Manufacturing Practices compliant laboratory. Blastomere cells have served as a source to derive the hESCs and the xeno-free culture was demonstrated to be more safe and effective in clinical therapeutic application of hESCs. All the patients showed a remarkable improvement in their conditions and no serious adverse events were reported. This study concluded that hESC lines could be scalable and used in the treatment of various neurological disorders such as SCI, CP, and PD.

PMID: 28533935

11. Both antenatal and postnatal inflammation contribute information about the risk of brain damage in extremely preterm newborns.

Yanni D, Korzeniewski S, Allred EN, Fichorova RN, O'Shea TM, Kuban K, Dammann O, Leviton A.

Pediatr Res. 2017 May 26. doi: 10.1038/pr.2017.128. [Epub ahead of print]

BACKGROUNDPreterm newborns exposed to intrauterine inflammation are at increased risk of neurodevelopmental disorders. We hypothesized that adverse outcomes are more strongly associated with a combination of antenatal and postnatal inflammation than with either of them alone. METHODS We defined antenatal inflammation as histologic inflammation in the placenta. We measured the concentrations of seven inflammation-related proteins in blood obtained on postnatal days 1, 7, and 14 from 763 infants born before 28 weeks of gestation. We defined postnatal inflammation as a protein concentration in the highest quartile on at least 2 days. We used logistic regression models to evaluate the contribution of antenatal and postnatal inflammation to the risk of neurodevelopmental disorders.RESULTSThe risk of white matter damage was increased when placental inflammation was followed by sustained elevation of CRP or ICAM-1. We found the same for spastic cerebral palsy when placental inflammation was followed by elevation of TNF-α or IL-8. The presence of both placental inflammation and elevated levels of IL-6, TNF-α, or ICAM-1 was associated with an increased risk for microcephaly.CONCLUSIONCompared to a single hit, two inflammatory hits are associated with stronger risk for abnormal cranial ultrasound, spastic cerebral palsy, and microcephaly at 2 years.Pediatric Research accepted article preview online, 26 May 2017. doi:10.1038/pr.2017.128.

PMID: 28549057

12. Region specific oligodendrocyte transcription factor expression in a model of neonatal hypoxic injury.

Affeldt BM, Obenaus A, Chan J, Pardo AC.

Int J Dev Neurosci. 2017 May 22. pii: S0736-5748(17)30040-0. doi: 10.1016/j.ijdevneu.2017.05.001. [Epub ahead of print]

White matter injury (WMI) of prematurity is associated with a spectrum of neurological disorders ranging from mild cognitive and behavioral deficits to cerebral palsy. Translational studies have implicated impaired oligodendrocyte development after hypoxia as the primary cause of WMI, but the underlying mechanisms remain poorly understood. The goal of this study was to identify alterations in the expression of oligodendrocyte precursor cell transcription factors in a mouse model of transient mild global hypoxia. Postnatal day (P) 7 mouse pups were exposed to hypoxia (7.5% O2) for 60minutes. We compared oligodendrocyte differentiation and subsequent myelin formation between hypoxia and sham animals at P9, P14 and P28 by examining the expression of key transcription factor regulators of oligodendrocyte differentiation (Ascl1, Olig1, Olig2, and Nkx2.2), as well as APC, a mature oligodendrocyte marker, in the major white matter regions including the corpus callosum, external capsule and anterior commissure. We also examined the effect on myelin formation by examining two myelin specific protein constituents, myelin associated glycoprotein (MAG) and myelin basic protein (MBP), in white matter tracts and whole brain lysate respectively. We found that transient hypoxia at P7 altered the expression of Ascl1, Olig1 and Nkx2.2, resulting in delayed myelination in the external capsule. In addition, our study showed that oligodendrocyte progenitor cells specified several days prior to a hypoxic event are more susceptible to maturation arrest than those specified shortly prior to hypoxia. Our results suggest that alterations of Ascl1, Olig1 and Nkx2.2 underlie impaired oligodendrocyte differentiation and deficient myelination in WMI. These transcription factors are potential therapeutic targets for the treatment of WMI in preterm infants.

PMID: 28546087

13. Update on Postnatal Steroids.

Halliday HL.

Neonatology. 2017;111(4):415-422. doi: 10.1159/000458460. Epub 2017 May 25.

Antenatal steroid treatment to enhance fetal lung maturity and surfactant treatment to prevent or treat respiratory distress syndrome have been major advances in perinatal medicine in the past 40 years contributing to improved outcomes for preterm infants. Use of postnatal steroids to prevent or treat chronic lung disease in preterm infants has been less successful and associated with adverse neurodevelopmental outcomes. Although early (in the first week of life) postnatal steroid treatment facilitates earlier extubation and reduces the risk of chronic lung disease, it is associated with adverse effects, such as hyperglycemia, hypertension, gastrointestinal bleeding and perforation, hypertrophic cardiomyopathy, growth failure, and cerebral palsy, and cannot be recommended. Early treatment with hydrocortisone may also improve survival without chronic lung disease, but concerns remain about possible adverse effects such as gastrointestinal perforation and sepsis, particularly in very preterm infants. Early inhaled budesonide also reduces the incidence of chronic lung disease but there are concerns that this may occur at the expense of increased risk of death. More studies of early low-dose steroids with adequate long-term follow-up are needed before they can be recommended for the prevention of chronic lung disease. Late (after the first week of life) postnatal steroids may have a better benefit-to-harm ratio than early steroids. A Cochrane Review shows that late steroid treatment reduces chronic lung disease, the combination of death and chronic lung disease at both 28 days and 36 weeks' corrected age, and the need for later rescue dexamethasone. Adverse effects include hyperglycemia, hypertension, hypertrophic cardiomyopathy, and severe retinopathy of prematurity but without an increase in blindness. Long-term neurodevelopmental effects are not significantly increased by late postnatal steroid treatment. Current recommendations are that postnatal steroid treatment should be reserved for preterm infants who are ventilator-dependent after the first 7-14 days of life and any course should be low dose and of short duration to facilitate endotracheal extubation. Budesonide/surfactant mixtures show some promise as a means of reducing chronic lung disease in preterm infants with severe respiratory distress syndrome, but further larger studies with long-term follow-up are needed before this treatment can be recommended as a routine intervention.

PMID: 28538237

14. White matter injury in the preterm infant: pathology and mechanisms.

Back SA.

Acta Neuropathol. 2017 May 22. doi: 10.1007/s00401-017-1718-6. [Epub ahead of print]

The human preterm brain is particularly susceptible to cerebral white matter injury (WMI) that disrupts the normal progression of developmental myelination. Advances in the care of preterm infants have resulted in a sustained reduction in the severity of WMI that has shifted from more severe focal necrotic lesions to milder diffuse WMI. Nevertheless, WMI remains a global health problem and the most common cause of chronic neurological morbidity from cerebral palsy and diverse neurobehavioral disabilities. Diffuse WMI involves maturation-dependent vulnerability of the oligodendrocyte (OL) lineage with selective degeneration of late oligodendrocyte progenitors (preOLs) triggered by oxidative stress and other insults. The magnitude and distribution of diffuse WMI are related to both the timing of appearance and regional distribution of susceptible preOLs. Diffuse WMI disrupts the normal progression of OL lineage maturation and myelination through aberrant mechanisms of regeneration and repair. PreOL degeneration is accompanied by early robust proliferation of OL progenitors that regenerate and augment the preOL pool available to generate myelinating OLs. However, newly generated preOLs fail to differentiate and initiate myelination along their normal developmental trajectory despite the presence of numerous intact-appearing axons. Disrupted preOL maturation is accompanied by diffuse gliosis and disturbances in the composition of the extracellular matrix and is mediated in part by inhibitory factors derived from reactive astrocytes. Signaling pathways implicated in disrupted myelination include those mediated by Notch, WNT-beta catenin, and hyaluronan. Hence, there exists a potentially broad but still poorly defined developmental window for interventions to promote white matter repair and myelination and potentially reverses the widespread disturbances in cerebral gray matter growth that accompanies WMI.

PMID: 28534077