Mailleux L, Feys H.

PMID: 30888051

2. Parent’s perception of constraint induced movement therapy in cerebral palsy management in rehabilitation centers of Lahore.
Manzoor N, Kashif M, Haroon B, Dastgir A, Iram H.


OBJECTIVE: To assess the perceptions of parents about constraint-induced movement therapy to treat their children with cerebral palsy. METHODS: The qualitative study was conducted in three rehabilitation centres situated in Lahore, Pakistan, from January to July 2014, and comprised parents with enough experience of constraint-induced movement therapy. Therapy session was given to children with hemiplegic spastic cerebral palsy for 4-5 hours per day for at least a month. The interview was recorded and then transcribed verbatim. RESULTS: There were 5 sets of parents whose children were aged 4-12 years. Five main themes emerged from the interviews and they were: child behaviour towards the therapy is variable; increase in cognitive level of the child; group therapy is more beneficial than individual therapy; after therapy the children developed a habit to use the affected hand in their activities; and other than change in the physical condition, parents also observed change in the social behaviour. CONCLUSIONS: Constraint-induced movement therapy seemed to offer a promising opportunity to tackle and promote both social and physical outcomes in cerebral palsy children.

PMID: 30890830

Sidiropoulos AN, Chen S, Kaminski TRM, Gordon AM.


Motor function difficulties associated with unilateral spastic cerebral palsy (USCP) impact gait inter-limb coordination.
between the upper and lower extremities. Two motor learning based, upper extremity treatments, Constraint Induced Movement Therapy (CIMT) and Hand Arm Bimanual Therapy (HABIT), have resulted in improvements in coordination and function between the arms in children with USCP. However, no study has investigated whether coordination between the upper and lower extremities improves after either intervention during a functional task, such as walking. Gait analysis was performed before and after participation in intensive (3 weeks, 90 h total) CIMT and HABIT interventions to determine if intensive upper extremity treatment can improve inter-limb coordination between the upper and lower extremities of children (n = 20, 6-17 years old) with USCP. While upper extremity clinical evaluations indicated hand function improvements, there were no changes in lower extremity parameters for either treatment. However, we found that 10 out of 11 children with a 2:1 arm swing-to-stride ratio at pre-test improved to a 1:1 ratio at post-test. Temporal synchronicity of contralateral limbs, swing displacement of the more affected arm, and arm swing side symmetry unexpectedly decreased. Positive changes in coordination were observed in children who demonstrated poor coordination during walking at pre-test, yet the changes were not robust. Principle component analysis did not indicate changes in limb coupling. While more coordinated, gross-motor training of the upper and lower extremity may reveal greater changes, lower extremity gait patterns were not improved in high functioning children with USCP.

PMID: 30888460

Sala DA, Grissom HE, Delsole EM, Chu ML, Godfried DH, Bhattacharyya S, Karamitopoulos MS, Chu A.

AIM: To assess the accuracy of consumer available wrist-based and hip-based activity trackers in quantitatively measuring ambulation in children with cerebral palsy (CP). METHOD: Thirty-nine children (23 males, 16 females; mean age [SD] 9y 7mo [3y 5mo]; range 4-15y) with CP were fitted with trackers both on their wrist and hip. Each participant stood for 3 minutes, ambulated in a hallway, and sat for 3 minutes. The number of steps and distance were recorded on trackers and compared to manually counted steps and distance. Pearson correlation coefficients were determined for the number of steps during ambulation from each tracker and a manual count. Mean absolute error (MAE) and range of errors were calculated for steps during ambulation for each tracker and a manual count and for distance for each tracker and hallway distance. RESULTS: For the number of steps, a weak inverse relationship ($r=-0.033$) was found for the wrist-based tracker and a strong positive relationship ($r=0.991$) for the hip-based tracker. The MAE was 88 steps for the wrist-based and seven steps for the hip-based tracker. INTERPRETATION: Only the hip-based tracker provided an accurate step count; neither tracker was accurate for distance. Thus, ambulation of children with CP can be accurately quantified with readily available trackers.

PMID: 30883727

5. Muscle fibre morphology and microarchitecture in cerebral palsy patients obtained by 3D synchrotron X-ray computed tomography.
Borg L, Sporring J, Dam EB, Dahl VA, Dyrby TB, Feidenhans'l R, Dahl AB, Pingel J.

BACKGROUND: Synchrotron X-ray computed tomography (SXCT) allows for three-dimensional imaging of objects at a very high resolution and in large field-of-view. PURPOSE: The aim of this study was to use SXCT imaging for morphological analysis of muscle tissue, in order to investigate whether the analysis reveals complementary information to two-dimensional microscopy. METHODS: Three-dimensional SXCT images of muscle biopsies were taken from participants with cerebral palsy and from healthy controls. We designed morphological measures from the two-dimensional slices and three-dimensional volumes of the images and measured the muscle fibre organization, which we term orientation consistency. RESULTS: The muscle fibre cross-sectional areas were significantly larger in healthy participants than in participants with cerebral palsy when carrying out the analysis in three dimensions. However, a similar analysis carried out in two dimensions revealed no patient group difference. The present study also showed that three-dimensional orientation consistency was significantly larger for healthy participants than for participants with cerebral palsy. CONCLUSION: Individuals with CP have smaller muscle fibres than healthy control individuals. We argue that morphometric measures of muscle fibres in two dimensions are generally trustworthy only if the fibres extend perpendicularly to the slice plane, and otherwise three-dimensional aspects should be considered. In addition, the muscle tissue of individuals with CP showed a decreased level of orientation consistency when compared to healthy control tissue. We suggest that the observed disorganization of the tissue may be induced by atrophy caused by physical inactivity and insufficient neural activation.

PMID: 30878888
6. Distal Rectus Femoris Tendon Transfer for the Correction of Stiff-Knee Gait in Cerebral Palsy.

INTRODUCTION: Distal rectus femoris tendon transfer is the standard surgical procedure for the treatment of stiff-knee gait in patients with cerebral palsy and is commonly performed during single-event multilevel surgery. STEP 1 POSITIONING AND APPROACH: With the patient supine, make a 3 to 4-cm longitudinal incision 2 to 3 cm above the patellar proximal pole. STEP 2 PREPARATION OF THE RECTUS FEMORIS TENDON: Separate the rectus femoris tendon from the vasti; avoid releasing the entire quadriceps at all cost. STEP 3 PREPARATION OF THE GRACILIS OR SEMITENDINOSUS TENDON FOR TRANSFER: Isolate the gracilis tendon proximally, release it from its muscle belly, and pull it out distally through a small incision at the pes anserinus insertion. STEP 4 TRANSFERRING THE GRACILIS TENDON TO THE RECTUS FEMORIS TENDON: Insert a long tendon passer above the fascia and beneath the sartorius muscle belly from anterior to posterior to the mini-incision in the pes anserinus region to grasp and transfer the gracilis tendon to the anterior approach. STEP 5 TENDON TENSIONING AND SUTURING: Weave the gracilis tendon into the released rectus femoris tendon with the interlacing technique described by Pulvertaft. RESULTS: Various studies have demonstrated good initial results, with an improvement in peak knee flexion in swing phase and knee motion in swing phase, following distal rectus femoris tendon transfer. WHAT TO WATCH FOR: IndicationsContraindicationsPitfalls & Challenges.

PMID: 30881736

7. Contribution of corticospinal drive to ankle plantar flexor muscle activation during gait in adults with cerebral palsy.
Frisk RF, Lorentzen J, Nielsen JB.

Impaired plantar flexor muscle activation during push-off in late stance contributes importantly to reduced gait ability in adults with cerebral palsy (CP). Here we used low-intensity transcranial magnetic stimulation (TMS) to suppress soleus EMG activity during push-off as an estimate of corticospinal drive in CP adults and neurologically intact (NI) adults. Ten CP adults (age 34 years, SD 14.6, GMFCS I-II) and ten NI adults (age 33 years, SD 9.8) walked on a treadmill at their preferred walking speed. TMS of the leg motor cortex was elicited just prior to push-off during gait at intensities below threshold for motor-evoked potentials. Soleus EMG from steps with and without TMS were averaged and compared. Control experiments were performed while standing and in NI adults during gait at slow speed. TMS induced a suppression at a latency of about 40 ms. This suppression was similar in the two populations when differences in control EMG and gait speed were taken into account (CP 18%, NI 16%). The threshold of the suppression was higher in CP adults. The findings suggest that corticospinal drive to ankle plantar flexors at push-off is comparable in CP and NI adults. The higher threshold of the suppression in CP adults may reflect downregulation of cortical inhibition to facilitate corticospinal drive. Interventions aiming to facilitate excitability in cortical networks may contribute to maintain or even improve efficient gait in CP adults.

PMID: 30900000

8. Gait synergetic neuromuscular control in children with Cerebral Palsy at different Gross Motor Function Classification System levels.
Yu Y, Chen X, Cao S, Wu, Zhang X, Chen X.

Cerebral palsy (CP) is a neural developmental disease featured with gait abnormalities. CP gait assessment is usually performed with the Gross Motor Function Classification System (GMFCS) in clinics, which does not involve a thorough assessment of neuromuscular control. To understand how the neuromuscular control disorders lead to gait abnormalities, we explored the relationship between GMFCS levels and the gait synergetic control characteristics in this study. In total, 18 children with CP at different GMFCS levels (mean age: 4.41 ± 1.30 years ) and 8 age-matched typically developing (TD) children (mean age: 4.43 ± 1.36 years) were recruited to perform a straight walking task, and the surface electromyographic (sEMG) signals from 8 lower limb muscles on each side and accelerometer data were collected. A non-negative Matrix Factorization method was applied to obtain the muscle synergies from the sEMG signals. Next, synergy structures were projected onto the basic gait synergies to test the completeness of those structures. Subsequently, synergy activations parameters, including total activation duration and co-activation index, were compared across the participants. This study
showed that children with CP at GMFCS levels I and II and the TD children had similar synergy structures, but the synergy activations of these children with CP were different from those of TD children. In addition, similar as previous research, we also found children with CP at GMFCS level III could not access all the four basic synergies on both sides. Based on the synergy analysis results, a gait assessment paradigm was proposed to facilitate the clinical CP gait evaluation.

PMID: 30892974


BACKGROUND: Consensus opinion supports standing frame use as part of postural management for non-ambulant young people with cerebral palsy (CP). Most young people with CP in the UK who use standing frames, use them at nursery or school, rather than at home. In this paper we report professionals' and parents' experiences and views of standing frame use specifically in educational settings. This research was conducted as part of a large mixed methods study to determine the acceptability and inform the design of a future trial of standing frames. METHODS: Qualitative methods were used: focus groups with educational professionals, parents, and clinicians (paediatricians, physiotherapists, and occupational therapists) were convened. Data was analysed thematically using Framework analysis. RESULTS: Five focus groups were conducted. The overarching theme "flexibility" encompassed four subordinate themes: (i) 'balancing education and therapy', which described the way education professionals had to juggle different priorities from health professionals within a multi-disciplinary team; (ii) 'young people's autonomy' which highlighted participants' belief that standing frame use should be centred on the individual young person and their needs; (iii) 'working within logistical boundaries', which demonstrated that "ideal" standing frame use was not always possible due to logistical issues (e.g., staffing, standing frame availability); and (iv) 'competence and confidence' which highlighted that educational professionals felt that they lacked the training to confidently position young people in their standing frame. CONCLUSIONS: This paper highlights the complexity of standing frame use in the educational setting. If a standing frame programme is prescribed to be delivered in an educational setting, strong multi-disciplinary and inter-agency communication is essential to balance therapy versus education. Training is required to ensure staff are competent in using the standing frame with the young person understanding their individual requirements. A flexible approach - inclusive of the young person's needs, logistical demands, and resource - is necessary. This article is protected by copyright. All rights reserved.

PMID: 30883842

10. The efficacy of physical therapy on the improvement of the motor components of visual attention in children with cerebral palsy: a case series study.

Abuin-Porras V, Pedersini P, Berjano P, Villafañe JH.


This paper has attempted to compare the effects of Bobath's concept with control's session on the improvement of visual attention in children with cerebral palsy. A 10 children sample (7 girls and 3 boys) aged 6 to 16 years (median, 12 years) was collected. The group who had received Bobath-based treatment crossed-over to control treatment and the previous control group received Bobath-based treatment for once a week. Measures were assessed at pre- and posttreatment. Outcome measure included the visual attention, we used Conners' Kiddie Continuous Performance Test (K-CPT). Bobath's session targeted to crossed-over participants produced greater improvements in K-CPT(RT) (difference=33.1, P<0.05) at posttreatment compared to the control's session group, whereas the improvement of K-CPT did not differ between groups. The results of this case series study showed a significant improvement on visual attention through the improvement of motor control functions after the Bobath's session over the control's session.

PMID: 30899744


AIM: To investigate whether motor performance in school-age children without cerebral palsy, cooled for neonatal encephalopathy, is associated with perinatal factors and 18-month developmental scores and to explore relationships between school-age motor and cognitive performance. METHODS: Motor and cognitive performance was assessed in 29 previously cooled children at 6–8 years using the Movement Assessment Battery for Children-2 (MABC-2) and the Wechsler Intelligence Scale for Children (WISC-IV). Associations between MABC-2 scores less than/equal (<)=15th centile and perinatal factors, social/family background, 18-month Bayley-III scores and WISC-IV scores were explored. RESULTS: Eleven/29(38%) children had MABC-2 scores <15th centile including 7(24%) <5th centile. No significant perinatal or socio-economic risk factors were identified. Motor scores <85 at 18 months failed to identify children with MABC-2 scores <15th centile. MABC-2 scores <15th centile were associated with lower Full Scale IQ (p=0.045), Working Memory (p=0.03) and Perceptual Reasoning (p=0.005) scores at 6–8 years and receiving greater support in school (p=0.01). CONCLUSION: A third of cooled children without cerebral palsy had MABC-2 scores indicating motor impairment at school-age that was not identified at 18 months by Bayley-III. Most children with low MABC-2 scores needed support at school. Sub-optimal MABC-2 scores indicate need for detailed school-age cognitive evaluation. This article is protected by copyright. All rights reserved.

PMID: 30883895


AIM: To describe current practices of physiotherapists and occupational therapists when training two-wheel bike skills in children with cerebral palsy (CP) within an International Classification of Functioning, Disability and Health (ICF) framework. METHODS: Ninety-five physiotherapists and occupational therapists working with children with CP in Australia completed a customized online survey. Survey questions related to: eligibility, initial assessment, intervention characteristics, and evaluation of effectiveness. Open-ended responses were analyzed using deductive content analysis. Close-ended questions were analyzed using descriptive statistics. The ICF was used as a framework for coding and reporting. RESULTS: Body structure and function factors were most frequently considered in eligibility (56% of observations) and assessment (47%). Activity and participation-related factors were considered more in intervention (42%) and evaluation (75%). While functional training approaches were predominant, intervention characteristics varied markedly. Excepting goal-related tools, few measures were identified for assessment or evaluation of effectiveness. Environmental and personal factors were seldom considered across practice areas. CONCLUSIONS: Current two-wheel bike skills training for children with CP in Australia appears highly variable. Development and testing of bike skills-specific outcome measures and interventions and guidance for therapists on consideration of environmental and personal factors are warranted.

PMID: 30880531


AIM: Brain alterations in very preterm children at risk for developmental coordination disorder were investigated. METHODS: Infants born very preterm with gestation age <30 weeks or birthweight <1,250g were recruited from Royal Women's Hospital Melbourne from 2001 to 2003. Volumetric imaging was performed at term equivalent age; at seven years volumetric imaging and diffusion tensor imaging were performed. At seven years, 53 of 162 children without cerebral palsy had scores ≤16th percentile on the Movement Assessment Battery for Children-Second Edition and were considered at risk for developmental coordination disorder. RESULTS: At term equivalent age, smaller brain volumes were found for total brain tissue, cortical grey matter, cerebellum, caudate accumbens, pallidum and thalamus in children at risk for developmental coordination disorder (p<0.05); similar patterns were present at seven years. There was no evidence for catch-up brain growth in at risk children. At seven years, at risk children displayed altered microstructural organisation in many white matter tracts (p<0.05). CONCLUSION: Infants born very preterm at risk for developmental coordination disorder displayed smaller brain volumes at term equivalent age and seven years, and altered white matter microstructure at seven years, particularly in motor areas. There was no catch-up growth from infancy to seven years. This article is protected by copyright. All rights reserved.

PMID: 30891804
14. Automated pose estimation captures key aspects of General Movements at 8-17 weeks from conventional videos.
Marchi V, Hakala A, Knight A, D’Acunto F, Scattoni ML, Guzzetta A, Vanhatalo S. 

AIM: General movement assessment requires substantial expertise for accurate visual interpretation. Our aim was to evaluate an automated pose estimation method, using conventional video records, to see if it could capture infant movements using objective biomarkers. METHODS: We selected archived videos from 21 infants aged 8-17 weeks who had taken part in studies at the IRCCS Stella Maris Foundation (Italy), from 2011-2017. Of these, 14 presented with typical low-risk movements, while seven presented with atypical movements and were later diagnosed with cerebral palsy. Skeleton videos were produced using a computational pose estimation model adapted for infants and these were blindly assessed to see whether they contained the information needed for classification by human experts. Movements of skeletal key points were analysed using kinematic metrics to provide a biomarker to distinguish between groups. RESULTS: The visual assessments of the skeleton videos were very accurate, with Cohen's K of 0.90 when compared with the classification of conventional videos. Quantitative analysis showed that arm movements were more variable in infants with typical movements. CONCLUSION: It was possible to extract automated estimation of movement patterns from conventional video records and convert them to skeleton footage. This could allow quantitative analysis of existing footage. This article is protected by copyright. All rights reserved.

PMID: 30883894

15. The Impact of Early Neuroimaging and Developmental Assessment in a Preterm Infant Diagnosed with Cerebral Palsy.
Gullion L, Stansell J, Moss H, Jenkins D, Aljuhani T, Coker-Bolt P.

Premature infants are at risk for cerebral palsy (CP) that is typically diagnosed between 18-24 months. We present a case study of an infant who was discharged from the neonatal intensive care unit (NICU) without obvious neurological deficits but was later diagnosed with hemiplegic CP. The infant was enrolled in an infant motor study, which included neuroimaging and developmental motor assessments. At term, anatomical MRI showed bilateral periventricular leukomalacia, abnormal brain metabolites in frontal white matter via MR spectroscopy (MRS), and low fractional anisotropy (FA) values obtained from diffusional kurtosis imaging (DKI) in several cortical white matter tracts compared to a group of typically developing infants without neuroimaging abnormalities. In addition, the infant scored below average on a developmental assessment administered at term and three months as well as on the standard Bayley III assessment at 12 months. Abnormal neuroimaging and low scores on the early developmental assessment prompted referral for intervention services at two months. With intensive therapy, by 45 months, the infant was average in self-care, mobility, and communication skills, although below average in visual motor and gross motor coordination. This case highlights the clinical impact of early detection and referral using combined neuroimaging and developmental testing.

PMID: 30881719

Magee LA, De Silva DA, Sawchuck D, Synnes A, von Dadelszen P.

OBJECTIVE: The objective is to provide guidelines for the use of antenatal magnesium sulphate for fetal neuroprotection of the preterm infant. OPTIONS: Antenatal magnesium sulphate administration should be considered for fetal neuroprotection when women present at ≤33 + 6 weeks with imminent preterm birth, defined as a high likelihood of birth because of active labour with cervical dilatation ≥4 cm, with or without preterm pre-labour rupture of membranes, and/or planned preterm birth for fetal or maternal indications. There are no other known fetal neuroprotective agents. OUTCOMES: The outcomes measured are the incidence of cerebral palsy (CP) and neonatal death. EVIDENCE: Published literature was retrieved through searches of PubMed or Medline, CINAHL, and the Cochrane Library in December 2017, using appropriate controlled vocabulary and key words (magnesium sulphate, cerebral palsy, preterm birth). Results were restricted to systematic reviews, randomized controlled trials, and relevant observational studies. There were no date or language restrictions. Searches were updated on a regular basis and incorporated in the guideline to December 2017. Grey (unpublished) literature was identified through searching the websites of health technology assessment and health technology assessment-related agencies, clinical practice
guideline collections, clinical trial registries, and national and international medical specialty societies. VALUES: The quality of evidence was rated using the criteria described in the Report of the Canadian Task Force on Preventive Health Care (Table 1). BENEFITS, HARMS, AND COSTS: Antenatal magnesium sulphate for fetal neuroprotection reduces the risk of "death or CP" (relative risk [RR] 0.85; 95% confidence interval [CI] 0.74-0.98; 4 trials, 4446 infants), "death or moderate-severe CP" (RR 0.85; 95% CI 0.73-0.99; 3 trials, 4250 infants), "any CP" (RR 0.71; 95% CI 0.55-0.91; 4, trials, 4446 infants), "moderate-to-severe CP" (RR 0.60; 95% CI 0.43-0.84; 3 trials, 4250 infants), and "substantial gross motor dysfunction" (inability to walk without assistance) (RR 0.60; 95% CI 0.43-0.83; 3 trials, 4287 women) at 2 years of age. Results were consistent between trials and across the meta-analyses. There is no anticipated significant increase in health care-related costs because women eligible to receive antenatal magnesium sulphate will be judged to have imminent preterm birth. VALIDATION: Australian National Clinical Practice Guidelines were published in March 2010 by the Antenatal Magnesium Sulphate for Neuroprotection Guideline Development Panel. Antenatal magnesium sulphate was recommended for fetal neuroprotection in the same dosage as recommended in these guidelines. However, magnesium sulphate was recommended only at <30 weeks gestation, based on 2 considerations. First, no single gestational age subgroup was considered to show a clear benefit. Second, in the face of uncertainty, the committee felt it was prudent to limit the impact of their clinical practice guidelines on resource allocation. In March 2010, the American College of Obstetricians and Gynecologists issued a Committee Opinion on magnesium sulphate for fetal neuroprotection. It stated "the available evidence suggests that magnesium sulfate given before anticipated early preterm birth reduces the risk of cerebral palsy in surviving infants." No official opinion was given on a gestational age cut-off, but it was recommended that physicians develop specific guidelines around the issues of inclusion criteria, dosage, concurrent tocolysis, and monitoring in accordance with 1 of the larger trials. Similarly, the World Health Organization also strongly recommends use of magnesium sulphate for fetal neuroprotection in its 2015 recommendations on interventions to improve preterm birth outcomes but cites further researching on dosing regimen and re-treatment. SPONSORS: Canadian Institutes of Health Research (CIHR). SUMMARY STATEMENT: RECOMMENDATIONS.

PMID: 30879485


The purpose of this study was to create growth-percentiles for Caucasian children with cerebral palsy (CP). The studied parameters were height and age. In a retrospective analysis, we converted measurements collected in our center to create disorder-specific percentiles of normative data. Patients were stratified due to sex (male and female) and to mobility levels using the gross motor function classification system (GMFCS) (A = walking; GMFCS I-III, B = non walking; GMFCS IV-V) into four groups. In total, 2363 measurements in patients 0-18 years were collected. The mean age for group "Am" was 6.8 years (n = 862), group "Bm" 7.6 years (n = 563), group "Am" 7.7 years (n = 600), and group "Bm" 8.2 years (n = 366). The created percentiles for all groups were below the reference percentiles for healthy Caucasian children (KiGGS). The median curve for children with GMFCS levels I-III is slightly above the 3rd percentile, whereas the 50th percentile for GMFCS levels IV-V is mostly below the 3rd KiGGS centile. Conclusion: In conclusion, children with cerebral palsy are smaller than healthy children. The difference between 50th percentile of CP patients compared to healthy children supports the need for the use of disorder-specific growth charts. Those charts can help clinicians differentiate growth disorders in patients with CP. What is Known: • Children with cerebral palsy are shorter than healthy children and height is influenced by level of ambulation. • Currently, only reference percentiles of American children with mixed ethnic backgrounds are available to evaluate growth. What is New: • This paper presents disorder-specific reference percentiles for longitudinal growth of Caucasian children with cerebral palsy depending on motor function. • These percentiles allow to assess longitudinal growth in children with cerebral palsy to detect other additional diseases impairing growth.

PMID: 30877384

18. Suboptimal Nutrition and Low Physical Activity Are Observed Together with Reduced Plasma Brain-Derived Neurotrophic Factor (BDNF) Concentration in Children with Severe Cerebral Palsy (CP).


Brain-derived neurotrophic factor (BDNF) is a mediator of exercise and nutrition-induced neural plasticity. In children with cerebral palsy (CP), neuromuscular deficits and mobility impairment have a negative impact on their physical activity level and nutritional status, but whether these children have reduced BDNF concentrations is unknown. Therefore, the aim of the present
study was to investigate the plasma BDNF concentration, nutritional status, and physical activity level in children with mild to severe CP. Blood sampling, dietary registration, and questionnaires were completed for children with mild CP (gross motor function classification system (GMFCS) I-II, n = 31, age 10.6 ± 0.6 years), severe CP (GMFCS IV-V, n = 14, age 10.9 ± 1.1 years) and typically developed (TD) children (n = 22, age 10.9 ± 0.6 years). Children with severe CP had ~40% lower plasma BDNF concentration than TD children (p < 0.05). Furthermore, children with severe CP had lower daily physical activity level than TD children (p < 0.01), and a daily intake of energy, n-3 fatty acids, and dietary fibers that was only ~50% of TD (p > 0.001). Reduced plasma BDNF concentrations were observed in children with severe CP. This may be of significance for optimal neural growth and plasticity. This was observed together with low physical activity levels and a suboptimal intake of energy, n-3 fatty acids, and dietary fibers.

PMID: 30875771

Trivić I, Hojsak I.

The majority of children with cerebral palsy (CP) have feeding difficulties and are especially prone to malnutrition. The early involvement of a multidisciplinary team should aim to prevent malnutrition and provide adequate nutritional support. Thorough nutritional assessment, including body composition, should be a prerequisite for the nutritional intervention. As in typically-developed children nutritional support should start with dietary advice and the modification of oral feeding, if safe and acceptable. However, for prolonged feeding, in the presence of unsafe swallowing and inadequate oral intake, enteral nutrition should be promptly initiated and early gastrostomy placement should be evaluated and discussed with parents/caregivers. Gastrointestinal problems (oropharyngeal dysfunction, gastroesophageal disease, and constipation) in children with CP are frequent and should be actively detected and adequately treated as they can further worsen the feeding process and nutritional status.

PMID: 30899688

20. Reliability and Validity of the Neurogenic Bladder Symptom Score in Adults with Cerebral Palsy.

OBJECTIVES: To examine the utility of the Neurogenic Bladder Symptom Score (NBSS) in adults with cerebral palsy (CP).
METHODS: Patients participated in a structured intake which included bladder management. Patients (or caregivers, if patients unable) completed NBSS and SF-Qualiveen twice over a two-week period. Validity was determined using Cronbach's alpha and correlation testing between NBSS, intake, and SF-Qualiveen. Reliability was determined using test-retest method and intraclass correlation coefficients (ICCs).
RESULTS: 54 patients were included. 36 patients (67%) used a wheelchair. 35 patients (66%) required a caregiver to complete questionnaires. Median NBSS subdomain scores were 12/29 for incontinence, 9/22 for storage/voiding, 2/23 for consequences and 1/4 for quality of life (QOL). Lower scores reflect fewer symptoms. Reliability was high (ICC = 0.90). There was a moderate correlation (R=0.70) between NBSS QOL and SF-Qualiveen. Bladder management method, as determined by the NBSS, was indwelling catheter in 4, intermittent catheterization in 6, voiding into a toilet in 33 and missing in 11. Importantly, there was no option for voiding into a diaper, which was common in this population.
CONCLUSIONS: For adults with CP, the NBSS has high reliability and statistically, it demonstrated appropriate validity, but it has limitations. Its face validity is questionable given that diapers were not an option. The validity of caregiver completion needs further assessment. The NBSS may have a floor effect for detecting urinary consequences or QOL, reflected by consistently low scores in these subdomains. The development of a specific urinary symptom/QOL tool for adults with CP is needed.

PMID: 30890419

McPhee PG, Benner JL, Balemans ACJ, Verschuren O, van den Berg-Emons RJG, Hurvitz EA, Peterson MD, van der Slot WMA, Roebroeck ME, Gorter JW.
BACKGROUND: Estimates of multimorbidity, defined as the presence of at least two chronic conditions, some of which attributable to modifiable behaviours, are high in adults with cerebral palsy (CP). An assessment protocol evaluating multimorbidity risk is needed in order to develop and evaluate effective interventions to optimize lifelong health in individuals with CP. The aim of this protocol paper is to describe the development of a core outcome set (COS) for assessing multimorbidity risk in adolescents and adults with CP, to be used in clinic and research. METHODS: The expert consortium will first define the target population and outcomes to be measured. Through a process of literature review and an international Delphi survey with expert clinicians and researchers, we will then determine which outcome measurement instruments (OMIs) can best measure those outcomes. The resulting OMIs will be used in a feasibility study with adolescents and adults with CP from an international clinical research network. Finally, a face-to-face stakeholder meeting with adolescents and adults with CP, their families/caregivers and researchers and clinicians who are experts in CP, will be organized to reach final agreement on the COS. DISCUSSION: This COS will guide clinicians and researchers in assessing multimorbidity risk in adolescents and adults with CP. The inclusion of experts and individuals with CP from international locations for establishing the COS lends strong support to its generalizability. Evidence of its feasibility and approval from all stakeholders will enable implementation in clinical practice, and guide future research using the COS in individuals with CP.

PMID: 30890152

Bromham N, Dworzynski K, Eunson P, Fairhurst C; Guideline Committee.

PMID: 30890528

23. Mortality risk among adults with cerebral palsy: alarming findings and lingering questions.
Landes SD.

PMID: 30895597


AIM: To describe the nature and extent of the literature addressing the medical and its re/habilitative management of cerebral palsy (CP) in India. METHOD: Online worldwide scholarly databases, research hosting directories, Indian publishing houses, and grey literature were used to identify papers published between 2005 and 2016. We retrieved 144 English language papers that described the medical and rehabilitative management of Indian children with CP. RESULTS: Quantitative, qualitative, and mixed research designs are published by a variety of health care professionals in India. Intervention (45%) and observational studies (30%) predominate. Outcomes were categorized using the World Health Organization's International Classification of Functioning, Disability and Health framework, with body structure and function most reported and activity/participation least reported; 57% described its re/habilitation interventions and 43% were medical interventions. INTERPRETATION: There is a substantial body of CP research in India that focuses on interventions to reduce impairments, with minimal attention given to activities and participation, environmental, and personal factors. Twenty-six per cent of studies are published in what appear to be 'predatory journals'. This paper serves as an alert about the presence of 'predatory journals' in medicine that may introduce publication bias, which can distort results reported in those studies individually, or from conclusions drawn in reviews that contain those studies. WHAT THIS PAPER ADDS: Cerebral palsy research in India focuses on interventions to reduce impairment. Activities, participation, and environmental factors are minimally addressed. Quantitative studies are more common than qualitative studies. Many Indian studies are published in journals that are not indexed in worldwide databases of scholarly journals.

PMID: 30883735
Ziegler L, Schulte R, Gharagabhi A.


BACKGROUND: Motor imagery (MI) engages cortical areas in the human brain similar to motor practice. Corticospinal excitability (CSE) is facilitated during but not after MI practice. We hypothesized that lasting CSE changes could be achieved by associatively pairing this endogenous modulation with exogenous stimulation of the same intracortical circuits. METHODS: We combined MI with a disinhibition protocol (DIS) targeting intracortical circuits by paired-pulse repetitive transcranial magnetic stimulation in one main and three subsequent experiments. The follow-up experiments were applied to increase effects, e.g., by individualizing inter-stimulus intervals, adding neuromuscular stimulation and expanding the intervention period. CSE was captured during (online) and after (offline) the interventions via input-output changes and cortical maps of motor evoked potentials. A total of 35 healthy subjects (mean age 26.1 ± 2.6 years, 20 females) participated in this study.

RESULTS: A short intervention (48 stimuli within ∼90s) increased CSE. This plasticity developed rapidly, was associative (with MIon, but not MIoff or REST) and persisted beyond the intervention period. Follow-up experiments revealed the relevance of individualizing inter-stimulus intervals and of consistent inter-burst periods for online and offline effects, respectively. Expanding this combined MI/DIS intervention to 480 stimuli amplified the sustainability of CSE changes. When concurrent neuromuscular electrical stimulation was applied, the plasticity induction was cancelled. CONCLUSIONS: This novel associative stimulation protocol augmented plasticity induction in the human motor cortex within a remarkably short period of time and in the absence of active movements. The combination of endogenous and exogenous disinhibition of intracortical circuits may provide a therapeutic backdoor when active movements are no longer possible, e.g., for hand paralysis after stroke.

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IMPORTANCE: Neonatal hyperbilirubinemia can cause lifelong neurodevelopmental impairment (kernicterus) even in high-resource settings. A better understanding of the incidence and processes leading to kernicterus may help in the design of preventive measures. OBJECTIVES: To determine incidence rates of hazardous hyperbilirubinemia and kernicterus among near-term to term newborns and to evaluate health care professional adherence to best practices. DESIGN, SETTING, AND PARTICIPANTS: This population-based nationwide cohort study used prospectively collected data on the highest serum bilirubin level for all infants born alive at 35 weeks’ gestation or longer and admitted to neonatal care at all 46 delivery and 37 neonatal units in Sweden from 2008 to 2016. Medical records for newborns with hazardous hyperbilirubinemia were evaluated for best neonatal practices and for a diagnosis of kernicterus up to 2 years of age. Data analyses were performed between September 2017 and February 2018. EXPOSURES: Extreme (serum bilirubin levels, ≥25.0 mg/dL [≥510 μmol/L]) and hazardous (serum bilirubin levels, ≥30.0 mg/dL [≥510 μmol/L]) neonatal hyperbilirubinemia. MAIN OUTCOMES AND MEASURES: The primary outcome was kernicterus, defined as hazardous neonatal hyperbilirubinemia followed by cerebral palsy, sensorineural hearing loss, gaze paralysis, or neurodevelopmental retardation. Secondary outcomes were health care professional adherence to national guidelines using a predefined protocol with 10 key performance indicators for diagnosis and treatment as well as assessment of whether bilirubin-associated brain damage might have been avoidable. RESULTS: Among 992 378 live-born infants (958 051 term births and 34 327 near-term births), 494 (320 boys; mean [SD] birth weight, 3505 [29.9 mg/dL [425-509 μmol/L]) developed extreme hyperbilirubinemia (50 per 100 000 infants), 6.8 per 100 000 infants developed hazardous hyperbilirubinemia, and 1.3 per 100 000 infants developed kernicterus. Among 13 children developing kernicterus, brain injury was assessed as potentially avoidable for 11 children based on the presence of 1 or several of the following possible causes: untimely or lack of predischarge bilirubin screening (n = 6), misinterpretation of bilirubin values (n = 2), untimely or delayed initiation of treatment with intensive phototherapy (n = 1), untimely or no treatment with exchange transfusion (n = 6), or lack of repeated exchange transfusions despite indication (n = 1). CONCLUSIONS AND RELEVANCE: Hazardous hyperbilirubinemia in near-term or term newborns still occurs in Sweden and was associated with disabling brain damage in 13 per million births. For most of these cases, health care professional noncompliance with best practices was identified, suggesting that a substantial proportion of these cases might have been avoided.

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27. Cerebral Palsy Rate of Very Low Birth Weight Infants Born at 36 Weeks of Gestation. Park HS.


PMID: 30886548


Neonatal encephalopathy due to hypoxia ischemia (HI) leads to severe, life-long morbidities in thousands of neonates born in the US and worldwide each year. Varying capacities of long-term episodic memory, verbal working memory and learning can present without cerebral palsy and have been associated with the severity of neonatal encephalopathy sustained at birth. Among children who sustain a moderate degree of HI at birth, girls have larger hippocampal volumes compared to boys. Clinical studies indicate that female neonatal brains are more resistant to the effects of neonatal HI, resulting in better long-term cognitive outcomes as compared to males with comparable brain injury. Our most recent mechanistic studies have addressed the origins and cellular basis of sex differences in hippocampal neuroprotection following neonatal HI-related brain injury, and implicate estrogen receptor α (ERα) in the neurotrophin receptor-mediated hippocampal neuroprotection in female mice. This review summarizes the recent findings on ERα dependent, neurotrophin-mediated hippocampal neuroprotection, and weighs the evidence that this mechanism plays an important role in preserving long-term memory and learning following HI in females.

PMID: 30884486


BACKGROUND: Fever and increased maternal interleukin-6 (IL-6) plasma levels in labor are associated with an increased risk of adverse events in offspring, including neonatal seizures, cerebral palsy, and low intelligence scores at school age. However, the neural changes in the neonate that might mediate the adverse effects of maternal noninfectious fever are not fully characterized. This study was designed to test the hypothesis that induced maternal noninfectious fever alters neonatal neural progenitor cell proliferation and enhances microglial activation in the rat dentate gyrus of the hippocampus. METHODS: Systemic vehicle or IL-6 was given 3 times to near-term pregnant rats (n = 7/group) every 90 minutes, and maternal core temperature was recorded. Neonatal brains were processed and analyzed for dentate gyrus cell proliferation (using Ki-67, n = 10/group, and glial fibrillary acidic protein, n = 6/group) and resident microglia activation (using ionized calcium-binding adaptor protein-1 [Iba-1], n = 6/group). In separate studies, the authors assessed microglia proliferation using Ki-67/Iba-1 co-staining (n = 5/group). RESULTS: Compared to controls, exposure to IL-6 resulted in significant maternal temperature increase [mean temperature difference 0.558°C (95% CI, 0.417-0.698; P < .0001)]. Following maternal IL-6, Ki-67 cell proliferation in the dentate gyrus was 55% higher in neonates whose mother received IL-6 (38.8 ± 9.2) compared with those that received vehicle (25.1 ± 7.8); mean difference 13.7 (95% CI, 5.68-21.71); (P = .0021). Glial fibrillary acidic protein cell proliferation was 40% higher in the neonatal dentate gyrus whose mother received IL-6 when compared to controls (713 ± 85.52 vs 500 ± 113); mean difference 212 (95% CI, 82.2-343.4); (P = .004). Resident microglial activation was 90% higher in the dentate gyrus of neonates whose mother received IL-6 when compared to controls (71.8 ± 9.3 vs 37.8 ± 5.95); mean Iba-1 in stained cells was significantly different between IL-6 and vehicle groups 34 (95% CI, 23.94-44.05); (P < .0001). Proliferating microglia, determined by the colocalization of Ki-67 and Iba-1, were not different in the vehicle (8.8% ± 3.19%) and the IL-6 (5.6% ± 2.3%) groups (mean difference 3.2% (95% CI, -0.8-7.25) (P = .1063). CONCLUSIONS: IL-6 is sufficient to induce maternal systemic temperature increases in near-term pregnant rats as well as neuronal, glial, and neuroinflammatory changes in the dentate gyrus of the neonatal hippocampus. These alterations might disrupt fetal neurodevelopment during a vulnerable period.

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Hyperoxia plays a key role in the development of bronchopulmonary dysplasia (BPD), a chronic lung disease of preterm infants. Infants with BPD often have brain injury that leads to long-term neurodevelopmental impairment, but the underlying mechanisms controlling BPD-induced neurodevelopmental impairment remain unclear. Our previous studies have shown that hyperoxia-induced BPD in rodents is associated with lung inflammasome activation. Here we tested the hypothesis that hyperoxia-induced lung and brain injury is mediated by inflammasome activation and that inhibition of caspase-1, a key component of the inflammasome, attenuates hyperoxia-induced lung and brain injury in neonatal mice. C57/BL6 mouse pups were randomized to receive daily intraperitoneal injections of Ac-YVAD-CMK, an irreversible caspase-1 inhibitor, or placebo during exposure to room air or hyperoxia (85% O2) for 10 days. We found that hyperoxia activated the NLRP1 inflammasome, increased production of mature IL-1β and upregulated expression of p30 gasdermin-D (GSDMD), the active form of GSDMD responsible for the programmed cell death mechanism of pyroptosis in both lung and brain tissue. Importantly, we show that inhibition of caspase-1 decreased IL-1β activation and p30 GSDMD expression and improved alveolar and vascular development in hyperoxia-exposed lungs. Moreover, caspase-1 inhibition also promoted cell proliferation in the subgranular zone and subventricular zone of hyperoxia-exposed brains resulting in lessened atrophy of these zones. Thus, the inflammasome plays a critical role in hyperoxia-induced neonatal lung and brain injury, and targeting this pathway may be beneficial in the prevention of lung and brain injury in preterm infants.

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