1. Children and adolescents with cerebral palsy flexibly adapt grip control in response to variable task demands
Sarah M Schwab, Francis M Grover, Drew H Abney, Paula L Silva, Michael A Riley


Background: Children and adolescents with cerebral palsy demonstrate impairments in grip control with associated limitations in functional grasp. Previous work in cerebral palsy has focused on grip control using relatively predictable task demands, a feature which may limit generalizability of those study results in light of recent evidence in typically developing adults suggesting that grip control strategies are task-dependent. The purpose of this study was to determine whether and how varying upper extremity task demands affect grip control in children and adolescents with cerebral palsy. Methods: Children and adolescents with mild spastic cerebral palsy (n = 10) and age- and gender-matched typically developing controls (n = 10) participated. Participants grasped an object while immersed in a virtual environment displaying a moving target and a virtual representation of the held object. Participants aimed to track the target by maintaining the position of the virtual object within the target as it moved in predictable and unpredictable trajectories. Findings: Grip control in children with cerebral palsy was less efficient and less responsive to object load force than in typically developing children, but only in the predictable trajectory condition. Both groups of participants demonstrated more responsive grip control in the unpredictable compared to the predictable trajectory condition. Interpretation: Grip control impairments in children with cerebral palsy are task-dependent. Children and adolescents with cerebral palsy demonstrated commonly observed grip impairments in the predictable trajectory condition. Unpredictable task demands, however, appeared to attenuate impairments and, thus, could be exploited in the design of therapeutic interventions.

PMID: 32829238

2. Mechanisms of reduced plantarflexor function in Cerebral palsy: smaller triceps surae moment arm and reduced muscle force
Tessa L Gallinger, Jared R Fletcher, Brian R MacIntosh


Both muscle forces, and moment arm (MA) could contribute to reduced muscle moment in people with Cerebral Palsy (CP). Current reports in CP are conflicting. The tendon travel method of estimating MA requires constant force, but passive force is high and variable in CP, and range of motion is limited. Therefore, the purpose of this study was to examine triceps surae muscle MA in 12 subjects with mild to moderate CP (15-32 years) and 10 typically developing peers (TD, 17-26 years) by tendon travel and by visually measuring the apparent MA. MA was calculated at 90° and at a reference angle (~106°) with zero net passive moment. The tendon travel (28.8 ± 5.6 mm) and visual methods (29.1 ± 5.5 mm) yielded similar MA in CP (p = 0.94) at the reference angle. TD had significantly larger triceps surae muscle MA than CP subjects (p = 0.002), 35.4 ± 4.1

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mm at the reference angle for tendon travel and 35.4 ± 3.6 mm by the visual method. Test/retest revealed less bias (0.8 mm) using the visual method. Calculated active peak isometric force was significantly less in CP (1983.8 ± 887.0 N) than TD (4104.9 ± 1154.9 N, p < 0.001). There are challenges in estimating MA in CP, but the visual method is more reliable. Although a shorter moment arm would reduce the joint moment, joint angular velocity for a given velocity of muscle shortening would be enhanced. Strength training may mitigate the effects of the smaller moment arm and reduced joint moment generated in those with CP.

PMID: 32827781

3. Postural deformity in children with cerebral palsy: Why it occurs and how is it managed
Haruhiko Sato


Despite the fact that children with cerebral palsy may not have any deformities at the time of birth, postural deformities, such as scoliosis, pelvic obliquity, and windswept hip deformity, can appear with increasing age. This may lead to respiratory function deterioration and, in more severe cases, affects survival. To date, postural care is believed to help improve the health and quality of life of children with cerebral palsy. This review provides an overview of the cause and clinical management of postural deformity that is seen in children with cerebral palsy.

PMID: 32850273

4. Safety of the LCP Pediatric Hip Plate in Proximal Femoral Osteotomy in Children with Cerebral Palsy
Omar Q Samarah, Majd A Shaheen, Rana A Tehabsim, Bayan A Shaheen, Marah B Makahleh, Mahmoud M Almustafa, Fadi A Al Hadidi, Lutfi A Hussein, Yazan S Hammad


Purpose: Proximal femoral osteotomy in cerebral palsy patients is a demanding procedure. The fixation of the osteotomy can fail due to the weak osteoporotic bone. The LCP pediatric hip plate with its good grip makes these procedures safe. The aims of the present study are to evaluate the radiological outcome of proximal femoral osteotomy that was fixed with the pediatric LCP in cerebral palsy patients and to raise safety issues regarding its low rate of complications. Patients and methods: Sixteen patients with cerebral palsy who were operated in our department were included in this retrospective study. Data collected from medical charts and X-ray measurements retrospectively reviewed. Results: In total, 16 patients (21 hips), ie, 9 males and 7 females, were included in this analysis. The mean age at the time of the index surgery was 11.9 years (5.9-18.0). The mean follow-up period was 4.78 years (1.5-8.0). Five patients had bilateral hip involvement and 11 had unilateral involvement. All patients had spastic cerebral palsy. The mean values of varus correction and de-rotation were 25° (0°-45°) and 35° (20°-50°), respectively. Neck shaft angle and the Reimer's migration index were significantly improved postoperatively (p<0.01 for both). Seventeen hips showed complete consolidation within 14 weeks of fixation and four hips needed 16 weeks. These four hips were in three patients who were 16 years of age or older. The correlation between age at surgery and the time needed for consolidation was statistically significant (p=0.01 for both). Avascular necrosis, revision surgeries, failure of fixation, acetabular penetration, screw loosening or fracture of the femur were not seen in this study. Conclusion: The LCP pediatric hip plate can be used safely in CP patients. The plate provides a strong stable fixation on osteoporotic bone with a low rate of complications.

PMID: 32848407

5. An analytical insight into how walking speed and spatial- and temporal-symmetry are related to ankle dysfunctions in children with hemiplegic cerebral palsy
Ragab K Elnaggar


Objective: To identify the major determining factors among ankle dysfunctions for walking speed and symmetry in children
with hemiplegic cerebral palsy (hCP). Design: This was a prospective analysis that included 52 children with hCP, aged between 5-8 years, had mild spasticity, and were functioning at Gross Motor Function Classification System level I or II. The dorsi and plantar flexors strength, dynamic spasticity (represented by gastrocnemius muscle-lengthening velocity during stance phase), plantar flexors stiffness, ankle joint position-sense, and walking performance (spatiotemporal parameter) were assessed. Results: The least absolute shrinkage and selection operator regression analyses showed that the dorsiflexor strength of the paretic limb was the major determining factor of walking speed (R = 0.38, P<.001). Dynamic spasticity of the plantar flexors explained a portion of the variance in walking speed (R = 0.15, P<.001) and the highest portion of the variance in spatial walking-symmetry (R = 0.18, P=.002). In addition, the ankle joint position-sense was the primary determinant of temporal walking-symmetry (R = 0.10, P=.021). Conclusion: In children with hCP, walking speed is mostly influenced by dorsiflexor muscles strength, temporal walking-symmetry is associated with the joint position-sense, while spatial walking-symmetry is explicated by the dynamic spasticity of the plantar flexor muscles.

PMID: 32858535

6. Multi-segment foot model reveals distal joint kinematic differences between habitual heel-toe walking and non-habitual toe walking

Elijah C Kuska, Joaquin A Barrios, Allison L Kinney


Toe walking is observed in pathological populations including cerebral palsy, stroke, and autism spectrum disorder. To understand pathological toe walking, previous studies have analyzed non-habitual toe walking. These studies found sagittal plane deviations between heel-toe and toe walking at the hip, knee, and ankle. Further investigation is merited as toe walking may involve altered biomechanics at more distal joints, such as the midtarsal joint. The purpose of this study was to examine biomechanical differences between rearfoot strike walking (RFSW) and non-rearfoot strike walking (NRFSW) in the midfoot and ankle. We hypothesized that during NRFSW, midtarsal kinematics would diverge from those during RFSW in all three cardinal planes and ankle kinematics would display increased supination. Twenty-four healthy females walked overground with both walking patterns. Motion capture, electromyography (EMG), and force plate data were collected. A validated multi-segment foot model was used with mean difference waveform analyses to compare walking conditions during stance. Significantly different kinematics were found in all three planes for the midtarsal and ankle joint during NRFSW. The NRFSW midtarsal joint exhibited increased plantarfexion, eversion, and adduction with the largest differences occurring at initial contact and in the sagittal plane. The NRFSW ankle exhibited increased supination at initial contact and during early stance. These findings indicate that toe walking alters both distal and proximal foot joint kinematics in multiple planes. This may further the understanding of altered biomechanics during toe walking while providing a basis for future analyses of pathological gait.

PMID: 32827776

7. The Effectiveness of Hippotherapy to Recover Gross Motor Function in Children with Cerebral Palsy: A Systematic Review and Meta-Analysis

Laura De Guindos-Sanchez, David Lucena-Anton, Ines Carmona-Barrientos, Jose A Moral-Munoz, Alejandro Salazar


Cerebral palsy (CP) is a permanent disorder of the posture and movement, which can result in impairments of gross motor function, among others. Hippotherapy (HPT) is an emerging intervention to promote motor recovery in patients with neurological disorders, providing a smooth, precise, rhythmic, and repetitive pattern of movement to the patient. The main objective of this systematic review and meta-analysis of randomized controlled clinical trials was to analyze the effectiveness of HPT interventions on gross motor function in subjects with CP. The following databases were searched in May 2019: PubMed, Scopus, Embase, and Web of Science. The methodological quality of the randomized controlled trials was assessed using the Physiotherapy Evidence Database (PEDro) scale. A total of 10 studies were analyzed in this review, involving 452 participants. Favorable effects were obtained on the gross motor function (Gross Motor Function Measure-66, standardized mean difference (SMD) = 0.81, 95% confidence interval (CI) = 0.47-1.15, Gross Motor Function Measure-88 dimension A SMD = 0.64, 95% CI = 0.30-0.97, dimension B SMD = 0.42, 95% CI = 0.09-0.75, and dimension E SMD = 0.40, 95% CI = 0.06-0.73). The results obtained in the present review show the potential benefit of HPT intervention in improving gross motor function in children with CP.
The pendulum test assesses quadriceps spasticity by dropping the lower leg of a relaxed patient from the horizontal position and observing limb movement. The first swing excursion (FS) decreases with increasing spasticity severity. Our recent simulation study suggests that the reduced initial swing results from muscle short-range stiffness and its interaction with reflex hyper-excitability. Short-range stiffness emerges from the thixotropic behavior of muscles where fiber stiffness upon stretch increases when the muscle is held isometric. Fiber stiffness might thus be higher during the first swing of the pendulum test than during consecutive swings. In addition, it has recently been suggested that muscle spindle firing reflects fiber force rather than velocity and therefore, reflex activity might depend on fiber stiffness. If this hypothesized mechanism is true, we expect to observe larger first swing excursions and reduced reflex muscle activity when the leg is moved rather than kept isometric before release, especially in patients with increased reflex activity. We performed the pendulum test in 15 children with cerebral palsy (CP) and 15 age-matched typically developing (TD) children in two conditions. In the hold condition, the leg was kept isometric in the extended position before release. In the movement condition, the leg was moved up and down before release to reduce the contribution of short-range stiffness. Knee kinematics and muscle activity were recorded. Moving the leg before release increased first swing excursion (p < 0.001) and this increase was larger in children with CP (21°) than in TD children (8°) (p < 0.005). In addition, pre-movement delayed reflex onset by 87 ms (p < 0.05) and reduced reflex activity as assessed through the area under the curve of rectus femoris electromyography (p < 0.05) in children with CP. The movement history dependence of pendulum kinematics and reflex activity supports our hypothesis that muscle short-range stiffness and its interaction with reflex hyper-excitability contribute to joint hyper-resistance in spastic CP. Our results have implications for standardizing movement history in clinical tests of spasticity and for understanding the role of spasticity in functional movements, where movement history differs from movement history in clinical tests.

The association between physical activity and health has been clearly established, and the promotion of physical activity should be viewed as a cost-effective approach that is universally prescribed as a first-line treatment for nearly every chronic disease. Health care providers involved in the care for individuals with cerebral palsy (CP) are encouraged to take an active role in promoting their health and well-being. Balancing activity behaviours across the whole day, with improved physical activity, reduced sedentary time, and healthy sleep behaviours, can set up infants, preschool-, and school-aged children with CP for a healthy trajectory across their lifetime. However, most clinicians do not apply a systematic surveillance, assessment, and management approach to detect problems with physical activity or sleep in children with CP. Consequently, many children with CP miss out on an important first line of treatment. This article presents an evidence-informed clinical practice guide with practical pointers to help practitioners in detecting 24-hour activity problems as a critical step towards adoption of healthy lifestyle behaviours for children with CP that provide long-term health benefits. WHAT THIS PAPER ADDS: The 24-hour activity checklist detects problems in children with cerebral palsy (CP). A CP-specific infographic facilitates effective 24-hour activity counselling and education.

Purpose: The objective of this study was to determine risk factors for epilepsy and drug-resistant epilepsy (DRE) development in children with cerebral palsy. Method: Two hundred twenty-nine patients presenting to the pediatric neurology clinic and diagnosed as having cerebral palsy between November 2016 and November 2019 were included in the study. Medical histories and clinical, laboratory, and radiological findings were examined retrospectively from patient records in the hospital data system. Results: Girls represented 103 patients (45%) and boys 126 (55%). The patients' mean age was 8.39 ± 4.54 years. Epileptic seizures were present in 120 (52.4%) patients and drug-resistant seizures in 64 (27.9%). The risk of epilepsy was significantly higher in patients with motor or speech impairment, with hearing impairment, or undergoing first seizure in the neonatal period. We also observed a higher risk of epilepsy in patients with psychiatric comorbidity, particularly autism spectrum disorder. The risk of epilepsy was also higher in patients with microcephaly or quadriplegic cerebral palsy and in patients with focal and generalized epileptiform abnormality on electroencephalograms (EEGs). However, no significant difference was identified when all these factors were evaluated in terms of the risk of developing DRE. Conclusion: Patients with cerebral palsy have high comorbid epilepsy rates. We think that the risk of epilepsy may be higher in patients undergoing first seizure in the neonatal period, with microcephaly, with quadriplegic type cerebral palsy, and with additional psychiatric comorbidity. The rate of DRE development was very low in patients with normal EEG findings or with only background rhythm abnormalities on first EEGs during neonatal seizures. This may be regarded as a good prognostic factor for nondevelopment of DRE.

PMID: 32858364

11. Factors associated with spoken language comprehension in children with cerebral palsy: a systematic review


Aim: To identify factors that are relevant for spoken language comprehension in children with cerebral palsy (CP), following the International Classification of Functioning, Disability and Health - Children and Youth (ICF-CY) framework. Method: A systematic literature search was conducted using the electronic literature databases PubMed, Embase, PsycInfo, and Cochrane Library, from January 1967 to December 2019. Included studies involved children with CP, results regarding spoken language comprehension, and analysis of at least one associated factor. Factors were classified within ICF-CY domains. Results: Twenty-one studies met inclusion criteria. Factors in the ICF-CY domains of body functions and structure were most frequently reported. White brain matter abnormalities, motor type, functional mobility, and intellectual functioning appear to be relevant factors in spoken language comprehension in CP. Factors in the domain of activities and participation, as well as contextual factors, have rarely been studied in the context of spoken language comprehension in CP. Interpretation: Most factors known to be important for spoken language comprehension in typically developing children and/or known to be susceptible to change by interventions are understudied in CP.

PMID: 32852786

12. Complementary and Alternative Therapy Use in Children with Cerebral Palsy
Maryam Oskoui, Pamela Ng, Michele Zaman, David Buckley, Adam Kirton, Esias van Rensburg, Ellen Wood, Michael Shevell, Annette Majnemer


PMID: 32854793

13. Decreasing cerebral palsy prevalence in multiple births in the modern era: a population cohort study of European data
Oliver Perr, Judith Rankin, Mary Jane Platt, Elodie Sellier, Catherine Arnaud, Javier De La Cruz, Ingeborg Krägeloh-Mann, David G Sweet, Solveig Bjellmo

PMID: 32852505
Multiple births (twins or higher order multiples) are increasing in developed countries and may present higher risk for cerebral palsy (CP). However, few studies can reliably investigate trends over time because these outcomes are relatively rare.

Objectives: We pooled data from European CP registers to investigate CP birth prevalence and its trends among single and multiple births born between 1990 and 2008. Design: Population cohort study. Setting: 12 population-based registers from the Surveillance of Cerebral Palsy in Europe collaboration. Participants: 4 446 125 single and multiple live births, of whom 8416 (0.19%) had CP of prenatal or perinatal origin. Main outcomes: CP diagnosis ascertained in childhood using harmonised methods; CP subtype; Motor impairment severity among CP cases. Results: The rate of multiple births increased from 1990. Multiples displayed higher risk for CP (RR=4.27, 95% CI 4.00 to 4.57). For singletons and multiples alike, risk for CP was higher among births of lower gestational age (GA) or birth weight (BW). However, CP birth prevalence declined significantly among very preterm (<32 weeks) and very low BW (<1500 g) multiples. Singletons and multiples with CP displayed similar severity of motor impairment. Conclusions: Between 1990 and 2008, CP birth prevalence decreased steadily among multiples with low GA or BW. Furthermore, multiples with CP display similar profiles of severe motor impairment compared with CP singletons. Improvements in management of preterm birth since the 1990s may also have been responsible for providing better prospects for multiples.
implants for specific characteristics and, on expenditure side, not exceeding funding of direct expenses intended for this treating process.

PMID: 32856814

16. Polypharmacy Among Privately Insured Adults with Cerebral Palsy: A Retrospective Cohort Study
Daniel G Whitney, Mary Schmidt, Mark D Peterson, Heidi Haapala


Background: Adults with cerebral palsy (CP) have increased risk for developing various secondary chronic diseases, especially when they have other neurodevelopmental disabilities (NDDs). Multiple medications are likely prescribed to manage the greater morbidity-related burden for adults with CP; however, because health care delivery and care coordination is suboptimal for this population, adults with CP may have an increased risk for polypharmacy. To date, very little is known about the prescribing practices and extent of polypharmacy for adults with CP. Objective: To determine the prevalence and adjusted odds of polypharmacy among adults with CP only and those with CP+NDDs, compared with adults without CP. Methods: Data from 2017 Optum Clinformatics Data Mart, a U.S. private administrative database, was used for this retrospective cohort study. Diagnosis codes were used to identify adults (aged ≥ 18 years) with CP, NDDs (e.g., intellectual disabilities, epilepsy, and autism spectrum disorders), and 24 relevant morbidities. Polypharmacy was examined as 0-4 versus ≥ 5, 0-9 versus ≥ 10, and 0-14 versus ≥ 15 medications. Logistic regression estimated the OR and 95% CI of polypharmacy before and after adjusting for age, sex, region of residence, and multimorbidity (as 0, 1, 2, 3, 4-5, and ≥ 6 morbidities). Exploratory analyses were conducted to compare polypharmacy among young (18-40 years) and middle-aged (41-64 years) adults with CP only and CP + NDDs with elderly (≥ 65 years) adults without CP. Results: Adults with CP only (n = 5,603) and CP + NDDs (n = 2,474) had higher unadjusted prevalence and adjusted OR for each polypharmacy definition compared with adults without CP (n = 9.0 million; e.g., ≥ 5 medications: adjusted OR for CP only = 1.38, 95% CI = 1.30-1.47; CP + NDDs: OR = 2.42, 95% CI = 2.20-2.67). Adults with CP+NDDs had higher unadjusted prevalence and adjusted OR of each polypharmacy definition compared with CP only. Compared with elderly without CP, the unadjusted prevalence of polypharmacy was lower for young adults with CP only (e.g., ≥ 5 medications: 60.2%, 43.8%), similar for young adults with CP+NDDs (e.g., ≥ 15 medications: 10.9%, 12.5%), and elevated for middle-aged CP only and CP + NDDs (e.g., ≥ 10 medications: 28.7%, 34.3%, 41.7%). Conclusions: Privately insured adults with CP only and CP + NDDs have an elevated prevalence of polypharmacy compared with adults without CP, even after accounting for multimorbidity. Importantly, adults aged 18-40 years with CP have a similar (CP + NDDs) prevalence of polypharmacy compared with the general geriatric population, with the prevalence increasing further for CP by middle age. Disclosures: Whitney was supported by the University of Michigan Office of Health Equity and Inclusion Diversity Fund and the American Academy of Cerebral Palsy and Developmental Medicine. These funding sources had no role in the design or conduct of the study; collection, management, analysis, or interpretation of the data; preparation, review, or approval of the manuscript; or the decision to submit the manuscript for publication. The other authors have no conflicts of interest to disclose.

PMID: 32857655

Syed Ahmar Shah, Peter Brown, Hortensia Gimeno, Jean-Pierre Lin, Verity M McClelland


Background: While Deep Brain Stimulation (DBS) of the Globus pallidus internus is a well-established therapy for idiopathic/genetic dystonia, benefits for acquired dystonia are varied, ranging from modest improvement to deterioration. Predictive biomarkers to aid DBS prognosis for children are lacking, especially in acquired dystonias, such as dystonic Cerebral Palsy. We explored the potential role of machine learning techniques to identify parameters that could help predict DBS outcome. Methods: We conducted a retrospective study of 244 children attending King's College Hospital between September 2007 and June 2018 for neurophysiological tests as part of their assessment for possible DBS at Evelina London Children's Hospital. For the 133 individuals who underwent DBS and had 1-year outcome data available, we assessed the potential predictive value of six patient parameters: sex, etiology (including cerebral palsy), baseline severity (Burke-Fahn-Marsden Dystonia Rating Scale-motor score), cranial MRI and two neurophysiological tests, Central Motor Conduction Time (CMCT) and Somatosensory Evoked Potential (SEP). We applied machine learning analysis to determine the best combination of these features to aid DBS prognosis. We developed a classification algorithm based on Decision Trees (DTs) with k-fold cross validation for independent
testing. We analyzed all possible combinations of the six features and focused on acquired dystonias. Results: Several trees resulted in better accuracy than the majority class classifier. However, the two features that consistently appeared in top 10 DTs were CMCT and baseline dystonia severity. A decision tree based on CMCT and baseline severity provided a range of sensitivity and specificity, depending on the threshold chosen for baseline dystonia severity. In situations where CMCT was not available, a DT using SEP alone provided better than the majority class classifier accuracy. Conclusion: The results suggest that neurophysiological parameters can help predict DBS outcomes, and DTs provide a data-driven, highly interpretable decision support tool that lends itself to being used in clinical practice to help predict potential benefit of DBS in dystonic children. Our results encourage the introduction of neurophysiological parameters in assessment pathways, and data collection to facilitate multi-center evaluation and validation of these potential predictive markers and of the illustrative decision support tools presented here.

PMID: 32849251

18. Does caesarean delivery in the first pregnancy increase the risk for adverse outcome in the second? A registry-based cohort study on first and second singleton births in Norway
Solveig Bjellmo, Guro L Andersen, Sissel Hjelle, Kari Klungsoyr, Lone Krebs, Stian Lydersen, Pål Richard Romundstad, Torstein Vik


Objective: To explore if newborns in the second pregnancy following a previous caesarean delivery (CD) have higher risk of perinatal mortality or cerebral palsy than newborns in pregnancies following a previous vaginal delivery (VD). Design: Cohort study with information from the Medical Birth Registry of Norway and the Cerebral Palsy Registry of Norway. Setting: Births in Norway. Participants: 294,598 women with their first and second singleton delivery during 1996-2015. Main outcome measures: Stillbirth, perinatal mortality, neonatal mortality and cerebral palsy. Results: Among 294,598 included women, 42,962 (15%) had a CD in their first pregnancy while 251,636 (85%) had a VD. Compared with the second delivery of mothers with a previous VD, the adjusted OR (adjOR), for stillbirth in the second pregnancy following a previous CD was 1.45, 95% CI 1.22 to 1.73; for perinatal death the adjOR was 1.42 (1.22 to 1.73) and for neonatal death 1.13 (0.86 to 1.49). Among children who survived the neonatal period, the adjOR for cerebral palsy was 1.27 (0.99 to 1.64). Secondary outcomes, including small for gestational age, preterm and very preterm birth, uterine rupture and placental complications (eg, postpartum haemorrhage and pre-eclampsia) were more frequent in the subsequent pregnancy following a previous CD compared with a previous VD, in particular for uterine rupture adjOR 86.7 (48.2 to 156.1). Adjustment for potential confounders attenuated the ORs somewhat, but the excess risk in the second pregnancy persisted for all outcomes. Conclusion: A previous CD was in this study associated with increased risk for stillbirth and perinatal death compared with a previous VD. Although less robust, we also found that a previous CD was associated with a slightly increased risk of cerebral palsy among children surviving the neonatal period. The aetiology behind these associations needs further investigation.

PMID: 32830116

19. A Maternal-Administered Multimodal Neonatal Bundle in Hospitalized Very Preterm Infants: A Pilot Study
Lisa Letzkus, Corrie Alonzo, Elizabeth Connaughton, Nancy Kelly, Santina Zanelli


Background: Premature infants are at an increased risk for developing cerebral palsy (CP). Evidence-based strategies designed to promote healthy brain development and facilitate adaptation after brain injury in infants still admitted to the neonatal intensive care unit (NICU) represent a novel approach that may lead to improved long-term outcomes. Purpose: To investigate the feasibility of a maternal-administered early intervention bundle in very preterm infants prior to NICU discharge. Methods: A pilot trial evaluating a maternal-administered NICU-based bundle of interventions in preterm infants (≤32 weeks’ gestational age and/or ≤1500 g birth weight). The impact of the bundle on short-term developmental outcomes of infants, as well as maternal stress, anxiety, and depression, is evaluated. Results: The intervention bundle was implemented in 11 mother-infant dyads (including 1 set of twins) for a median of 8 weeks and was overall well received. Vocal soothing, scent exchange, and comforting touch were feasible, performed at or above the predetermined goal of 71% of the time (5/7 days), while kangaroo care and infant massage were not. Maternal stress, anxiety, and depression were decreased during the study time. Implications to practice: A neonatal multimodal intervention bundle provided by mothers is feasible. Implications to research: Additional randomized controlled studies are needed to determine whether this type of bundled interventions can (1) improve the
neurodevelopmental outcomes of participating infants and (2) improve long-term parental outcomes, including decreased burden of anxiety and depression, as well as improved attachment and optimal patterns of social interaction.

PMID: 32826409

20. Muscle Microbiopsy to Delineate Stem Cell Involvement in Young Patients: A Novel Approach for Children With Cerebral Palsy
Marlies Corvelyn, Nathalie De Beukelaer, Robin Duelen, Jorieke Deschrevel, Anja Van Campenhout, Sandra Prinsen, Ghislaine Gayan-Ramirez, Karen Maes, Guido Weide, Kaat Desloovere, Maurilio Sampaolesi, Domiziana Costamagna


Cerebral palsy (CP), the single largest cause of childhood physical disability, is characterized firstly by a lesion in the immature brain, and secondly by musculoskeletal problems that progress with age. Previous research reported altered muscle properties, such as reduced volume and satellite cell (SC) numbers and hypertrophic extracellular matrix compared to typically developing (TD) children (>10 years). Unfortunately, data on younger CP patients are scarce and studies on SCs and other muscle stem cells in CP are insufficient or lacking. Therefore, it remains difficult to understand the early onset and trajectory of altered muscle properties in growing CP children. Because muscle stem cells are responsible for postnatal growth, repair and remodeling, multiple adult stem cell populations from young CP children could play a role in altered muscle development. To this end, new methods for studying muscle samples of young children, valid to delineate the features and to elucidate the regenerative potential of muscle tissue, are necessary. Using minimal invasive muscle microbiopsy, which was applied in young subjects under general anesthesia for the first time, we aimed to isolate and characterize muscle stem cell-derived progenitors of TD children and patients with CP. Data of 15 CP patients, 3-9 years old, and 5 aged-matched TD children were reported. The muscle microbiopsy technique was tolerated well in all participants. Through the explant technique, we provided muscle stem cell-derived progenitors from the Medial Gastrocnemius. Via fluorescent activated cell sorting, using surface markers CD56, ALP, and PDGFRA, we obtained SC-derived progenitors, mesoangioblasts and fibro-adipogenic progenitors, respectively. Adipogenic, skeletal, and smooth muscle differentiation assays confirmed the cell identity and ability to give rise to different cell types after appropriate stimuli. Myogenic differentiation in CP SC-derived progenitors showed enhanced fusion index and altered myotube formation based on MYOSIN HEAVY CHAIN expression, as well as disorganization of nuclear spreading, which were not observed in TD myotubes. In conclusion, the microbiopsy technique allows more focused muscle research in young CP patients. Current results show altered differentiation abilities of muscle stem cell-derived progenitors and support the hypothesis of their involvement in CP-altered muscle growth.

PMID: 32848872

21. Effect of antenatal magnesium sulphate on MRI biomarkers of white matter development at term equivalent age: The magnum study
Tanya Poppe, Benjamin Thompson, James P Boardman, Mark E Bastin, Jane Alsweiler, Gerard Deib, Jane E Harding, Caroline A Crowther, MagNUM Study Group


Background: Magnesium sulphate given to women immediately prior to very preterm birth protects the perinatal brain, so fewer babies die or develop cerebral palsy. How magnesium sulphate exerts these beneficial effects remains uncertain. The aim of the MagNUM Study was to assess the effect of exposure to antenatal magnesium sulphate on MRI measures of brain white matter microstructure at term equivalent age. Methods: Nested cohort study within the randomised Magnesium sulphate at 30 to <34 weeks' Gestational age Neuroprotection Trial (MAGENTA). Mothers at risk of preterm birth at 30 to <34 weeks' gestation were randomised to receive either 4 g of magnesium sulphate heptahydrate [8 mmol magnesium ions], or saline placebo, infused over 30 min when preterm birth was planned or expected within 24 h. Participating babies underwent diffusion tensor MRI at term equivalent age. The main outcomes were fractional anisotropy across the white matter tract skeleton compared using Tract-based Spatial Statistics (TBSS), with adjustment for postmenstrual age at birth and at MRI, and MRI site. Researchers and families were blind to treatment group allocation during data collection and analyses. Findings: Of the 109 participating babies the demographics of the 60 babies exposed to magnesium sulphate were similar to the 49 babies exposed to placebo. In babies whose mothers were allocated to magnesium sulphate, fractional anisotropy was higher within the corticospinal tracts and corona radiata, the superior and inferior longitudinal fasciculi, and the inferior fronto-occipital fasciculi compared to babies whose mothers were allocated placebo (P < 0.05). Interpretation: In babies born preterm, antenatal
magnesium sulphate exposure promotes development of white matter microstructure in pathways affecting both motor and cognitive function. This may be one mechanism for the neuroprotective effect of magnesium sulphate treatment prior to preterm birth. Funding: Health Research Council of New Zealand.

PMID: 32858399