
Shikako-Thomas K, Fehlings D, Germain M, Gordon AM, Maynard D, Majnemer A.


BACKGROUND: Intensive upper extremity training (IUET) has demonstrated efficacy in clinical and functioning outcomes in children with hemiplegia. However, implementation in the clinical context requires novel service models and knowledge translation. AIMS: To map implementation of IUET in Canada, to identify factors associated with the implementation and best practices for implementation. METHODS: Mixed-methods design; descriptive statistics, chi-square tests. Individual phone interviews and focus groups with purposeful sampling. Thematic analysis; telephone surveys with managers of 31 pediatric rehabilitation centers across Canada. Four focus groups across Canada and one in the Netherlands. RESULTS: Implementation of IUET group interventions is limited in Canada (7/31). Barriers included beliefs and values related to evidence-based practice, opportunities for continuing education, researchers-clinicians partnerships, access to scientific literature, and the presence of a champion. Pressure from parents and media presenting IUET as a novel and effective therapy, support and flexibility of families, having the critical mass of clients and a managerial willingness to accommodate new ideas and restructure service provision were some facilitators. CONCLUSIONS: Uptake of the evidence requires many steps described in the knowledge translation cycle. Factors identified in the study could be considered in most clinical settings to facilitate the uptake of research evidence for IUET.

PMID: 28509591

2. Combined transcranial Direct Current Stimulation and robotic upper limb therapy improves upper limb function in an adult with cerebral palsy.

Friel KM, Lee P, Soles LV, Smorenburg ARP, Kuo HC, Edwards DJ.


BACKGROUND: Robotic therapy can improve upper limb function in hemiparesis. Excitatory transcranial direct current stimulation (tDCS) can prime brain motor circuits before therapy. OBJECTIVE: We tested safety and efficacy of tDCS plus robotic therapy in an adult with unilateral spastic cerebral palsy (USCP). METHODS: In each of 36 sessions, anodal tDCS (2 mA, 20min) was applied over the motor map of the affected hand. Immediately after tDCS, the participant completed robotic therapy, using the shoulder, elbow, and wrist (MIT Manus). The participant sat in a padded chair with affected arm abducted, forearm supported, and hand grasping the robot handle. The participant controlled the robot arm with his affected arm to move a cursor from the center of a circle to each of eight targets (960 movements). Motor function was tested before, after, and six
months after therapy with the Wolf Motor Function Test (WMFT) and Fugl-Meyer (FM). RESULTS: Reaching accuracy on the robot task improved significantly after therapy. The WMFT and FM improved clinically meaningful amounts after therapy. Improvements were maintained six months after therapy. CONCLUSIONS: Combined tDCS and robotics safely improved upper limb function in an adult with USCP.

PMID: 28505986

3. The influence of a constraint and bimanual training program using a variety of modalities on endurance and on the cardiac autonomic regulation system of children with unilateral cerebral palsy: A self-control clinical trial.

Cohen-Holzer M, Sorek G, Schweizer M, Katz-Leurer M.


BACKGROUND: An intensive hybrid program, combining constraint with bimanual training, improves upper extremity function as well as walking endurance of children with unilateral cerebral palsy (UCP). Endurance improvement may be associated with the cardiac autonomic regulation system (CARS) adaptation, known to be impaired among these children. OBJECTIVE: To examine the influence of an intensive hybrid program on CARS, walking endurance and the correlation with upper extremity function of children with UCP. METHODS: 24 children aged 6-10 years with UCP participated in a hybrid program, 10 days, 6 hours per day. Data were collected pre-, post- and 3-months post-intervention. Main outcome measures included the Polar RS800CX for heart rate (HR) and heart rate variability (HRV) data, the 6-Minute Walk Test (6MWT) for endurance, and the Assisting Hand Assessment (AHA) and Jebsen-Taylor Test of Hand Function (JTTHF) for bimanual and unimanual function. RESULTS: A significant reduction in HR and an increase in HRV at post- and 3-month post-intervention was noted ($\chi^2=8.3$, $p=0.016$) along with a significant increase in 6MWT with a median increase of 81 meters ($\chi^2=11.0$, $p=0.004$) at the same interval. A significant improvement was noted in unimanual and bimanual performance following the intervention. CONCLUSIONS: An intensive hybrid program effectively improved CARS function as well as walking endurance and upper extremity function in children with UCP (213).

PMID: 28505992


Öunpuu S, Solomito M, Bell K, Pierz K.


External femoral derotation osteotomy (FDO) is an orthopaedic intervention to correct increased femoral anteversion and associated excessive internal hip rotation and internal foot progression during gait in children with cerebral palsy. The resulting functional issues may include clearance problems and hip abductor lever-arm dysfunction. The purpose of this study was to evaluate long-term gait outcomes of FDO. Twenty ambulatory patients (27 sides) with cerebral palsy who underwent pre-operative (P0) and a one year post-operative (P1) gait analysis as part of the standard of care had a second post-operative analysis (P2) approximately 11 years post-surgical intervention. Mean hip rotation in stance showed statistically significant decreases in internal rotation at P1 post-surgical intervention that were maintained long-term (mean hip rotation P0: 21±9, P1: 0±9 and P2: 6±12 degrees internal). Similar results were seen with mean foot progression (P0: 9±16 degrees internal, P1: 14±13 degrees external, P2: 13±16 degrees external). However, 2/27 sides (9%) showed a recurrence of internal hip rotation of >15° at the 11year follow-up. The reasons for this recurrence could include age, surgical location and ongoing disease process all of which need to be further examined. We conclude that FDO can show long-term kinematic and functional benefits when performed in the prepubescent child with cerebral palsy in comparison to the natural progression of of hip rotation in cerebral palsy.

PMID: 28521149
5. Knee Recurvatum in Children With Spastic Diplegic Cerebral Palsy.

Bauer J, Patrick Do K, Feng J, Pierce R, Aiona M.


BACKGROUND: The purpose of this study is to determine which factors drive patients with diplegic cerebral palsy to walk without knee recurvatum despite hyperextension of the knee on physical examination. METHODS: A retrospective review was conducted of all data collected in the Gait Analysis Laboratory between 1999 and 2014. Patients with spastic diplegic cerebral palsy and at least 5 degrees of knee extension on clinical examination were identified for the study. After IRB approval, a total of 60 children ranging in age from 4 to 17 were included in the study. There were 27 female patients. Gross Motor Function Classification System level was distributed in the population as follows: 34 patients at Gross Motor Function Classification System level I, 18 at level II, and 8 at level III. Patients were excluded from this study if they had extrapyramidal involvement, history of selective dorsal rhizotomy or lower extremity surgery. Patient who received botulinum toxin A injections within 1 year of the study were excluded as well. Patients were divided into 2 groups: children that walked with knee hyperextension (KH) and children that walked without knee hyperextension (KF, "knee flexion"). There were 15 subjects in the KH group and 45 subjects in the KF group. Motion laboratory evaluation included a comprehensive examination, kinematics, and kinetic analysis with a VICOM system. All data were analyzed with unpaired t test to detect differences between the 2 groups. All statistical analysis was done only for the right legs (unless the right leg did not meet the exclusion then the left leg was analyzed) to meet the statistical requirement for independence. The Pearson correlation was applied to correlate the maximum knee extension in stance with maximum ankle dorsiflexion in stance. RESULTS: The static measurement of dorsiflexion with knee flexed showed statistically significant difference (P=0.004) with KH group having 2.3±11.6 degrees and KF group having 13.1±12.2 degrees. There was also a statistically significant difference in the static measurement of dorsiflexion with knee extended (P=0.0014) with KH group having -3.3±9.0 degrees and KF group having 5.8±9.1 degrees. Maximum dorsiflexion in stance phase also showed significant difference (P=0.0022) with the KH group having 0.1±14.0 degrees and KF group having 11.5±11.2 degrees. Maximum dorsiflexion in stance phase also showed significant difference (P<0.001) with the DH group having 0.1 (SD) 14.0 degrees and KF group having 11.5 (SD) 12.0 degrees. There were no significant differences in popliteal angle measurements or any strength measurement. CONCLUSIONS: Our study shows that the plantar flexion knee extension couple is the major contributing factor to cause patients with passive knee hyperextension to walk in a recurvatum pattern. This would have implications of further treatment of the knee hyperextension in stance.

PMID: 28520679

6. Treadmill exercise improves motor and memory functions in cerebral palsy rats through activation of PI3K-Akt pathway.

Jung SY, Kim DY.


Cerebral palsy (CP) is a chronic disorder characterized by physical disability and disruption of brain function. We evaluated the effects of treadmill exercise on motor and memory functions in relation with phosphatidylinositol 3-kinase (PI3K)-Akt pathway using CP rat model. Rota-rod test, step-down avoidance task, 5-bromo-2'-deoxyuridine (BrdU) immunohistochemistry, and western blot for synapsin I, postsynaptic density-95 (PSD-95), PI3K, Akt, and glycogen synthase kinase-3β (GSK-3β) were performed. CP was induced by maternal lipopolysaccharide (LPS)-injection with sensorimotor restriction. Five weeks after birth, the rats in the exercise groups were made to run on the treadmill for 30 min per one day, 5 times a week, during 4 weeks. Motor and memory functions were impaired in the LPS-induced CP rats and treadmill exercise increased motor and memory functions in the CP rats. Cell proliferation in the hippocampus was suppressed in the LPS-induced CP rats and treadmill exercise increased hippocampal cell proliferation in the CP rats. Expressions of synapsin I, PSD-95, phosphorylated (p)-PI3K, and p-Akt were decreased in the LPS-induced CP rats and treadmill exercise enhanced the expressions of synapsin I, PSD-95, p-PI3K, and p-Akt in the CP rats. GSK-3β expression was increased in the LPS-induced CP rats and treadmill exercise suppressed GSK-3β expression in the CP rats. The present results suggest that treadmill exercise might improve motor and memory functions through activation of PI3K-Akt pathway.

PMID: 28503524


OBJECTIVE: To investigate the immediate effect of a single session of whole body vibration (WBV) on lower extremity spasticity in children with cerebral palsy (CP). METHODS: Seventeen children with spastic CP were included. A single session of WBV was administered: 10-minute WBV, 1-minute rest, and 10-minute WBV. The effects of WBV were clinically assessed with the Modified Ashworth Scale (MAS) and Modified Tardieu Scale (MTS) before and immediately, 30 minutes, 1 hour, 2 hours, 3 hours, and 4 hours after WBV. RESULTS: Spasticity of the ankle plantarflexor, as assessed by MAS and MTS scores, was reduced after WBV. Post-hoc analysis demonstrated that, compared to baseline, the MAS significantly improved for a period of 1 hour after WBV, and the R1 and R2-R1 of the MTS significantly improved for a period of 2 hours after WBV. CONCLUSION: A single session of WBV improves spasticity of ankle plantarflexors for 1-2 hours in children with CP. Future studies are needed to test whether WBV is an effective preparation before physiotherapy and occupational therapy.

PMID: 28503461


BACKGROUND AND PURPOSE: Improving functional mobility is often a desired outcome for adolescents with cerebral palsy (CP). Traditional neurorehabilitation approaches are frequently directed at impairments; however, improvements may not be carried over into functional mobility. The purpose of this case report was to describe the examination, intervention, and outcomes of a task-oriented physical therapy intervention program to improve dynamic balance, functional mobility, and dual-task performance in an adolescent with CP. CASE DESCRIPTION: The participant was a 15-year-old girl with spastic triplegic CP (Gross Motor Classification System Level II). Examination procedures included the Canadian Occupational Performance Measure, 6-minute walk test, Muscle Power Sprint Test, 10 x 5-meter sprint test, Timed Up and Down Stairs Test, Gross Motor Function Measure, Gillette Functional Assessment Questionnaire, and functional lower extremity strength tests. Intervention focused on task-oriented dynamic balance and mobility tasks that incorporated coordination and speed demands as well as task-specific lower extremity and trunk strengthening activities. Dual task demands were integrated into all intervention activities. OUTCOMES: Post-intervention testing revealed improvements in cardiovascular endurance, anaerobic power, agility, stair climbing, gross motor skills, and mobility. DISCUSSION: The participant appeared to benefit from a task-oriented program to improve dynamic balance, functional mobility, and dual-task performance.

PMID: 28509631

9. Relationship Between Mobility and Self-Care Activity in Children With Cerebral Palsy.


OBJECTIVE: To investigate the factors influencing the development of self-care activity, and the association between mobility and self-care activity in children with cerebral palsy (CP). METHODS: A total of 63 CP children aged ≥4 years, were studied retrospectively. Children with severe intellectual disability or behavioral problems were excluded. The relationship between the Gross Motor Function Classification System (GMFCS), the Manual Ability Classification System (MACS), and the Pediatric Evaluation of Disability Inventory (PEDI) was analyzed. Simple and multiple linear regression analyses were conducted for continuous variables, such as verbal intelligence quotient (IQ) and PEDI subscales. RESULTS: Final evaluation was done for 25 children, ranging from 4 to 11 years of age. According to GMFCS levels, the differences in PEDI-self care scores, showed statistically borderline significance (p=0.051). Conversely, differences in PEDI-self care scores according to CP types and MACS levels were not statistically significant. Simple linear regression analysis showed that PEDI mobility and PEDI social function significantly influence the PEDI self-care. Multiple linear regression analysis showed that PEDI mobility was the only
factor significantly influencing PEDI self-care in children aged ≥7 years (R²=0.875, p=0.03). CONCLUSION: Mobility is important for the acquisition of self-care abilities in children with CP aged ≥7 years.

PMID: 28503460


Michmizos KP, Krebs HI.


BACKGROUND: Robot-aided sensorimotor therapy imposes highly repetitive tasks that can translate to substantial improvement when patients remain cognitively engaged into the clinical procedure, a goal that most children find hard to pursue. Knowing that the child's brain is much more plastic than an adult's, it is reasonable to expect that the clinical gains observed in the adult population during the last two decades would be followed up by even greater gains in children. Nonetheless, and despite the multitude of adult studies, in children we are just getting started. There is scarcity of pediatric robotic rehabilitation devices that are currently available and the number of clinical studies that employ them is also very limited. PURPOSE: We have recently developed the MIT's pedi-Anklebot, an adaptive habilitation robotic device that continuously motivates physically impaired children to do their best by tracking the child's performance and modifying their therapy accordingly. The robot's design is based on a multitude of studies we conducted focusing on the ankle sensorimotor control. In this paper, we briefly describe the device and the adaptive environment we built around the impaired children, present the initial clinical results and discuss how they could steer future trends in pediatric robotic therapy. CONCLUSIONS: The results support the potential for future interventions to account for the differences in the sensorimotor control of the targeted limbs and their functional use (rhythmic vs. discrete movements and mechanical impedance training) and explore how the new technological advancements such as the augmented reality would employ new knowledge from neuroscience.

PMID: 28505989


Nguyen AT, Armstrong EA, Yager JY.


Neurodevelopmental reflex testing is commonly used in clinical practice to assess the maturation of the nervous system. Neurodevelopmental reflexes are also referred to as primitive reflexes. They are sensitive and consistent with later outcomes. Abnormal reflexes are described as an absence, persistence, reappearance, or latency of reflexes, which are predictive indices of infants that are at high risk for neurodevelopmental disorders. Animal models of neurodevelopmental disabilities, such as cerebral palsy, often display aberrant developmental reflexes, as would be observed in human infants. The techniques described assess a variety of neurodevelopmental reflexes in neonatal rats. Neurodevelopmental reflex testing offers the investigator a testing method that is not otherwise available in such young animals. The methodology presented here aims to assist investigators in examining developmental milestones in neonatal rats as a method of detecting early-onset brain injury and/or determining the effectiveness of therapeutic interventions. The methodology presented here aims to provide a general guideline for investigators.

PMID: 28518104

12. Cerebral palsy.

Dean E.


New guidelines from the National Institute for Health and Care Excellence (NICE) focus on children with cerebral palsy.

PMID: 28513388

Nyman A, Lohmander A.


Babbling is an important precursor to speech, but has not yet been thoroughly investigated in children with neurodevelopmental disabilities. Canonical babbling ratio (CBR) is a commonly used but time-consuming measure for quantifying babbling. The aim of this study was twofold: to validate a simplified version of the CBR (CBRUTTER), and to use this measure to determine if early precursors to speech and language development could be detected in children with different neurodevelopmental disabilities. Two different data sets were used. In Part I, CBRUTTER was compared to two other CBR measures using previously obtained phonetic transcriptions of 3571 utterances from 38 audio recordings of 12-18 month old children with and without cleft palate. In CBRUTTER, number of canonical utterances was divided by total number of utterances. In CBRsyl, number of canonical syllables was divided by total number of syllables. In CBRutt, number of canonical syllables was divided by total number of utterances. High agreement was seen between CBRUTTER and CBRsyl, suggesting CBRUTTER as an alternative. In Part II, babbling in children with neurodevelopmental disability was examined. Eighteen children aged 12-22 months with Down syndrome, cerebral palsy or developmental delay were audio-video recorded during interaction with a parent. Recordings were analysed by observation of babbling, consonant production, calculation of CBRUTTER, and compared to data from controls. The study group showed significantly lower occurrence of all variables, except for of plosives. The long-term relevance of the findings for the speech and language development of the children needs to be investigated.

PMID: 28521525


Westbom L, Rimstedt A, Nordmark E.


AIM: To explore pain screening in CPUP, a follow-up surveillance programme for people with cerebral palsy (CP), specifically to describe reported pain prevalence, localizations, patterns of distribution; to compare with studies using psychometrically sound assessment instruments; and to assess agreement between pain documented in CPUP and medical records. METHOD: Registry study of a population with CP, born 1993 to 2008, living in Skåne, Sweden in 2013. Descriptive data, cross-tabulations, and chi-square tests to characterize and compare the study groups. Kappa analysis to test the concordance between register and medical record reports on pain. RESULTS: Pain was reported by 185 out of 497 children (37%; females 40%, males 35%). Level V in both Gross Motor Function Classification System (GMFCS) and Manual Ability Classification System (MACS) was associated with highest prevalence of pain (50% and 54%), and level I with lowest prevalence of pain (30% and 32%). Pain was most frequent in dyskinetic CP (46%) and least frequent in unilateral spastic CP (33%). Feet and knees were the dominant localizations. Fair-moderate agreement (kappa 0.37, prevalence-adjusted bias-adjusted kappa [PABAK] 0.44) was found between documented pain in CPUP and medical records, although more seldom recognized in medical records. INTERPRETATION: The distribution of pain between CP subtypes, functional levels, sex, and age in CPUP is concordant with previous population-based studies, indicating the validity of the CPUP pain screening. Despite this, further clinical evaluation with extended pain assessments and pain management were largely neglected in children reporting chronic pain.

PMID: 28509356

Adolfsson M, Johnson E, Nilsson S.


BACKGROUND: Children with cerebral palsy (CP) face particular challenges, e.g. daily pain that threaten their participation in school activities. This study focuses on how teachers, personal assistants, and clinicians in two countries with different cultural prerequisites, Sweden and South Africa, manage the pain of children in school settings. METHOD: Participants' statements collected in focus groups were analysed using a directed qualitative content analysis framed by a Frequency of attendance-Intensity of involvement model, which was modified into a Knowing-Doing model. RESULTS: Findings indicated that pain management focused more on children's attendance in the classroom than on their involvement, and a difference between countries in terms of action-versus-reaction approaches. Swedish participants reported action strategies to prevent pain whereas South African participants primarily discussed interventions when observing a child in pain. CONCLUSION: Differences might be due to school- and healthcare systems. To provide effective support when children with CP are in pain in school settings, an action-and-reaction approach would be optimal and the use of alternative and augmentative communication strategies would help to communicate children's pain. As prevention of pain is desired, structured surveillance and treatment programs are recommended along with trustful collaboration with parents and access to "hands-on" pain management when needed. Implications for rehabilitation • When providing support, hands-on interventions should be supplemented by structured preventive programs and routines for parent collaboration (action-and-reaction approach). • When regulating support, Sweden and South Africa can learn from each other; ○ In Sweden, the implementation of a prevention program has been successful. ○ In South Africa, the possibilities giving support directly when pain in children is observed have been beneficial.

PMID: 28521563


Bourke-Taylor HM, Cotter C, Lalor A, Johnson L.


PURPOSE: This qualitative study investigated perceived successful school experiences for students with cerebral palsy in Australia. Participation and appropriate support in school are complex concepts, although few studies have investigated all stakeholders' perspectives. METHODS: Phenomenology informed the study that centered on the concept of a successful school experience. In-depth interviews occurred with students (n = 7), parents (n = 11), teachers (n = 10), school principals (n = 9) and allied health practitioners (n = 10) to gain the perspective from multiple vantage points. Specific research questions, interview guides and demographic questionnaires were configured for each group. Interviews were analyzed thematically within and between groups. RESULTS: Three key themes emerged: Collaborative partnerships between families, schools and outside organizations; School culture and attitude is key; and, allied health practitioners are part of home and school teams. CONCLUSIONS: Student and school success was impacted substantially by the capacity of adults in the student's life to collaborate - family, school professionals and allied health practitioners. An inclusive school culture was crucial to students with cerebral palsy. All parties needed to prioritize promotion of an open and positive school culture built around problem-solving inclusive practices. Involved people, such as allied health practitioners, bring knowledge and skills that are not otherwise readily available in school environments. Implications for rehabilitation Students with cerebral palsy have high needs at school and allied health practitioners have a role advocating for, educating and providing support to students within the school. Teachers of students with cerebral palsy need education, training and support from allied health practitioners. The need for allied health and rehabilitation services continues for children and youth with cerebral palsy outside of school and across the schooling years. School professionals; allied health practitioners; families and students can work together to improve the student experience.

PMID: 28524702
17. Validation of an MRI Brain Injury and Growth Scoring System in Very Preterm Infants Scanned at 29- to 35-Week Postmenstrual Age.

George JM, Fiori S, Fripp J, Pannek K, Bursle J, Moldrich R, Guzzetta A, Coulthard A, Ware RS, Rose SE, Colditz PB, Boyd RN.


BACKGROUND AND PURPOSE: The diagnostic and prognostic potential of brain MR imaging before term-equivalent age is limited until valid MR imaging scoring systems are available. This study aimed to validate an MR imaging scoring system of brain injury and impaired growth for use at 29 to 35 weeks postmenstrual age in infants born at <31 weeks gestational age.

MATERIALS AND METHODS: Eighty-three infants in a prospective cohort study underwent early 3T MR imaging between 29 and 35 weeks' postmenstrual age (mean, 32±2 ± 1±3 weeks; 49 males, born at median gestation of 28±4 weeks; range, 23+6 -30+6 weeks; mean birthweight, 1068 ± 312 g). Seventy-seven infants had a second MR scan at term-equivalent age (mean, 40+6 ± 1+3 weeks). Structural images were scored using a modified scoring system which generated WM, cortical gray matter, deep gray matter, cerebellar, and global scores. Outcome at 12-months corrected age (mean, 12 months 4 days ± 1+2 weeks) consisted of the Bayley Scales of Infant and Toddler Development, 3rd ed. (Bayley III), and the Neuro-Sensory Motor Developmental Assessment. RESULTS: Early MR imaging global, WM, and deep gray matter scores were negatively associated with Bayley III motor (regression coefficient for global score $\beta = -1.31; 95\% CI, -2.39 to -0.23; P = .02$), cognitive ($\beta = -1.52; 95\% CI, -2.39 to -0.65; P < .01$) and the Neuro-Sensory Motor Developmental Assessment outcomes ($\beta = -1.73; 95\% CI, -3.19 to -0.28; P = .02$). Early MR imaging cerebellar scores were negatively associated with the Neuro-Sensory Motor Developmental Assessment ($\beta = -5.99; 95\% CI, -11.82 to -0.16; P = .04$). Results were reconfirmed at term-equivalent age MR imaging. CONCLUSIONS: This clinically accessible MR imaging scoring system is valid for use at 29 to 35 weeks postmenstrual age in infants born very preterm. It enables identification of infants at risk of adverse outcomes before the current standard of term-equivalent age.

PMID: 28522659

Prevention and Cure

18. Association between the use of Magnesium Sulfate as Neuroprotector in Prematurity and the Neonatal Hemodynamic Effects.

Nunes RD, Schutz FD, Traebert JL.


PURPOSE: Cerebral palsy is often associated with prematurity and magnesium sulfate (MgSO4), has been used as neuroprotector, with favorable results. However, its mechanism of action has not been fully elucidated. This study aimed to evaluate the association between MgSO4 at the imminent premature delivery and neonatal hemodynamic effects.

MATERIALS AND METHODS: A cross-sectional study involving 94 newborns (NB) between 24 and 32 weeks at a Brazilian hospital was performed. Bivariate analysis between the use or the nonuse of MgSO4 and hemodynamic characteristics were performed, using chi-square test. RESULTS: NB were evaluated between those who received MgSO4 (27.7) and those who did not (72.3%). Normal heart rate was verified in 62.8% of NB, normal respiratory rate in 70.2% and normal temperature in 22.3%. Oxygen saturation higher or equal than 95% was evidenced in 85.1% of NB, normal hemoglucotest in 74.5% and hemoglobin greater or equal than 16.4 g/dL in 30.9%. Non-invasive ventilation was performed in 48.9% of NB, while 51.1% were submitted to endotracheal ventilation. There was no significance relation detected between the use of MgSO4 and the hemodynamic characteristics. CONCLUSIONS: MgSO4 does not appear to influence hemodynamic factors as cause of the neuroprotection in premature NB.

PMID: 28521581
19. Intravenous injection of umbilical cord-derived mesenchymal stromal cells attenuates reactive gliosis and hypomyelination in a neonatal intraventricular hemorrhage model.


Intraventricular hemorrhage (IVH) is a frequent complication of preterm newborns, resulting in cerebral palsy and cognitive handicap as well as hypoxic ischemic encephalopathy and periventricular leukomalacia. In this study, we investigated the restorative effect on neonatal IVH by umbilical cord-derived mesenchymal stromal cells (UC-MSCs) cultured in serum-free medium (RM medium) for clinical application. UC-MSCs were cultured with αMEM medium supplemented with FBS or RM. A neonatal IVH mouse model at postnatal day 5 was generated by intraventricular injection of autologous blood, and mice were intravenously administered $1 \times 10^5$ UC-MSCs two days after IVH. Brain magnetic resonance imaging was performed at postnatal day 15, 22 and neurological behavioral measurements were performed at postnatal day 23, accompanied by histopathological analysis and cytokine bead assays in serum after IVH with or without UC-MSCs. Both UC-MSCs cultured with αMEM and RM met the criteria of MSCs and improved behavioral outcome of IVH mice. Moreover the RM group exhibited significant behavioral improvement compared to the control group. Histopathological analysis revealed UC-MSCs cultured with RM significantly attenuated periventricular reactive gliosis, hypomyelination, and periventricular cell death observed after IVH. Furthermore, human brain-derived neurotrophic factor and hepatocyte growth factor were elevated in the serum, cerebrospinal fluid and brain tissue of neonatal IVH model mice 24h after UC-MSCs administration. These results suggest UC-MSCs attenuate neonatal IVH by protecting gliosis and apoptosis of the injured brain, and intravenous injection of UC-MSCs cultured in RM may be feasible for neonatal IVH in clinic.

PMID: 28504197

20. ADCY5-related movement disorders: Frequency, disease course and phenotypic variability in a cohort of paediatric patients.


INTRODUCTION: ADCY5 mutations have been recently identified as an important cause of early-onset hyperkinetic movement disorders. The phenotypic spectrum associated with mutations in this gene is expanding. However, the ADCY5 mutational frequency in cohorts of paediatric patients with hyperkinetic movement disorders has not been evaluated.

METHODS: We performed a screening of the entire ADCY5 coding sequence in 44 unrelated subjects with genetically undiagnosed childhood-onset hyperkinetic movement disorders, featuring chorea alone or in combination with myoclonus and dystonia. All patients had normal CSF analysis and brain imaging and were regularly followed-up in tertiary centers for paediatric movement disorders. RESULTS: We identified five unrelated subjects with ADCY5 mutations (11% of the cohort). Three carried the p. R418W mutation, one the p. R418Q and one the p. R418G mutation. Mutations arose de novo in four cases, while one patient inherited the mutation from his similarly affected father. All patients had delayed motor and/or language milestones with or without axial hypotonia and showed generalized chorea and dystonia, with prominent myoclonic jerks in one case. Episodic exacerbations of the baseline movement disorder were observed in most cases, being the first disease manifestation in two patients. The disease course was variable, from stability to spontaneous improvement during adolescence. CONCLUSION: Mutations in ADCY5 are responsible for a hyperkinetic movement disorder that can be preceded by episodic attacks before the movement disorder becomes persistent and is frequently misdiagnosed as dyskinetic cerebral palsy. A residual degree of neck hypotonia and a myopathy-like facial appearance are frequently observed in patients with ADCY5 mutations.

PMID: 28511835