1. Medial Gastrocnemius Muscle-Tendon Junction and Fascicle Lengthening across the Range of Motion Analyzed in 2-D and 3-D Ultrasound Images.


Ultrasound imaging modalities offer a clinically viable method to visualize musculoskeletal structures. However, proper data comparison between investigations is compromised because of a lack of measurement error documentation and method standardization. This investigation analyzes the reliability and validity of extracting medial gastrocnemius belly and fascicle lengths and pennation angles in different ankle joint positions, across the full range of motion, in a cohort of 11 children with spastic cerebral palsy and 11 typically developed children. Each of these parameters was extracted from two consecutive acquisitions, using both 2-D and 3-D ultrasound images. The findings suggest that the muscle tendon junction extraction in 2-D images can be a suitable parameter for analyzing medial gastrocnemius muscle length in typically developed children and children with spastic cerebral palsy, although averaging over multiple measurements is recommended to reduce variability. More caution should be taken when performing analyses based on fascicle length.

PMID: 30172570


OBJECTIVE: The purpose of this study was the construction of a new semi-automated experimental setup for the evaluation of the stiffness of ankle foot orthoses (AFOs) around an axis aligned to the anatomical ankle joint during the second rocker of the gait. The setup, developed in close collaboration with the orthopedic device company V!GO NV (Wetteren, Belgium), allows measurement of plantarflexion and dorsiflexion in the sagittal plane for a maximal range of motion of 50° (−25° plantarflexion up to 25° dorsiflexion) in a non-destructive way. RESULTS: The mechanical properties of four 3D printed AFOs are investigated, based on the ranges of motion derived from the gait assessment of the patients when they walked with their AFO. The reliability of the stiffness measures was studied by the evaluation of the test-retest repeatability and the intra-tester and inter-tester variability. These studies revealed that the ankle stiffness can be measured with high reliability (ICC = 0.94-1.00). The obtained outcomes indicate that the experimental setup could be applied to measure the ankle stiffness of any topology of AFOs and, in the future, help finding the correlation with the information coming from the gait assessment of the patients.

PMID: 30185209
3. [Physician and family perception of the results of multiple orthopedic surgeries in children with cerebral palsy].
Turriago C, Ortiz-Corredor F, Baquero M, Arbeláez-Huertas F.

OBJECTIVE: To compare the perception of physicians and families regarding the results of multilevel orthopedic surgery of the lower limbs to improve gait in children with cerebral palsy. METHODS: An evaluation of medical records and pre- and postoperative videos of children attended in the walking laboratory was carried out. The outcome of the surgical treatment was evaluated by applying not only the physician rating scale, but also the Gillette functional assessment questionnaire (FAQ), as well as perception questionnaires to assess the relatives' perspective. RESULTS: 243 patients were evaluated. According to the functional evaluation questionnaire, 45 cases worsened, 103 improved and 95 remained stable (p<0.001). The physician rating scale showed that gait got worse in 13 cases, improved in 210 and was the same in 20. The overall perception of the treatment outcome was favorable among relatives. A weak but significant correlation between the change in the physician's average score and family satisfaction (r=0.15; p=0.016) was found, as well as between the physician's overall perception and the family's perception (r=1, 5; p=0.015). CONCLUSIONS: The results of the surgical treatment were favorable for both the physician and the family. Although most cases retained functional status according to the gross motor function classification system (GMFCS), a significant proportion of patients improved according to the Gillette functional assessment questionnaire (FAQ).

PMID: 30183957

4. BMI does not capture the high fat mass index and low fat-free mass index in children with cerebral palsy and proposed statistical models that improve this accuracy.
Whitney DG, Miller F, Pohlig RT, Modlesky CM.

BACKGROUND/OBJECTIVES: Children with cerebral palsy (CP) are at risk for having a misclassified overweight/obesity status based on BMI thresholds due to their lower fat-free mass and similar fat mass compared with typically developing children. The primary objective was to determine if BMI could predict fat mass index (FMI) and fat-free mass index (FFMI) in children with CP. SUBJECTS/METHODS: Forty-two children with CP and 42 typically developing children matched to children with CP for age and sex participated in the study. Dual-energy X-ray absorptiometry was used to assess body composition. Children with CP who could ambulate without assistance were considered ambulatory (ACP) and the rest were considered nonambulatory (NACP). RESULTS: Children with CP had higher percent body fat (%Fat) and FMI and lower fat-free mass and FFMI than controls (p<0.05) but no difference in fat mass (p=0.10). When BMI was statistically controlled, NACP had higher %Fat, fat mass and FMI and lower FFMI than ACP and controls (p<0.05). NACP also had lower fat-free mass than controls (p<0.05). ACP had higher %Fat and FMI and lower fat-free mass and FFMI than controls (p<0.05). BMI was a strong predictor of FMI (R²=0.83) and a moderately strong predictor of FFMI (R²=0.49) in children with CP (both p<0.01). Prediction of FMI (R²=0.86) and FFMI (R²=0.66) from BMI increased (p<0.05) when age, sex and ambulatory status were included. CONCLUSION: Compared with typically developing children, children with CP have a higher BMI and lower FFMI for a given BMI, which is more pronounced in NACP than ACP. The finding suggests that the prevalence of overweight/obesity status may be underestimated in children with CP.

PMID: 30181652

5. Hammersmith Infant Neurological Examination Asymmetry Score Detects Hemiplegic Cerebral Palsy From Typical Development.

BACKGROUND: The Hammersmith Infant Neurological Examination is one of several useful tools for early identification of cerebral palsy; however, cut-off scores for cerebral palsy do not consistently distinguish infants with hemiplegia from those typically developing. We hypothesized that use of an asymmetry score, in addition to the assessment's standard total cutoff score, could remedy this problem in a clinical setting. METHODS: This retrospective study of a neonatal intensive care follow-up program with consistent clinical use of the Hammersmith Infant Neurological Examination matched infants with a diagnosis of cerebral palsy to infants without motor delays or evidence of neurodevelopmental impairments. Groups had same corrected
and gestational ages at Hammersmith Infant Neurological Examination assessment. Asymmetry presence was recorded.

RESULTS: Of 74 infants with cerebral palsy, 28 had quadriplegia, 11 had diplegia, and 35 had hemiplegia. Median total Hammersmith Infant Neurological Examination and asymmetry scores for hemiplegia were 57.5 and 10 versus 76 and 0 for those without cerebral palsy. Sensitivity and specificity to distinguish hemiplegia from typical development by combining a total Hammersmith Infant Neurological Examination score <63 and an asymmetry score >5 were 91.8% and 100%, respectively. CONCLUSIONS: In a clinical setting, combining total Hammersmith Infant Neurological Examination and asymmetry scores can help providers differentiate infants with hemiplegia from those typically developing.

PMID: 30190180

LeBrun DG, Banskota B, Banskota AK, Rajbhandari T, Baldwin KD, Spiegel DA.


BACKGROUND: Cerebral palsy (CP) comprises a heterogeneous group of disorders whose clinical manifestations and epidemiologic characteristics vary across socioeconomic and geographic contexts. The functional severity of untreated CP in low-income countries has been insufficiently studied; a better understanding of how these children present for care in resource-constrained environments is important because it will better characterize the natural history of CP, guide clinical decision-making, and aid in the prognostication of children with untreated CP. QUESTIONS/PURPOSES: The purposes of this study were (1) to determine the etiologies, motor subtypes, topographic distributions, and functional classifications of a large cohort of Nepali children with untreated CP presenting to a large pediatric rehabilitation center in Nepal; and (2) to compare the Gross Motor Function Classification System (GMFCS), the Manual Ability Classification System (MACS), and the Communication Function Classification System (CFCS) scores of a subset of patients with spastic CP in the Nepali cohort with control subjects from high-income countries. METHODS: A cross-sectional study was conducted at the Hospital and Rehabilitation Centre for Disabled Children in Nepal. Two hundred six consecutive Nepali children (76 girls; median age 4.0 years [interquartile range {IQR}, 2.5-9.0 years]) were evaluated to determine the demographic, clinical, and functional characteristics of a cohort of Nepali children with untreated CP. A systematic review of the Medline and Cochrane databases was then performed to obtain reference classification scores from high-income countries. Cross-sectional, noninterventional studies reporting at least one functional classification system with a sample size of at least 50 participants were included. Only studies of patients with spastic CP were included to allow for compatible comparisons with a subset of our study sample with spastic CP. A random-effects analysis was used to pool functional scores from participants in the included studies. Among the 206 children in our sample, 102 had spastic CP (35 girls; median age 5.5 years [IQR, 3.5-9.0 years]). Functional scores from these children were compared with pooled scores obtained from the systematic review by assessing the proportions of children in each sample with GMFCS, MACS, and CFCS score categories of I or II versus III to V. RESULTS: Children with spastic hemiplegia from high-income countries were more likely to have a GMFCS score of I or II (96% [95% confidence interval {CI}, 92%-99%] versus 78% [95% CI, 62%-89%]) and a MACS score of I or II (83% [95% CI, 77%-88%] versus 50% [95% CI, 32%-68%]) relative to those from Nepal, but they were less likely to have a CFCS score of I or II (67% [95% CI, 51%-80%] versus 97% [95% CI, 87%-99%]). No differences were seen in children with spastic diplegia or quadriplegia. CONCLUSIONS: Children in Nepal with hemiplegic CP have greater functional disability despite less motor impairment compared with children from high-income settings. Targeted interventions to maintain functional status in Nepali children with CP may reduce this disparity. Additional studies demonstrating the association between socioeconomic status and the prognosis of CP in resource-limited populations are needed. LEVEL OF EVIDENCE: Level II, prognostic study.

PMID: 30179955

7. Day/night melatonin content in cerebral palsy.
Santos JS, Giacheti CM, Dornelas LS, Silva NC, Souza ALDM, Guissoni Campos LM, Pinato L.


Changes in the sleep-wake cycle are frequent and may impair quality of life in individuals with cerebral palsy (CP). To investigate if a lack of a day/night variation of melatonin content could be related with sleep disorders (SD), the SD were evaluated with a Sleep Questionnaire and the melatonin content using ELISA in 33 individuals with CP and 24 controls. The indicative of SD were present in 47% of CP group, and the most frequent was the indicative of sleep breathing disorder. The CP group showed higher diurnal and lower nocturnal melatonin content than controls. Individuals with CP that had indicative of SD showed lower nocturnal content of melatonin than those without SD. These results showed that the lack of the day/night variation of melatonin was related to SD in individuals with CP.

PMID: 30176339
8. Interdisciplinary Management of a Class III Anterior Open Bite Malocclusion in a Patient With Cerebral Palsy.
Michelogiannakis D, Vorrasi JS, Kotsailidi EA, Rossouw PE.


Dentofacial disharmony in patients with cerebral palsy (CP) can lead to low self-esteem and functional limitations. However, medical and behavioral challenges in patients with developmental disorders often prevent dental practitioners from offering the necessary treatment. This report describes the clinical interdisciplinary management of a 20-year-old man with CP, including orthodontic, periodontal, and orthognathic surgery therapy. The patient presented with the chief complaint of having difficulty chewing, was wheelchair dependent, had poor orofacial muscle control, and exhibited a Class III malocclusion with a skeletal anterior open bite. The lower midline was shifted 3 mm to the right, there was severe maxillary spacing, and the patient had gingival overgrowth. A combined orthodontic, periodontal, and orthognathic surgery treatment approach was chosen to meet the patient's interdisciplinary needs. Because of his physical limitations, it was necessary to avoid complicated and prolonged orthodontic treatment mechanics. Interdisciplinary therapy improved the patient's oral function, periodontal health, and facial esthetics and led to a good occlusion, which remained stable 1 year after treatment. Regardless of the treatment challenges, combined orthodontic and surgical therapy in the present patient with CP led to favorable treatment results and improved the patient's self-esteem, confidence in social interactions, and speaking and chewing abilities.

PMID: 30193117

Yogi H, Alves LAC, Guedes R, Ciamponi AL.


INTRODUCTION: Cerebral palsy (CP) is an encephalic static lesion characterized as a nonprogressive disorder of movements and posture with functional deficits that may favor the occurrence of various malocclusions. We looked for a possible association between overall functional impairment and malocclusion in this population. METHODS: Seventy patients from the Center of Attendance for Special Needs Patients, ages 6 to 18 years and with a CP diagnosis, were involved in the research. The overall degree of functional impairment was assessed with the Gross Motor Function Classification System, and malocclusion was evaluated with the criteria established by the World Health Organization and selected occlusion characteristics. To test the associations, univariate and multiple logistic Poisson regression analyses were used, and prevalence ratio values were calculated. RESULTS: Patients with limited or severely limited mobility (Gross Motor Function Classification of 4 or 5) (P = 0.003), parafunctional habits (P = 0.001), and a caregiver who was not the mother had 3 to 4 times more risk for open bite. Patients with dyskinetic CP are 4 times more likely to develop deepbite (P = 0.005). CONCLUSIONS: The results showed that the type of CP, the degree of motor involvement, and the presence of parafunctions are important factors to be considered to establish a correct diagnosis of malocclusion in persons with CP.

PMID: 30173844

10. Analysis of electroencephalogram-derived indexes for anesthetic depth monitoring in pediatric patients with intellectual disability undergoing dental surgery.


BACKGROUND: Patients with intellectual disability (ID) often require general anesthesia during oral procedures. Anesthetic depth monitoring in these patients can be difficult due to their already altered mental state prior to anesthesia. In this study, the utility of electroencephalographic indexes to reflect anesthetic depth was evaluated in pediatric patients with ID. METHODS: Seventeen patients (mean age, 9.6 ± 2.9 years) scheduled for dental procedures were enrolled in this study. After anesthesia induction with propofol or sevoflurane, a bilateral sensor was placed on the patient's forehead and the bispectral index (BIS) was recorded. Anesthesia was maintained with sevoflurane, which was adjusted according to the clinical signs by an anesthesiologist blinded to the BIS value. The index performance was accessed by correlation (with the end-tidal sevoflurane [EtSevo] concentration) and prediction probability (with a clinical scale of anesthesia). The asymmetry of the electroencephalogram between the left and right sides was also analyzed. RESULTS: The BIS had good correlation and prediction probabilities (above 0.5) in the majority of patients; however, BIS was not correlated with EtSevo or the clinical scale of anesthesia in patients with Lennox-Gastaut, West syndrome, cerebral palsy, and epilepsy. BIS showed better
INTRODUCTION: Drooling of saliva is the unintentional loss of saliva from the mouth resulting in excess pooling of saliva in the anterior portion of the oral cavity. It is considered normal in infants and usually resolves itself by 15-18 months of age. It is a common problem in pediatric patients with cerebral palsy or other neurological disorders. Drooling interferes with speech, impairs oral hygiene and contributes to oral dermatitis, aspiration pneumonias and fluid electrolyte imbalances. It has a profoundly negative impact on quality of life and contributes to social exclusion, self-esteem problems and significant discomfort, especially amongst school-aged children. In addition, it can present a serious challenge for caregivers. Various approaches to manage this condition have been described in the literature. Submandibular duct relocation allows salivary flow to be directed to the anterior portion of the oral cavity. It is considered normal in infants and usually resolves itself by 15-18 months of age.

OBJECTIVES: The aim of this study is to share our experience with the surgical approach to drooling children and to evaluate clinical outcomes and long-term caregiver satisfaction outcomes.

METHODS: The authors conducted a retrospective study with a review of the medical records of 43 children and adolescents who had been submitted to submandibular duct relocation in the Centro Hospitalar Tondela-Viseu, between January 2003 and December 2017. The authors analyzed the clinical history, bibs used per day before and after surgery, and caregivers' satisfaction was assessed by interview using a questionnaire. The results of this procedure, technical considerations and outcomes are presented in this work. RESULTS: Forty-three patients (15 girls and 28 boys), between the ages of 3 and 18 at time of surgery (mean age of 9), underwent bilateral submandibular duct transposition for drooling. All children have neurological disorders, with cerebral palsy being the predominant diagnosis. The majority were hospitalized for 1-2 days and no surgical complications were observed. The number of bib or clothing changes fell from more than ten in 23 patients (53%) pre-operatively to less than five in 33 patients (77%) post-operatively. 30% of caregivers were satisfied and 53% were very satisfied with the results of surgery. CONCLUSIONS: The results of this study show that submandibular duct relocation is an effective method in the resolution of uncontrolled drooling in children, contributing to the improvement of children's quality of life. The degree of satisfaction with the surgical results is in agreement with the published international studies, proving once again the effectiveness of the surgical technique implemented in our Hospital.

PMID: 30174011
13. [Risk Factors for Mental Health Problems in Children with Cerebral Palsy and Spina Bifida].

Klin Padiatr. 2018 Sep 4. doi: 10.1055/a-0664-0832. [Epub ahead of print] [Article in German; Abstract available in German from the publisher]

BACKGROUND: Children with cerebral palsy (CP) and spina bifida (SB) are at an increased risk for mental health problems. Aim of this study was to correlate disease specific and psychosocial risk factors with characteristic mental health problems.

PATIENTS: 271 children with CP and 84 with SB aged 3-17 years were included in a cross sectional study of 15 centers.

METHODS: Parents answered the Strengths and Difficulties Questionnaire (SDQ) for mental health problems, rated social participation of their children and gave data to their own educational and professional level. IQ and motor impairment were tested or rated by the caring pediatricians. RESULTS: Abnormal Total-Difficulties Scores were found in CP (30.2%) and SB (18.1%) as compared to the norm (10.0%). Increased prevalences persisted after controlling for IQ as covariate. In both groups, moderate correlations between externalizing problems and levels of cognitive and motor impairment were found. Emotional problems correlated with participation irrespective of level of impairment. Weak correlations were found with age and gender in both groups. After controlling for IQ as covariate mental health problems showed no systematic difference between both groups. DISCUSSION: Mental health problems in children and youth with CP and SB are frequent. They correlated with various risk factors (IQ, motor impairment, age, gender, participation). Early recognition, participation and psychotherapeutical facilities should be strengthened.

PMID: 30180264

Mensch SM, Echteld MA, Lemmens R, Oppewal A, Evenhuis HM, Rameckers EAA.


BACKGROUND: This study aimed to determine the relationship between motor abilities and quality of life in children with severe multiple disabilities. METHODS: In this cross-sectional study, motor abilities of 29 children (mean age 9.8 years; 45% girls) with severe multiple disabilities [IQ < 25; Gross Motor Function Motor Classification System level V] were measured with the MOtor eVAluation in Kids with Intellectual and Complex disabilities (Movakic) questionnaire (completed by the child's physical therapist). Quality of life was measured with the Quality of Life-Profound Multiple Disabilities (QoL-PMD) questionnaire (completed by the child's parents). RESULTS: A significantly moderate to high correlation was found between the total scores on the Movakic and the QoL-PMD (r = 0.40, P = 0.03), indicating that higher scores in motor abilities are associated with a higher level of quality of life. Furthermore, significantly moderate to high correlations were found between the total score on the Movakic and the dimension Physical Well-Being, Development and Activities of the QoL-PMD. In multiple linear regression models, all significant bivariate relationships between the Movakic total scores and QoL-PMD dimensions remained significant after controlling for the Gross Motor Function Motor Classification System level. CONCLUSIONS: In these children with severe multiple disabilities, motor abilities (as measured by Movakic) are moderately related to quality of life (as measured by the QoL-PMD).

PMID: 30175518

15. Long-term course of difficulty in participation of individuals with cerebral palsy aged 16 to 34 years: a prospective cohort study.
van Gorp M, Van Wely L, Dallmeijer AJ, de Groot V, Ketelaar M, Roebroeck ME; Perrin-Decade study group.


AIM: To determine the long-term course of difficulty in participation of individuals with cerebral palsy (CP) without intellectual disability between 16 years and 34 years of age. METHOD: One hundred and fifty-one individuals with CP aged 16 to 20 years were included (63% male, 37% female; Gross Motor Function Classification System [GMFCS] levels I-IV; without intellectual disability). The Assessment of Life Habits questionnaire 3.0 general short form was used up to three times biennially and at 13-year follow-up (13-year follow-up: n=98). Scores (range 0-10) reflect difficulty and assistance in participation in housing, education and employment, interpersonal relationships, recreation, community life, and responsibilities. Multilevel models were used to determine the course of difficulty in participation by GMFCS level. RESULTS: Despite high average participation levels, 41% to 95% of adolescents and young adults with CP experienced...
difficulty. Difficulty in participation in housing and interpersonal relationships increased from age 16 years onwards and in most other life areas in the mid- and late 20s. In adolescents in GMFCS levels III and IV, participation in recreation and community life improved up to age 23 years. INTERPRETATION: Individuals with CP experience increasing difficulties in participation in their mid- and late 20s. Clinicians should systematically check for participation difficulties in young adults with CP and offer timely personalized treatment. WHAT THIS PAPER ADDS: Many individuals with cerebral palsy (CP) aged 16 to 34 years experience difficulty in participation. Difficulty in participation increases in the mid- and late 20s for individuals with CP. Participation in recreation/community life improves before age 23 years for those in Gross Motor Function Classification System levels III and IV.

PMID: 30187926

Gigi M, Roth J, Eshel R, Constantini S, Bassan H.

AIM: To determine the health-related quality of life (HRQoL) of children born preterm (gestational age <32wks) after post-haemorrhagic hydrocephalus requiring shunt (PHH-S), and to examine the impact of perinatal and neurological morbidity on their QoL. METHOD: Forty infants (18 females, 22 males; aged 2y 2mo-8y 4.5mo) born preterm with PHH-S were matched for gestational age, birthweight, and sex with infants born preterm with normal cranial ultrasonography. Pediatric QoL Inventory parent-proxy report was administered at a mean age of 5 years 8 months. RESULTS: Children with PHH-S exhibited significantly lower mean HRQoL compared with controls in motor (36 [SD 34.9] vs 96.2 [SD 6.6]), emotional (59.8 [SD 26.7] vs 80.6 [SD 18.8]), social (55.6 [SD 29.7] vs 89.6 [SD 16.6]), and school (40.5 [SD 22.9] vs 89.7 [SD 15.2]) domains (p<0.001). Multivariate regression incorporating neonatal risk factors revealed an independent effect of parenchymal brain involvement (β=-0.6, p<0.01) and neonatal seizures (β=-0.2, p<0.02) on total HRQoL. Low HRQoL of children with PHH-S was associated with neurodevelopmental morbidities: cerebral palsy (CP), epilepsy, vision and feeding problems, low cognitive, personal-social, and adaptive scores (p<0.05). Multivariate analysis indicated an independent contribution from severe CP (β=-0.4, p<0.001) and low personal-social score (β=0.5, p<0.001). INTERPRETATION: Children born preterm after PHH-S exhibit significantly lower HRQoL scores compared with preterm born peers. HRQoL is associated with neonatal cerebral complications and neurodevelopmental morbidities. WHAT THIS PAPER ADDS: Children born preterm, after post-haemorrhagic hydrocephalus requiring shunt, have low health-related quality of life (HRQoL). A low HRQoL is associated with parenchymal brain involvement and with neurological morbidity. Severe cerebral palsy and low personal-social developmental scores have independent contributions to HRQoL.

PMID: 30187913

17. Factors affecting social participation of Iranian children with cerebral palsy.
Amini M, Saneii SH, Pashmdarfard M.

The purpose of this study was to identify the factors affecting the social participation of Iranian children with cerebral palsy (CP). Participants were 274 (male = 62%; female = 38%) children with CP, 6- to 12-years old (mean = 1.64) and their parents. Several standardized measures were used to assess social participation, gather environmental factors, and demographic questionnaires. The results of stepwise linear regression analysis indicated that the type of CP, Manual ability level and cognitive level (IQ) appear to be strong predictors of social participation between personal and environmental factors.

PMID: 30183435

18. Maternal smoking during pregnancy and long-term neurological morbidity of the offspring.
Gutvirtz G, Wainstock T, Landau D, Sheiner E.

OBJECTIVE: To evaluate the long-term pediatric neurological morbidity of children born to mothers who reported smoking
Cerebral Palsy has long been investigated to be associated with a range of motor and cognitive dysfunction. As the two most common CP subtypes, spastic cerebral palsy (SCP) and dyskinetic cerebral palsy (DCP) may share common and distinct elements in their pathophysiology. However, the common and distinct dysfunctional characteristics between SCP and DCP on the brain network level are less known. This study aims to detect the alteration of brain functional connectivity in children with CP. Methods: We recruited 16 DCP, 18 bilateral SCP, and 18 healthy children. Compared with healthy controls, altered functional connectivity within the brain network were found. These findings
indicate functional connectivity impairment and altered integration widely exist in children with CP, suggesting that the abnormal functional connectivity is a pathophysiological mechanism of motor and cognitive dysfunction of CP.

PMID: 30186320

Gupta M, Rajak BL, Bhatia D, Mukherjee A.


BACKGROUND: Neuromodulation is emerging as a new therapeutic field towards treatment of neurological disorders through advances in medical devices. Repetitive Transcranial Magnetic Stimulation (rTMS) is one such neuromodulatory device that has received increasing interest as a tool for modulating cortical excitability that influence motor activity in both normal and diseased population. However, the therapeutic effect of rTMS varies depending on stimulation frequency, intensity, pulse trains, duration, etc. Our previous studies had already demonstrated that higher frequency of 10 Hz was effective in improving the motor activity of spastic CP patients. OBJECTIVE: This study was aimed to evaluate the effect of different rTMS pulses on gross motor performance of spastic CP patients. METHOD: Thirty spastic CP patients were divided equally into three groups P1500, P2000 and P2500 with mean age (in years) 7.7 ± SD4.4, 6.8 ± SD5.3 and 7.2 ± SD5.1 respectively. Gross Motor Function Measure (GMFM) was employed as an outcome measure to assess the motor performance. Constant rTMS frequency of 10 Hz was delivered to each participant but the number of stimulation pulse varied according to the groups; which were 1500, 2000 and 2500 pulses for P1500, P2000 and P2500 group respectively. rTMS therapy of 15 minutes duration was followed by physical therapy of 30 minutes daily for 20 days. RESULT: Statistical analysis of pre versus post GMFM scores of different groups revealed significant result (p < .001) and the improvement in functional motor activity was 2.33% in P1500, 3.58% in P2000 and 5.17% in P2500 group. INTERPRETATION: The result demonstrated modulatory effect of rTMS pulse by improving motor function of spastic CP patients.

PMID: 30175934

Buizer AI, Martens BHM, Grandbois van Ravenhorst C, Schoonmade LJ, Becher JG, Vermeulen RJ.


AIM: To investigate the effects of continuous intrathecal baclofen (ITB) therapy in children with cerebral palsy (CP) and other neurological conditions. METHOD: This systematic review was conducted using standardized methodology, searching four electronic databases (PubMed, Embase, CINAHL, Cochrane Library) for relevant literature published between inception and September 2017. Included studies involved continuous ITB as an intervention and outcome measures relating to all International Classification of Functioning, Disability and Health: Children and Youth (ICF-CY) components. RESULTS: Thirty-three studies were identified, of which one, including 17 children with spastic CP, produced level II evidence, and the others, mainly non-controlled cohort studies, level IV and V. Outcomes at body function level were most frequently reported. Results suggest continuous ITB may be effective in reducing spasticity and dystonia in CP, as well as other neurological conditions, and may improve the ease of care and quality of life of children with CP, but the level of evidence is low. INTERPRETATION: Despite three decades of applying ITB in children and a relatively large number of studies investigating the treatment effects, a direct link has not yet been demonstrated because of the low scientific quality of the primary studies. Further investigation into the effects of continuous ITB at all levels of the ICF-CY is warranted. Although large, controlled trials may be difficult to realize, national and international collaborations may provide opportunities. Also, multicentre prospective cohort studies with a long-term follow-up, employing harmonized outcome measures, can offer prospects to expand our knowledge of the effects of continuous ITB therapy in children. WHAT THIS PAPER ADDS: There is low-level evidence for continuous intrathecal baclofen (ITB) in children with cerebral palsy. Continuous ITB is effective in reducing spasticity and dystonia in non-controlled cohort studies. Evaluation of individual goals and systematic assessment of long-term effects in large cohort studies are required.

PMID: 30187921
23. Botulinum toxin type A enhances the inhibitory spontaneous postsynaptic currents on the substantia gelatinosa neurons of the subnucleus caudalis in immature mice.
Jang SH, Park SJ, Lee CJ, Ahn DK, Han SK.

Botulinum toxin type A (BoNT/A) has been used therapeutically for various conditions including dystonia, cerebral palsy, wrinkle, hyperhidrosis and pain control. The substantia gelatinosa (SG) neurons of the trigeminal subnucleus caudalis (Vc) receive orofacial nociceptive information from primary afferents and transmit the information to higher brain center. Although many studies have shown the analgesic effects of BoNT/A, the effects of BoNT/A at the central nervous system and the action mechanism are not well understood. Therefore, the effects of BoNT/A on the spontaneous postsynaptic currents (sPSCs) in the SG neurons were investigated. In whole cell voltage clamp mode, the frequency of sPSCs was increased in 18 (37.5%) neurons, decreased in 5 (10.4%) neurons and not affected in 25 (52.1%) of 48 neurons tested by BoNT/A (3 nM). Similar proportions of frequency variation of sPSCs were observed in 1 and 10 nM BoNT/A and no significant differences were observed in the relative mean frequencies of sPSCs among 1-10 nM BoNT/A. BoNT/A-induced frequency increase of sPSCs was not affected by pretreated tetrodotoxin (0.5 µM). In addition, the frequency of sIPSCs in the presence of CNQX (10 µM) and AP5 (20 µM) was increased in 10 (53%) neurons, decreased in 1 (5%) neuron and not affected in 8 (42%) of 19 neurons tested by BoNT/A (3 nM). These results demonstrate that BoNT/A increases the frequency of sIPSCs on SG neurons of the Vc at least partly and can provide an evidence for rapid action of BoNT/A at the central nervous system.

PMID: 30181700

24. Risk of systemic adverse events after botulinum neurotoxin A treatment in cerebral palsy.
Papavasiliou AS.

PMID: 30171611

Gillard V, Chadie A, Ferracci FX, Brasseur-Daudruy M, Proust F, Marret S, Curey S.

BACKGROUND: Intraventricular hemorrhage (IVH) is a frequent complication in extreme and very preterm births. Despite a high risk of death and impaired neurodevelopment, the precise prognosis of infants with IVH remains unclear. The objective of this study was to evaluate the rate and predictive factors of evolution to post hemorrhagic hydrocephalus (PHH) requiring a shunt, in newborns with IVH and to report their neurodevelopmental outcomes at 2 years of age. METHODS: Among all preterm newborns admitted to the department of neonatology at Rouen University Hospital, France between January 2000 and December 2013, 122 had an IVH and were included in the study. Newborns with grade 1 IVH according to the Papile classification were excluded. RESULTS: At 2-year, 18% (n = 22) of our IVH cohort required permanent cerebro spinal fluid (CSF) derivation. High IVH grade, low gestational age at birth and increased head circumference were risk factors for PHH. The rate of death of IVH was 36.9% (n = 45). The rate of cerebral palsy was 55.9% (n = 43) in the 77 surviving patients (49.4%). Risk factors for impaired neurodevelopment were high grade IVH and increased head circumference. CONCLUSION: High IVH grade was strongly correlated with death and neurodevelopmental outcome. The impact of an increased head circumference highlights the need for early management. CSF biomarkers and new medical treatments such as antenatal magnesium sulfate have emerged and could predict and improve the prognosis of these newborns with PHH.

PMID: 30170570

26. Variants of the OLIG2 Gene are Associated with Cerebral Palsy in Chinese Han Infants with Hypoxic-Ischemic Encephalopathy.
Cerebral palsy (CP) is a leading cause of neurological disability among young children. Congenital and adverse perinatal clinical conditions, such as genetic factors, perinatal infection, and asphyxia, are risk factors for CP. Oligodendrocyte transcription factor (OLIG2) is a protein that is expressed in brain oligodendrocyte cells and is involved in neuron repair after brain injury. In this study, we employed a Chinese Han cohort of 763 CP infants and 738 healthy controls to study the association of OLIG2 gene polymorphisms with CP. We found marginal association of the SNP rs6517135 with CP (p = 0.044) at the genotype level, and the association was greatly strengthened when we focused on the subgroup of CP infants who suffered from hypoxic-ischemic encephalopathy (HIE) after birth, with p = 0.003 (OR = 0.558) at the allele level and p = 0.007 at the genotype level, indicating a risk-associated role of the T allele of the SNP rs6517135 under HIE conditions. The haplotype CTTG for rs6517135-rs1005573-rs6517137-rs9653711 in OLIG2 was also significantly associated with the occurrence of CP in infants with HIE (p = 0.01, OR = 0.521). Our results indicate that in the Han Chinese population, the polymorphisms of OLIG2 were associated with CP, especially in patients who had suffered HIE injury. This finding could be used to develop personalized care for infants with high susceptibility to CP.

PMID: 30178266

27. ST3GAL5-Related Disorders: A Deficiency in Ganglioside Metabolism and a Genetic Cause of Intellectual Disability and Choreoathetosis.
Gordon-Lipkin E, Cohen JS, Srivastava S, Soares BP, Levey E, Fatemi A.


GM3 synthase deficiency is due to biallelic pathogenic variants in ST3GAL5, which encodes a sialyltransferase that synthesizes ganglioside GM3. Key features of this rare autosomal recessive condition include profound intellectual disability, failure to thrive and infantile onset epilepsy. We expand the phenotypic spectrum with 3 siblings who were found by whole exome sequencing to have a homozygous pathogenic variant in ST3GAL5, and we compare these cases to those previously described in the literature. The siblings had normal birth history, subsequent developmental stagnation, profound intellectual disability, choreoathetosis, failure to thrive, and visual and hearing impairment. Ichthyosis and self-injurious behavior are newly described in our patients and may influence clinical management. We conclude that GM3 synthase deficiency is a neurodevelopmental disorder with consistent features of profound intellectual disability, choreoathetosis, and deafness. Other phenotypic features have variable expressivity, including failure to thrive, epilepsy, regression, vision impairment, and skin findings. Our analysis demonstrates a broader phenotypic range of this potentially under-recognized disorder.

PMID: 30185102

28. Early intervention at home in infants with congenital brain lesion with CareToy revised: a RCT protocol.
Sgandurra G, Beani E, Giampietri M, Rizzi R, Cioni G; CareToy-R Consortium.


BACKGROUND: Congenital brain lesions expose infants to be at high-risk for being affected by neurodevelopmental disorders such as cerebral palsy (CP). Early interventions programs can significantly impact and improve their neurodevelopment. Recently, in the framework of the European CareToy (CT) Project (www.caretoy.eu), a new medical device has been created to deliver an early, intensive, customized, intervention program, carried out at home by parents but remotely managed by expert and trained clinicians. Reviewing results of previous studies on preterm infants without congenital brain lesion, the CT platform has been revised and a new system created (CT-R). This study describes the protocol of a randomised controlled trial (RCT) aimed to evaluate, in a sample of infants at high-risk for CP, the efficacy of CT-R intervention compared to the Infant Massage (IM) intervention. METHODS/DESIGN: This RCT will be multi-centre, paired and evaluator-blinded. Eligible subjects will be preterm or full-term infants with brain lesions, in first year of age with predefined specific gross motor abilities. Recruited infants will be randomized into CT-R and IM groups at baseline (T0). Based on allocation, infants will perform an 8-week programme of personalized CareToy activities or Infant Massage. The primary outcome measure will be the Infant Motor Profile. On the basis of power calculation, it will require a sample size of 42 infants. Moreover, Peabody Developmental Motor Scales-Second Edition, Teller Acuity Cards, standardized video-recordings of parent infant interaction and wearable sensors (Actigraphs) will be included as secondary outcome measures. Finally, parents will fill out questionnaires (Bayley Social-Emotional, Parents Stress Index). All outcome measures will be carried out at the beginning (T0) and at end of 8-weeks intervention period, primary endpoint (T1). Primary outcome and some secondary outcomes will be carried out also after 2 months from T1 and at 18 months of age (T2 and T3, respectively). The Bayley Cognitive subscale will be used as additional assessment at T3. DISCUSSION: This study protocol paper is the first study aimed to test CT-R system in infants at high-risk for CP. This paper will present the scientific background and trial methodology. TRIAL REGISTRATION: NCT03211533 and NCT03234959 (www.clinicaltrials.gov).

PMID: 30185165

BACKGROUND: In low and middle-income settings, where access to support and rehabilitation services for children with disabilities are often lacking, the evidence base for community initiatives is limited. This study aimed to explore the impact of a community-based training programme for caregivers of children with cerebral palsy in Ghana. METHODS: A pre and post evaluation of an 11-month participatory training programme ("Getting to Know Cerebral Palsy") offered through a parent group model, was conducted. Eight community groups, consisting of a total of 75 caregivers and their children with cerebral palsy (aged 18 months-12 years), were enrolled from 8 districts across Ghana. Caregivers were interviewed at baseline, and again at 2 months after the completion of the programme, to assess: quality of life (PedsQL™ Family Impact Module); knowledge about their child's condition; child health indicators; feeding practices. Severity of cerebral palsy, reported illness, and anthropometric measurements were also assessed. RESULTS: Of the child-caregiver pairs, 64 (84%) were included in final analysis. There were significant improvements in caregiver quality of life score (QoL) (median total QoL 12.5 at baseline to 51.4 at endline, P<0.001). Caregivers reported significant improvements in knowledge and confidence in caring for their child (p<0.001), in some aspects of child feeding practices (p<0.001) and in their child's physical and emotional health (p= 0.001). Actual frequency of reported serious illness over 12-months remained high (67%) among children, however, a small reduction in recent illness episodes (past 2 weeks) was seen (64% to 50% p < 0.05). Malnutrition was common at both time points; 63% and 65% of children were classified as underweight at baseline and endline respectively (p = 0.5). CONCLUSION: Children with cerebral palsy have complex care and support needs which in low and middle-income settings need to be met by their family. This study demonstrates that a participatory training, delivered through the establishment of a local support group, with an emphasis on caregiver empowerment, resulted in improved caregiver QoL. Despite less effect on child health and no clear effect on nutritional status, this alone is an important outcome. Whilst further development of these programmes would be helpful, and is underway, there is clear need for wider scale-up of an intervention which provides support to families.

PMID: 30180171


INTRODUCTION: This study analysed the differences in play performance between preschool children with cerebral palsy and those with typical development and investigated the factors influencing functional mobility and manual dexterity on play in children with cerebral palsy. METHOD: Sixty preschool children (30 with cerebral palsy; 30 with typical development), were assessed by the revised Knox Preschool Play Scale, being that children with cerebral palsy were also classified according to their functional mobility and manual dexterity. RESULTS: On average, all measures were significantly smaller in the cerebral palsy group than the typical development group (p≤ .002). Manual function and functional mobility were negatively correlated with material (r = -.456, p = .011; r = -.487, p = .006) and space (r = -.494, p = .006; r = -.784, p = .000). Also the results pointed out a significant correlation with topography and manual function (r = .404, p = .027) and functional mobility (r = .718, p = .000). Pretend play and participation showed no correlation with topography (r = -.051, p = .788; r = -.312, p = .093), manual function (r = -.019, p = .921; r = -.322, p = .083) and functional mobility (r = -.085, p = .657; r = -.308, p = .097). CONCLUSION: Play performance of children with typical development was superior to those with cerebral palsy. The degree of impairment of functional mobility and manual function negatively was negatively associated with play exploration but did not relate to pretend play or social interaction in play.

PMID: 30186086


BACKGROUND/AIM: The functional Tactile Object Recognition Test (fTORT) is a measure of haptic object recognition capacity recently adapted for use with children with neurological impairment. The current study aimed to investigate preliminary evidence of construct validity and responsiveness of the fTORT and its association with a measure of upper limb
activity. METHODS: A cross-sectional study of 28 children with spastic hemiplegic cerebral palsy (CP) (mean age 10 years 8 months; SD two years four months; 16 male) and 39 typically developing (TD) children (mean age 11 years; SD two years nine months; 19 male) was utilised to investigate construct validity and association between measures. Sixteen children with CP (mean age 10 years 10 months; SD two years 8 months; 9 male) who were randomly allocated to either a treatment (n = 6) or control group (n = 10) were assessed at four time points to assess test responsiveness. RESULTS: There was a very significant difference (P value <0.0001) indicating greater haptic object recognition ability for the TD group (n = 39; median: 40; range: 33-42) than the group with CP (n = 28; median: 32.5; range: 3-41). fTORT scores demonstrated a significant association with scores on the activity measure (Pearson's r: 0.68; P = 0.0001). There were no significant changes over time in fTORT scores (P = 0.22) and no significant difference between the treatment and control groups (P = 0.47). CONCLUSION: The fTORT demonstrated preliminary construct validity, and was positively associated with an upper limb activity measure but scores did not change significantly following somatosensory training. This preliminary paper supports further research and future psychometric knowledge about the tool.

PMID: 30178484

32. Standardized and individualized care: do they complement or oppose each other? Schiariti V; National Institute of Neurological Disorders and Stroke, and American Academy for Cerebral Palsy and Developmental Medicine Common Data Elements working groups.


PMID: 30187468


AIM: To analyse the health care usage of individuals with cerebral palsy (CP) as a function of age and ambulatory status. METHOD: In total, 970 self-administered questionnaires relating to health care usage were sent, via a clinical network of professionals and institutions, to children and adults with CP in Brittany, France. Frequency of use of different aspects of health care were analysed as a function of age and ambulatory status. Multivariate logistic regression evaluated differences in the frequency of each health care type with age; the transition from childhood to adulthood was specifically analysed. RESULTS: The response rate was 53% (282 adults, 230 children). Use of medication (particularly psychotropic and analgesic) increased with age, while physical-types of health care (rehabilitation, physical medicine and rehabilitation follow-up, and equipment) decreased with age, independently of ambulatory status. Use of other treatments, such as botulinum toxin injections, was not influenced by age. The provision of rehabilitation was particularly affected by the period of transition. INTERPRETATION: Although health care needs change naturally in adulthood, the large decrease in usage of specific types of rehabilitation after the transition to adulthood suggested individuals had difficulty accessing this type of health care after childhood. These results provide objectives for the development of patient-centred, transitional consultations, and longitudinal studies. WHAT THIS PAPER ADDS: Use of medication, particularly psychotropic and analgesic drugs, increased with age in individuals with cerebral palsy. Use of orthoses, physical medicine and rehabilitation physician follow-up, and rehabilitation decreased with age. Transition from childhood to adulthood involved significant changes in health care usage.

PMID: 30171608


AIM: To investigate trends in birth prevalence of cerebral palsy (CP) overall and by gestational age, and examine the distribution of motor type, spastic topography, and severity using Australian CP Register data from 1995 to 2009. METHOD: Prenatal and perinatal CP data were collated from state/territory CP registers. Birth prevalence estimates per 1000 live births and per 1000 neonatal survivors (NNS) were calculated in five epochs. Data from three state registers with population-level
ascertainment were used to investigate birth prevalence trends by gestational age using Poisson regression. Distribution of motor type, spastic topography, and moderate to severe disability (IQ ≤50 and/or Gross Motor Function Classification System levels III-V) were evaluated within birthweight categories. RESULTS: Birth prevalence of CP varied across population-level states but within each state declined significantly over time (p<0.05). Birth prevalence per 1000 neonatal survivors declined amongst children born before 28 weeks (South Australia, Victoria p<0.001) and those born at or after 37 weeks (Victoria p<0.001, Western Australia p=0.002). Across Australia the percentage of children with bilateral spastic CP declined amongst those born less than 1000g. The percentage of children with moderate to severe disability decreased (48%-34%, p<0.001).

INTERPRETATION: Birth prevalence of CP declined. Encouragingly, the percentage of children with CP whose disability was moderate to severe also decreased. WHAT THIS PAPER ADDS: Birth prevalence of cerebral palsy (CP) differed but declined across Australian states (1995-2009). Australian CP birth prevalence declined significantly amongst children born before 28 weeks and those born at or after 37 weeks. The percentage of children with moderate to severe disability decreased.

PMID: 30187914

Prevention and Cure

Paton MCB, Allison BJ, Li J, Fahey MC, Sutherland AE, Nitsos I, Bischof RJ, Dean JM, Moss TJM, Polglase GR, Jenkin G, McDonald CA, Miller SL.

BACKGROUND: Infants born preterm following exposure to in utero inflammation/chorioamnionitis are at high risk of brain injury and life-long neurological deficits. In this study, we assessed the efficacy of early intervention umbilical cord blood (UCB) cell therapy in a large animal model of preterm brain inflammation and injury. We hypothesised that UCB treatment would be neuroprotective for the preterm brain following subclinical fetal inflammation. METHODS: chronically instrumented fetal sheep at 0.65 gestation were administered lipopolysaccharide (LPS, 150 ng, 055:B5) intravenously over 3 consecutive days, followed by 100 million human UCB mononuclear cells 6 h after the final LPS dose. Controls were administered saline instead of LPS and cells. Ten days after the first LPS dose, the fetal brain and cerebrospinal fluid were collected for analysis of subcortical and periventricular white matter injury and inflammation. RESULTS: LPS administration increased microglial aggregate size, neutrophil recruitment, astrogliosis and cell death compared with controls. LPS also reduced total oligodendrocyte count and decreased mature myelinating oligodendrocytes. UCB cell therapy attenuated cell death and inflammation, and recovered total and mature oligodendrocytes, compared with LPS. CONCLUSIONS: UCB cell treatment following inflammation reduces preterm white matter brain injury, likely mediated via anti-inflammatory actions.

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