**Interventions and Management**

1. **Effects of live and video form action observation training on upper limb function in children with hemiparetic cerebral palsy.**

Kim DH, An DH, Yoo WG.


PURPOSE: The purpose of this study was to investigate the effects of live and video form action observation training (AOT) on upper limb (UL) movement acceleration and function in children with cerebral palsy (CP). METHODS: In total, 12 children (7 boys, 5 girls) with CP participated in this study. The children were allocated randomly to live (experimental) and video (control) AOT groups. All children completed 20 treatment sessions, each 30 minutes in duration, 5 days per week for a month. Mediolateral (ML) and vertical (VT) acceleration data, Jebsen-Taylor Hand Function (JTHF) scores, and Box and Block Test (BBT) scores were obtained at baseline and at 4 weeks after the intervention. RESULTS: ML and VT movement acceleration and JTHF scores were significantly lower in the live group (p< 0.05). The BBT score was significantly higher in the live than in the video group (p< 0.05). CONCLUSIONS: Our findings suggest that live AOT is more effective than video AOT for improving UL movement acceleration and function. Clinically, our findings offer important insights for clinicians when planning AOT interventions to reduce UL movement acceleration and improve UL function.

PMID: 29710760

2. **Advantages of virtual reality in the rehabilitation of balance and gait: Systematic review.**

Cano Porras D, Siemonsma P, Inzelberg R, Zeilig G, Plotnik M.


BACKGROUND: Virtual reality (VR) has emerged as a therapeutic tool facilitating motor learning for balance and gait rehabilitation. The evidence, however, has not yet resulted in standardized guidelines. The aim of this study was to systematically review the application of VR-based rehabilitation of balance and gait in 6 neurologic cohorts, describing methodologic quality, intervention programs, and reported efficacy. METHODS: This study follows the Preferred Reporting Items for Systematic Reviews and Meta-Analyses. VR-based treatments of Parkinson disease, multiple sclerosis, acute and chronic poststroke, traumatic brain injury, and cerebral palsy were researched in PubMed and Scopus, including earliest available records. Therapeutic validity (CONTENT scale) and risk of bias in randomized controlled trials (RCT) (Cochrane Collaboration tool) and non-RCT (Newcastle-Ottawa scale) were assessed. RESULTS: Ninety-seven articles were included, 68 published in 2013 or later. VR improved balance and gait in all cohorts, especially when combined with conventional rehabilitation. Most studies presented poor methodologic quality, lacked a clear rationale for intervention programs, and did not utilize motor learning principles meticulously. RCTs with more robust methodologic designs were widely recommended. CONCLUSION: Our results suggest that VR-based rehabilitation is developing rapidly, has the potential to improve balance and gait in neurologic patients, and brings additional benefits when combined with conventional rehabilitation. This
systematic review provides detailed information for developing theory-driven protocols that may assist overcoming the observed lack of argued choices for intervention programs and motor learning implementation and serves as a reference for the design and planning of personalized VR-based treatments.

PMID: 29720544

3. Immersive Virtual Reality to Improve Walking Abilities in Cerebral Palsy: A Pilot Study.

Gagliardi C, Turconi AC, Biffi E, Maghini C, Marelli A, Cesareo A, Diella E, Panzeri D.


Immersive virtual reality (IVR) offers new possibilities to perform treatments in an ecological and interactive environment with multimodal online feedbacks. Sixteen school-aged children (mean age 11 ± 2.4 years) with Bilateral CP-diplegia, attending mainstream schools were recruited for a pilot study in a pre-post treatment experimental design. The intervention was focused on walking competences and endurance and performed by the Gait Real-time Analysis Interactive Lab (GRAIL), an innovative treadmill platform based on IVR. The participants underwent eighteen therapy sessions in 4 weeks. Functional evaluations, instrumental measures including GAIT analysis and parental questionnaire were utilized to assess the treatment effects. Walking pattern (stride length left and right side, respectively p = 0.001 and 0.003; walking speed p = 0.001), endurance (6MWT, p = 0.026), gross motor abilities (GMFM-88, p = 0.041) and most kinematic and kinetic parameters significantly improved after the intervention. The changes were mainly predicted by age and cognitive abilities. The effect could have been due to the possibility of IVR to foster integration of motor/perceptual competences beyond the training of the walking ability, giving a chance of improvement also to older and already treated children.

PMID: 29704186


Lucena-Antón D, Rosety-Rodríguez I, Moral-Munoz JA.


OBJECTIVE: The aim of the present study is to evaluate the effect of a 12 weeks hippotherapy intervention protocol on hip adductors spasticity in children with spastic cerebral palsy. DESIGN: Randomized controlled trial. SETTINGS/LOCATION: The intervention was conducted in an Equestrian and Therapeutic Association. Patients were recruited from a Rehabilitation Unit of Cerebral Palsy. SUBJECTS: A total of 44 children with spastic cerebral palsy (Gross Motor Function Classification System [GMFCS] levels IV-V; 28 boys and 16 girls; aged 8 years 10 months, SD 3 months) were assigned to a treatment (n = 22; mean age 9 years 6 months, SD 3 months) or a control group (n = 22; mean age 8 years 3 months, SD 3 months). INTERVENTIONS: The control group received conventional therapy, and the treatment group received hippotherapy in addition to their conventional treatment. The intervention consisted of a 12-weeks hippotherapy program (1 time/week, 45 min). OUTCOME MEASURES: Both groups were assessed before and after the full program with the Modified Ashworth Scale (MAS). RESULTS: There were significant differences in the MAS scores between the treatment and the control group in both adductors (left adductors: p = 0.040; right adductors: p = 0.047), after a 12-weeks hippotherapy intervention. CONCLUSIONS: A hippotherapy based treatment in addition to conventional therapy, in children with cerebral palsy, produces statistically significant changes in hip adductors spasticity after a 12-weeks intervention. Thus, it seems to produce benefits in the short-term.

PMID: 29705454

5. Micro-vascularisation is not a limiting factor for exercise in adults with Cerebral Palsy.

Andersen IT, Harrison A, Broholm R, Harder A, Nielsen JB, Bülow J, Pingel J.


OBJECTIVES: Muscle contractures are a common complication in patients with central nervous system (CNS) lesions which limit range of movement and cause joint deformities. Furthermore, it has previously been shown that muscles with contractures have a reduced number of capillaries, indicating decreased tissue vascularization. The aim of the present study was to investigate the microvascular volume (MV) at rest and after acute exercise in the muscle tissue of individuals with Cerebral...
Palsy (CP) and healthy control individuals. METHODS: Contrast enhanced ultrasound (CEUS) was used before and after 30 min of walking or running on a treadmill in 10 healthy control participants and 10 individuals with CP in order to detect MV of their skeletal muscle tissue. RESULTS: A significant increase in the MV was observed after exercise both in the adult CP group (21-53 years) and in the control group (21-52 years) (1.8 [plus minus] 0.8 dB to 3.1 [plus minus] 0.9 dB or 42.9% and 1.5 [plus minus] 0.6 dB to 2.5 [plus minus] 0.9 dB or 39.0%, respectively). Furthermore, a difference in the resting MV was observed between the most severe cases of CP (Gross motor function classification scale - GMFCS 3+4) (2.3 [plus minus] 0.5 dB) and the less severe cases (GMFCS 1+2) (1.5 [plus minus] 0.2 dB). When the CP group was walking (3.4 km/h), the lactate levels, Borg score, and heart rate matched the level of controls when they were running (9.8 km/h). CONCLUSION: Individuals with CP become exhausted at much lower exercise intensities than healthy individuals. This is not explained by impaired micro-vascularisation, since the MV of the individuals with CP respond normally to increased O2 demand during acute exercise.

PMID: 29722625

6. Natural history of scoliosis in cerebral palsy and risk factors for progression of scoliosis.

Yoshida K, Kajiura I, Suzuki T, Kawabata H.


BACKGROUND: Scoliosis in cerebral palsy (CP) often occurs and causes a disturbance in daily life. The purpose of this study was to investigate the natural history of scoliosis in cerebral palsy and determine risk factors for the progression of scoliosis using multivariate analyses. METHODS: We revised 113 patients with CP (47 males and 66 females) who had scoliosis with a curve of at least 10° were reviewed and retrospectively investigated these cases of scoliosis and analyzed the risk factors for the progression of this condition. RESULTS: The mean follow-up period was 16.5 years and the mean age at onset of scoliosis was 6.6 years (range: 1-16 years). In 59 patients (52%), the age at onset of scoliosis was under 6 years. On the final radiographs, the mean Cobb angle was 53.1° (range: 10° to 169°). After the age of 20 years, 13 of 40 patients (32.5%) had a progression of over 10° in scoliosis. Multivariate analyses showed the risk factors for the progression of scoliosis to be hip displacement (p = 0.0038), the onset of scoliosis before the age of 6 years (p = 0.0024), and 30° of the Cobb angle before the age of 10 years (p < 0.001). A subtype of CP (spastic quadriplegia) was identified as a potential risk factor. CONCLUSIONS: After the age of 20 years, 32.5% patients had a progression of over 10° in scoliosis. Risk factors for the progression of scoliosis in CP included hip displacement, early-onset scoliosis, and Cobb angle of 30° before the age of 10 years.

PMID: 29705176


Kulkarni VA, Davids JR, Boyles AD, Cung NQ, Bagley A.


PURPOSE: Hip surveillance programmes for children with cerebral palsy (CP) utilize the migration percentage (MP) measurement to initiate referrals and recommend treatment. This study assesses the reliability and efficiency of three methods of MP measurement on anteroposterior (AP) pelvis radiographs. METHODS: A total of 20 AP pelvis radiographs (40 hips) of children with CP were measured by three raters on two occasions using three methods: digital measurement (DM) on a Picture Archiving and Communication System monitor, computer-aided measurement (CA) using a digital templating tool and mobile device application measurement (MA) using a freely available MP measurement tool. For each method, the time required to complete the MP measurement of both hips on each AP pelvis radiograph was measured. Intra-class correlation coefficient (ICC) was used to determine reliability, and analysis of variance was used to compare groups. RESULTS: All three methods of determining MP showed excellent inter-rater and intra-rater reliability (ICC 0.976 to 0.989). The mean absolute difference in MP measurement was not significant between trials for a single rater (DM 2.8%, CA 1.9%, MA 2.2%) or between raters (DM 3.6%, CA 2.9%, MA 3.6%). The mean time to complete MP measurement was significantly different between methods, with DM = 151 seconds, CA = 73 seconds and MA = 80 seconds. CONCLUSION: All three MP measurement methods were highly reliable with clinically acceptable measurement error. The time required to measure a hip surveillance radiograph can be reduced by approximately 50% by utilizing a computer-based or mobile application-based MP measurement tool.

PMID: 29707053

Georgiadis AG, Dutt V, Truong WH, Novotny SA, Novacheck TF.


All patients with hypertonic cerebral palsy undergoing Bernese periacetabular osteotomy (PAO) between 2005 and 2014 were reviewed. Clinical and radiographic parameters, including the cerebral palsy hip classification and anterior and posterior wall indices were collected to assess acetabular reorientation. Twenty (83%) of 24 procedures involved the correction of posterolateral acetabular insufficiency and were 'anteverting PAOs'. All 20 experienced improvements in radiographic indices. Eleven (58%) of 19 PAOs in ambulatory patients were performed in the setting of other multilevel orthopedic surgery. The anteverting PAO is successful in correcting the posterolateral acetabular insufficiency present in spastic hip dysplasia, and can be performed in conjunction with a single-event multilevel surgery.

PMID: 29708908


Sung KH, Kwon SS, Chung CY, Lee KM, Kim J, Lee SY, Park MS.


BACKGROUND: Concurrent prophylactic femoral varization osteotomy (FVO) for stable hips has been performed in patients with cerebral palsy (CP) undergoing hip reconstructive surgery for the contralateral displaced hip. However, there is currently a lack of studies investigating the outcome after the prophylactic FVO in stable hip. This study investigated the outcomes after FVO in stable hips with CP and influencing factors. In addition, this study compared the outcomes with those after hip reconstructive surgery in the contralateral displaced hip. METHODS: This study included 119 CP patients with 224 hips (80 stable, 144 displaced) undergoing hip reconstructive surgery including FVO. Migration percentage (MP), neck-shaft angle (NSA), and head-shaft angle (HSA) were measured through preoperative and follow-up hip radiographs. All hips were divided into the stable (MP ≤ 33%) and displaced hip groups (MP > 33%) according to the preoperative radiographs, and the annual changes in the radiographic indices after FVO were analyzed. RESULTS: In stable hip group, MP did not significantly increase over time (p = 0.057) after prophylactic FVO. In displaced hip group, MP significantly increased over time (1.6%/year, p < 0.001). MP was significantly decreased in cases of concomitant Dega pelvic osteotomy in both stable (14.5%, p < 0.001) and displaced hips (18.9%, p < 0.001). CONCLUSIONS: Prophylactic FVO in the stable hip in patients with CP showed good surgical outcomes, without a risk of hip displacement throughout the follow-up duration, while hip reconstructive surgery in the displaced hip was associated with a risk of increased hip displacement.

PMID: 29703255


Brandenburg JE, Gransee HM, Fogarty MJ, Sieck GC.

J Neurophysiol. 2018 May 2. doi: 10.1152/jn.00186.2018. [Epub ahead of print]

Motor neuron (MN) development in early onset spasticity is poorly understood. For example, spastic cerebral palsy (sCP), the most common motor disability of childhood, is poorly predicted by brain imaging, yet research remains focused on the brain. By contrast, MNs, via the motor unit and neurotransmitter signaling, are the target of most therapeutic spasticity treatments and are the final common output of motor control. MN development in sCP is a critical knowledge gap as the late embryonic and postnatal periods are not only when the supposed brain injury occurs, but are critical times for spinal cord neuromotor development. Using an animal model of early onset spasticity (spa mouse [B6.Cg-Glrbspa/J] with a glycine (Gly) receptor mutation), we hypothesize that removal of effective glycinergic neurotransmitter inputs to MNs during development will influence MN pruning (including primary dendrites) and MN size. Spa (Glrb-/-) and wild-type (Glrb+/+) mice, ages 4-9 weeks, underwent unilateral retrograde labeling of the tibialis anterior muscle MNs via peroneal nerve dip in tetramethylrhodamine. After three days, mice were euthanized, perfused with 4% paraformaldehyde, and the spinal cord excised and processed for confocal imaging. Spa mice had ~61% fewer lumbar tibialis anterior MNs (P<0.01), disproportionately affecting larger MNs. Additionally, a ~23% reduction in tibialis anterior MN somal surface area (P<0.01) and a 12% increase in primary dendrites (P=0.046) were observed. Thus, MN pruning and MN somal surface area is abnormal in early onset spasticity. Fewer and smaller MNs may contribute to the spastic phenotype.

PMID: 29718808

Lintanf M, Bourseul JS, Houx L, Lempereur M, Brochard S, Pons C.


OBJECTIVE: To determine the effects of ankle-foot orthoses (AFOs) on gait, balance, gross motor function and activities of daily living in children with cerebral palsy. DATA SOURCES: Five databases were searched (PubMed, PsycINFO, Web of Science, Academic Search Premier and Cochrane Library) before January 2018. REVIEW METHODS: Studies of the effect of AFOs on gait, balance, gross motor function and activities of daily living in children with cerebral palsy were included. Articles with a modified PEDRO score ≥ 5/9 were selected. Data regarding population, AFO, interventions and outcomes were extracted. When possible, standardized mean differences (SMDs) were calculated from the outcomes. RESULTS: Thirty-two articles, corresponding to 56 studies (884 children) were included. Fifty-one studies included children with spastic cerebral palsy. AFOs increased stride length (SMD = 0.88, P < 0.001) and gait speed (SMD = 0.28, P < 0.001), and decreased cadence (SMD = -0.72, P < 0.001). Gross motor function scores improved (Gross Motor Function Measure (GMFM) D (SMD = 0.30, P = 0.004), E (SMD = 0.28, P = 0.02), Pediatric Evaluation of Disability Inventory (PEDI) (SMD = 0.57, P < 0.001)). Data relating to balance and activities of daily living were insufficient to conclude. Posterior AFOs (solid, hinged, supra-malleolar, dynamic) increased ankle dorsiflexion at initial contact (SMD = 1.65, P < 0.001) and during swing (SMD = 1.34, P < 0.001), and decreased ankle power generation in stance (SMD = -0.72, P < 0.001) in children with equinus gait. CONCLUSION: In children with spastic cerebral palsy, there is strong evidence that AFOs induce small improvements in gait speed and moderate evidence that AFOs have a small to moderate effect on gross motor function. In children with equinus gait, there is strong evidence that posterior AFOs induce large changes in distal kinematics.

PMID: 29714066


Størvold GV, Jahnson RB, Evensen KAI, Romild UK, Bratberg GH.


AIM: To examine associations between interventions and child characteristics; and enhanced gross motor progress in children with cerebral palsy (CP). METHODS: Prospective cohort study based on 2048 assessments of 442 children (256 boys, 186 girls) aged 2-12 years registered in the Cerebral Palsy Follow-up Program and the Cerebral Palsy Register of Norway. Gross motor progress estimates were based on repeated measures of reference percentiles for the Gross Motor Function Measure (GMFM-66) in a linear mixed model. Mean follow-up time: 2.9 years. RESULTS: Intensive training was the only intervention factor associated with enhanced gross motor progress (mean 3.3 percentiles, 95% CI: 1.0, 5.5 per period of ≥3 sessions per week and/or participation in an intensive program). Gross motor function was on average 24.2 percentiles (95% CI: 15.2, 33.2) lower in children with intellectual disability compared with others. Except for eating problems (-10.5 percentiles 95% CI: -18.5, -2.4) and ankle contractures by age (-1.9 percentiles 95% CI: -3.6, -0.2) no other factors examined were associated with long-term gross motor progress. CONCLUSIONS: Intensive training was associated with enhanced gross motor progress over an average of 2.9 years in children with CP. Intellectual disability was a strong negative prognostic factor. Preventing ankle contractures appears important for gross motor progress.

PMID: 29714626


Peterson MD, Kamdar N, Hurvitz EA.


AIM: To examine the longitudinal trends of cardiometabolic diseases in a large sample of adults with cerebral palsy (CP). METHOD: The Optum Clinformatics Data Mart is a de-identified nationwide claims database of beneficiaries from a single private payer. Beneficiaries were included if they had an International Classification of Diseases, Ninth Revision, Clinical Modification code for a diagnosis of CP. Adults with at least 3 years of continuous enrollment on a single plan between 2002 and 2009 were included in the final analyses (n=2659). We examined the longitudinal trends of incident diabetes mellitus, hypercholesterolemia, hypertension, cardiac dysrhythmias, and atherosclerosis, stratified by age categories: 18 to 39 years, 40 to 59 years, and 60 years and over. Kaplan-Meier product-limit survival curves were compared across age categories for each of the cardiometabolic outcomes, and a Cox proportional hazards regression was run to determine adjusted hazard ratios. RESULTS: The cumulative incidence of each of the cardiometabolic diseases ranged from 6.0% for atherosclerosis to 34.4%
for hypercholesterolemia at 3 years and over. Risk-adjusted Cox proportional hazard models revealed that age was a robust predictor of survival for each outcome, with higher hazard ratio ranges in middle age (hazard ratio 1.41-2.72) and older adults (hazard ratio 2.20-5.93) compared with young adults. INTERPRETATION: Adults with CP have high rates of cardiometabolic diseases; and disease-free survival shortens significantly with higher ages. WHAT THIS PAPER ADDS: Adults with cerebral palsy have high rates of cardiometabolic diseases. Disease-free survival of all cardiometabolic diseases shortens significantly with higher ages. The highest rates were for hypercholesterolemia and hypertension.

PMID: 29704244


Fortuna RJ, Holub A, Turk MA, Meccarello J, Davidson PW.

Fam Pract. 2018 Apr 27. doi: 10.1093/fampra/cmy027. [Epub ahead of print]

AIM: Health conditions in children with cerebral palsy (CP) are well described, yet health is less defined with advancing age. We examined health conditions, functional status and health care utilization in adults with CP across age groups. METHODS: We collected cross-sectional data on health conditions, functional status and utilization from the medical records of adults with CP across a large university-affiliated primary care network using the Rochester Health Status Survey IV (RHSS-IV), a 58-item validated survey. Data from the National Health and Nutrition Examination Survey and National Health Interview Survey provided prevalence estimates for the general population as comparison. RESULTS: Compared to the general population, adults with CP had higher rates of seizure disorder, obesity and asthma across all ages. Adults with CP under 30 years of age had higher rates of hypertension (16.7 versus 5.6%; P = 0.04), urinary incontinence (41.7 versus 10.5%; P < 0.001) and depression (16.7 versus 6.9%; P = 0.07). Conversely, there were lower rates of alcohol misuse, tobacco/nicotine and sexually transmitted illnesses. Independence with all activities of daily living decreased from 37.5% at 18-29 years of age to 22.5% in those 60 and over. Seizure disorders, urinary incontinence and gastroesophageal reflux disease were all independently associated with lower functional status. As expected, health care utilization increased with advancing age. CONCLUSIONS: Adults with CP should be monitored for conditions occurring at higher prevalence in CP, as well as common conditions occurring with advancing age. Age-related functional decline should be anticipated, especially with coexisting seizure disorders and urinary incontinence.

PMID: 29718268

15. Patient-reported mobility function and engagement in young adults with cerebral palsy: a cross-sectional sample.

Lennon N, Church C, Miller F.


PURPOSE: To describe self-reported life satisfaction and motor function of young adults with cerebral palsy (CP). METHODS: A total of 57 young adults with spastic CP classified as levels I (seven), II (25), III (16), IV (nine) by the Gross Motor Function Classification System, followed from childhood by our CP clinic, returned at a mean age of 27 years two months (SD 3 years 4 months). Self-reported life satisfaction and mobility status were measured by the Pediatric Outcomes Data Collection Instrument (PODCI), Patient-Reported Outcomes Measurement Information System (PROMIS), Functional Mobility Scale (FMS) and a project questionnaire. Surgical history and childhood mobility were confirmed from medical records. RESULTS: The Functional Mobility Scale demonstrated limited but stable mobility function from childhood to adulthood. The PROMIS and PODCI revealed limited motor function compared with a non-disabled normative reference (p < 0.05). Descriptive results showed high dependence on transportation, housing and income; although PROMIS subscales revealed satisfaction with social activities. Self-recall of childhood mobility function using the FMS correlated highly (r = 0.8; p < 0.0001) with historical records. CONCLUSION: Although functional mobility is limited and community independence is not fully achieved in young adults with CP, these participants maintained childhood levels of mobility function into young adulthood, were satisfied with social roles and had minimal reports of pain.

PMID: 29707060
16. Cryptorchidism in Boys With Cerebral Palsy Is Associated With the Severity of Disease and With Co-Occurrence of Other Congenital Anomalies.

Barthold JS, Wintner A, Hagerty JA, Rogers KJ, Hossain MJ.


BACKGROUND: Cryptorchidism is reported in 40-50% of small case series of cerebral palsy (CP) and attributed to hypothalamic-pituitary-gonadal axis abnormalities, intellectual disability (ID), or cremaster spasticity. We collected demographic and clinical data to define the frequency of cryptorchidism and clinical comorbidities in a large CP population.

METHODS: Electronic health record data were collected for all male patients ≥7 years of age seen in a large, multidisciplinary CP clinic between 2000 and 2016. Variables including age, testicular position, surgical findings, CP severity, birth history, and comorbidities were tested for association using univariable and stepwise backward logistic regression analyses. RESULTS: Of 839 established patients, testis position was scrotal in 553, undescended in 185 (24%), retractile in 38 (5%), and undocument in 63 cases. Cryptorchidism were diagnosed at a mean age of 5.8 years, with 20% documented as acquired, and testes were most commonly in the superficial inguinal pouch (41%) and associated with an inguinal hernia (56%). Severity was bilateral in 114/166 (69%) undescended and 24/36 (66%) retractile cases, respectively. Mean birth weight and the frequency of prematurity (55, 58, and 54%) and multiple birth (14, 13, and 9%) were not significantly different among the three groups. We observed a strong ordinal trend in the frequency of comorbidities, including quadriplegia, syndromic features/known genetic disease, intrauterine growth restriction (IUGR), death, brain malformations, seizures, gastrostomy, absent continence, ID and hearing, speech or visual impairment, with the retractile group holding the intermediate position for the majority. The stepwise multivariable analysis showed independent positive associations of cryptorchidism with quadriplegia, syndromic features/known genetic disease, hearing loss, and absent continence, and inverse associations with gestational age and multiple birth.

CONCLUSION: These data suggest that cryptorchidism is less common than previously reported in CP cases, but most strongly associated with quadriplegia. Delayed diagnosis may be related to an acquired condition or to the multiple additional functional deficits that occur in this population. Our data suggest that UDT and CP may both be components of malformation syndromes occurring in singleton births whose clinical features are more likely to include earlier delivery, IUGR, hearing loss, and/or global spasticity.

PMID: 29713311


Sigurdardottir S.


[This commentary is on the original article by Reid et al.]

PMID: 29707768

18. Opinions and observations of caregivers of children with cerebral palsy about changes seen after reflexology: A qualitative study.

Özkan F, Zincir H.


The aim of this research was to examine the effect of reflexology on the problems of children with cerebral palsy from perspective of caregivers. Qualitative study was made after 24-session reflexology program. 12 caregivers who have 2-18 year-old children with spastic type cerebral palsy receiving special education and received reflexology. The thematic questions were determined and in-depth interviews were conducted. Themes of the study were determined as; the caregiver's views on reflexology, the effect of reflexology on health of children with CP and the caregivers' observations on child after reflexology therapy, positive and negative aspects and causes of reflexology treatment. As a results; the caregivers expressed that there were increases in self-confidence of children, improvement in walking, reduced spasticity, relaxation, decreases in constipation, and increases in communication, speech and perception after reflexology.

PMID: 29705462


Cerebral palsy (CP) is the leading cause of motor impairment for children worldwide and results from perinatal brain injury (PBI). To test novel therapeutics to mitigate deficits from PBI, we developed a rat model of extreme preterm birth (<28 weeks of gestation) that mimics dual intrauterine injury from placental underperfusion and chorioamnionitis. We hypothesized that a sustained postnatal treatment regimen that combines the endogenous neuroreparative agents erythropoietin (EPO) and melatonin (MLT) would mitigate molecular, sensorimotor, and cognitive abnormalities in adult rats following prenatal injury. On embryonic day 18 (E18), a laparotomy was performed in pregnant Sprague-Dawley rats. Uterine artery occlusion was performed for 60 min to induce placental insufficiency via transient systemic hypoxia-ischemia, followed by intra-amniotic injections of lipopolysaccharide, and laparotomy closure. On postnatal day 1 (P1), approximately equivalent to 30 weeks of gestation, injured rats were randomized to an extended EPO + MLT treatment regimen, or vehicle (sterile saline) from P1 to P10. Behavioral assays were performed along an extended developmental time course (n = 6-29). Open field testing shows injured rats exhibit hypermobility and disinhibition and that combined neonatal EPO + MLT treatment repairs disinhibition in injured rats, while EPO alone does not. Furthermore, EPO + MLT normalizes hindlimb deficits, including reduced paw area and paw pressure at peak stance, and elevated percent shared stance after prenatal injury. Injured rats had fewer social interactions than shams, and EPO + MLT normalized social drive. Touchscreen operant chamber testing of visual discrimination and reversal shows that EPO + MLT at least partially normalizes these complex cognitive tasks. Together, these data indicate EPO + MLT can potentially repair multiple sensorimotor, cognitive, and behavioral realms following PBI, using highly translatable and sophisticated developmental testing platforms.

PMID: 29706928

20. Fetal Neuroprotection by Magnesium Sulfate: From Translational Research to Clinical Application.

Chollat C, Sentilhes L, Marret S.


Despite improvements in perinatal care, preterm birth still occurs regularly and the associated brain injury and adverse neurological outcomes remain a persistent challenge. Antenatal magnesium sulfate administration is an intervention with demonstrated neuroprotective effects for preterm births before 32 weeks of gestation (WG). Owing to its biological properties, including its action as an N-methyl-d-aspartate receptor blocker and its anti-inflammatory effects, magnesium is a good candidate for neuroprotection. In hypoxia models, including hypoxia-ischemia, inflammation, and excitotoxicity in various species (mice, rats, pigs), magnesium sulfate preconditioning decreased the induced lesions’ sizes and inflammatory cytokine levels, prevented cell death, and improved long-term behavior. In humans, some observational studies have demonstrated reduced risks of cerebral palsy after antenatal magnesium sulfate therapy. Meta-analyses of five randomized controlled trials using magnesium sulfate as a neuroprotectant showed amelioration of cerebral palsy at 2 years. A meta-analysis of individual participant data from these trials showed an equally strong decrease in cerebral palsy and the combined risk of fetal/infant death and cerebral palsy at 2 years. The benefit remained similar regardless of gestational age, cause of prematurity, and total dose received. These data support the use of a minimal dose (e.g., 4 g loading dose ± 1 g/h maintenance dose over 12 h) to avoid potential deleterious effects. Antenatal magnesium sulfate is now recommended by the World Health Organization and many pediatric and obstetrical societies, and it is requisite to maximize its administration among women at risk of preterm delivery before 32 WG.

PMID: 29713307
21. Comprehensive genomic analysis of patients with disorders of cerebral cortical development.


Eur J Hum Genet. 2018 Apr 30. doi: 10.1038/s41431-018-0137-z. [Epub ahead of print]

Malformations of cortical development (MCDs) manifest with structural brain anomalies that lead to neurologic sequelae, including epilepsy, cerebral palsy, developmental delay, and intellectual disability. To investigate the underlying genetic architecture of patients with disorders of cerebral cortical development, a cohort of 54 patients demonstrating neuroradiologic signs of MCDs was investigated. Individual genomes were interrogated for single-nucleotide variants (SNV) and copy number variants (CNV) with whole-exome sequencing and chromosomal microarray studies. Variation affecting known MCDs-associated genes was found in 16/54 cases, including 11 patients with SNV, 2 patients with CNV, and 3 patients with both CNV and SNV, at distinct loci. Diagnostic pathogenic SNV and potentially damaging variants of unknown significance (VUS) were identified in two groups of seven individuals each. We demonstrated that de novo variants are important among patients with MCDs as they were identified in 10/16 individuals with a molecular diagnosis. Three patients showed changes in known MCDs genes and a clinical phenotype beyond the usual characteristics observed, i.e., phenotypic expansion, for a particular known disease gene clinical entity. We also discovered 2 likely candidate genes, CDH4, and ASTN1, with human and animal studies supporting their roles in brain development, and 5 potential candidate genes. Our findings emphasize genetic heterogeneity of MCDs disorders and postulate potential novel candidate genes involved in cerebral cortical development.

PMID: 29706646