1. Development of an EMG-ACC-Based Upper Limb Rehabilitation Training System.

Liu L, Chen X, Lu Z, Cao S, Wu, Zhang X.


This paper focuses on the development of an upper limb rehabilitation training system designed for use by children with cerebral palsy (CP). It attempts to meet the requirements of in-home training by taking advantage of the combination of portable accelerometers (ACC) and surface electromyography (SEMG) sensors worn on the upper limb to capture functional movements. In the proposed system, the EMG-ACC acquisition device works essentially as wireless game controller, and three rehabilitation games were designed for improving upper limb motor function under a clinician's guidance. The games were developed on the Android platform based on a physical engine called Box2D. The results of a system performance test demonstrated that the developed games can respond to the upper limb actions within 210ms. Positive questionnaire feedbacks from twenty CP subjects who participated in the game test verified both the feasibility and usability of the system. Results of a long-term game training conducted with three CP subjects demonstrated that CP patients could improve in their game performance through repetitive training, and persistent training was needed to improve and enhance the rehabilitation effect. According to our experimental results, the novel multi-feedback SEMG-ACC-based user interface improved the users' initiative and performance in rehabilitation training.

PMID: 28113559


Preston N, Horton M, Levesley M, Mon-Williams M, O'Connor RJ.


BACKGROUND AND PURPOSE: Upper limb activity measures for children with cerebral palsy (CP) have a number of limitations, for example, lack of validity and poor responsiveness. To overcome these limitations, we developed the Children's Arm Rehabilitation Measure (ChARM), a parent-reported questionnaire validated for children with cerebral palsy aged 5-16 years. This paper describes both the development of the ChARM items and response categories and its psychometric testing and further refinement using the Rasch measurement model. METHODS: To generate valid items for the ChARM, we collected goals of therapy specifically developed by therapists, children with cerebral palsy, and their parents for improving activity limitation of the upper limb. The activities, which were the focus of these goals, formed the basis for the items. Therapists typically break an activity into natural stages for the purpose of improving activity performance, and these natural orders of achievement formed each item's response options. Items underwent face validity testing with health care
professionals, parents of children with cerebral palsy, academics, and lay persons. A Rasch analysis was performed on ChARM questionnaires completed by the parents of 170 children with cerebral palsy from 12 hospital paediatric services. The ChARM was amended, and the procedure repeated on 148 ChARMS (from children's mean age: 10 years and 1 month; range: 4 years and 8 months to 16 years and 11 months; 85 males; Manual Ability Classification System Levels I = 9, II = 26, III = 48, IV = 45, and V = 18). RESULTS: The final 19-item unidimensional questionnaire displayed fit to the Rasch model (chi-square p = .18), excellent reliability (person separation index = 0.95, α = 0.95), and no floor or ceiling effects. Items showed no response bias for gender, distribution of impairment, age, or learning disability. DISCUSSION: The ChARM is a psychometrically sound measure of upper limb activity validated for children with cerebral palsy aged 5-16 years. The ChARM is freely available for use to clinicians and nonprofit organisations.

PMID: 28112465

3. NICE publishes guideline on diagnosing and managing cerebral palsy in young people.

Torjesen I.


The National Institute for Health and Care Excellence (NICE) has published its first dedicated guideline on diagnosing and managing cerebral palsy in under 25s, in an attempt to improve recognition and treatment of the condition.

PMID: 28130209

4. Children with Spastic Cerebral Palsy Experience Difficulties Adjusting Their Gait Pattern to Weight Added to the Waist, While Typically Developing Children Do Not.


The prevalence of childhood overweight and obesity is increasing in the last decades, also in children with Cerebral Palsy (CP). Even though it has been established that an increase in weight can have important negative effects on gait in healthy adults and children, it has not been investigated what the effect is of an increase in body weight on the characteristics of gait in children with CP. In CP, pre and post three-dimensional gait analyses are performed to assess the effectiveness of an intervention. As a considerable amount of time can elapse between these measurements, and the effect of an alteration in the body weight is not taken into consideration, this effect of increased body weight is of specific importance. Thirty children with the predominantly spastic type of CP and 15 typically developing (TD) children were enrolled (age 3-15 years). All children underwent three-dimensional gait analysis with weight-free (baseline) and weighted (10% of the body weight added around their waist) trials. Numerous gait parameters showed a different response to the added weight for TD and CP children. TD children increased walking velocity, step- and stride length, and decreased double support duration with a slightly earlier timing of foot-off, while the opposite was found in CP. Similarly, increased ranges of motion at the pelvis (coronal plane) and hip (all planes), higher joint angular velocities at the hip and ankle, as well as increased moments and powers at the hip, knee and ankle were observed for TD children, while CP children did not change or even showed decreases in the respective measures in response to walking with added weight. Further, while TD children increased their gastrocnemius EMG amplitude during weighted walking, CP children slightly decreased their gastrocnemius EMG amplitude. As such, an increase in weight has a significant effect on the gait pattern in CP children. Clinical gait analysts should therefore take into account the negative effects of increased weight during pre-post measurements to avoid misinterpretation of treatment results. Overweight and obesity in CP should be counteracted or prevented as the increased weight has detrimental effects on the gait pattern.

PMID: 28123360
5. Effectiveness of virtual reality rehabilitation for children and adolescents with cerebral palsy: an updated evidence-based systematic review.

Ravi DK, Kumar N, Singhi P.


BACKGROUND: The use of virtual reality systems in the motor rehabilitation of children with cerebral palsy is new, and thus the scientific evidence for its effectiveness needs to be evaluated through a systematic review. OBJECTIVE: To provide updated evidence-based guidance for virtual reality rehabilitation in sensory and functional motor skills of children and adolescents with cerebral palsy. DATA SOURCES: PubMed, PEDro, Web of Science, OTseeker, PsycINFO and Cochrane Library were searched from their earliest records up to 1 June, 2016. STUDY SELECTION: Two reviewers applied the population intervention comparison outcome (PICO) question to screen the studies for this review. DATA EXTRACTION: Information on study design, subjects, intervention, outcome measures and efficacy results were extracted into a pilot-tested form. Method quality was assessed independently by two reviewers using the Downs and Black checklist. DATA SYNTHESIS: Thirty-one studies included 369 participants in total. Best evidence synthesis was applied to summarize the outcomes, which were grouped according to International Classification of Functioning, Disability and Health. Moderate evidence was found for balance and overall motor development. The evidence is still limited for other motor skills. CONCLUSIONS: This review uncovered additional literature showing moderate evidence that virtual reality rehabilitation is a promising intervention to improve balance and motor skills in children and adolescents with cerebral palsy. The technique is growing, so long-term follow-up and further research are required to determine its exact place in the management of cerebral palsy. Systematic review registration number PROSPERO 2015:CRD42015026048.

PMID: 28109566

6. Pain extent and function in youth with physical disabilities.

Miró J, de la Vega R, Tomé-Pires C, Sánchez-Rodríguez E, Castarlenas E, Jensen MP, Engel JM.


BACKGROUND: The aim of this study was to increase our understanding of the role that spatial qualities of pain (location and extent) play in functioning, among youths with disabilities and chronic pain. METHODS: One-hundred and fifteen youths (mean age 14.4 years; SD ±3.3 years) with physical disabilities and chronic pain were interviewed and were asked to provide information about pain locations and their average pain intensity in the past week, and to complete measures of pain interference, psychological function and disability. Most of the participants in this sample were males (56%), Caucasian (68%), and had a cerebral palsy (34%) or muscular dystrophy (25%) problem. Most participants did not report high levels of disability ( Formula: see text ), SD ±9.5, range 0-60) or global pain intensity ( Formula: see text ), SD ±2.4, range 0-10). RESULTS: Pain at more than one body site was experienced by 91% of participants. There were positive associations between pain extent with pain interference (r = 0.30) and disability (r = 0.30), and a negative association with psychological function (r = -0.38), over and above average pain intensity. Additionally, pain intensity in the back (as opposed to other locations) was associated with more pain interference (r = 0.29), whereas pain intensity in the shoulders was associated with less psychological function (r = -0.18), and pain intensity in the bottom or hips was associated with more disability (r = 0.29). CONCLUSION: The findings support the need to take into account pain extent in the assessment and treatment of youths with physical disabilities and chronic pain, call our attention about the need to identify potential risk factors of pain extent, and develop and evaluate the benefits of treatments that could reduce pain extent and target pain at specific sites.

PMID: 28115871

7. The Comparison of M-B CDI-K Short Form and K-ASQ as Screening Test for Language Development.

Kim SW, Kim JY, Lee SY, Jeon HR.


OBJECTIVE: To investigate the usefulness of the communication domain in the Korean version of Ages and Stages Questionnaire (K-ASQ), and short form of the Korean version of MacArthur-Bates Communicative Development Inventories (M-B CDI-K), as screening tests for language developmental delay. METHODS: Data was collected between April 2010 and December 2013, from children who visited either the Department of Physical Medicine and Rehabilitation or the
Developmental Delay Clinic, presenting with language development delay as their chief complaint. All the children took the short form of M-B CDI-K and K-ASQ as screening tests, and received diagnostic language assessments including Sequenced Language Scale for Infants (SELSI) or Preschool Receptive-Expressive Language Scale (PRES). RESULTS: A total of 206 children, mean age 29.7 months, were enrolled. The final diagnoses were developmental language disorder, global developmental delay, autism spectrum disorder, cerebral palsy, etc. The M-B CDI-K short form and the communication domain of the K-ASQ had 95.9% and 76.7% sensitivity, and 82.4% and 85.3% specificity, with regards to diagnostic language assessments. The M-B CDI-K short form showed higher negative predictive value and better accuracy than the communication domain of the K-ASQ. CONCLUSION: The screening ability of K-ASQ was not sufficient for children with language development delay, and the M-B CDI-K short form should be implemented for additional screening.

PMID: 28119842

8. The Impact of Contrastive Stress on Vowel Acoustics and Intelligibility in Dysarthria.

Connaghan KP, Patel R.


PURPOSE: To compare vowel acoustics and intelligibility in words produced with and without contrastive stress by speakers with spastic (mixed-spastic) dysarthria secondary to cerebral palsy (DYSCP) and healthy controls (HCs). METHOD: Fifteen participants (9 men, 6 women; age M = 42 years) with DYSCP and 15 HCs (9 men, 6 women; age M = 36 years) produced sentences containing target words with and without contrastive stress. Forty-five healthy listeners (age M = 25 years) completed a vowel identification task of DYSCP productions. Vowel acoustics were compared across stress conditions and groups using 1st (F1) and 2nd (F2) formant measures. Perceptual intelligibility was compared across stress conditions and dysarthria severity. RESULTS: F1 and F2 significantly increased in stressed words for both groups, although the degree of change differed. Mean Euclidian distance between vowels also increased with stress. The relative probability of vowels falling within the target F1 × F2 space was greater for HCs but did not differ with stress. Stress production resulted in greater listener vowel identification accuracy for speakers with mild dysarthria. CONCLUSIONS: Contrastive stress affected vowel formants for both groups. Perceptual results suggest that some speakers with dysarthria may benefit from a contrastive stress strategy to improve vowel intelligibility.

PMID: 28114612


Lund SK, Quach W, Weissling K, McKelvey M, Dietz A.


PURPOSE: The purpose of this study was to explore how speech-language pathologists (SLPs) who are augmentative and alternative communication (AAC) specialists approach the assessment process for 2 case studies, 1 child with cerebral palsy and 1 with autism spectrum disorder. The aim of the study was to answer the following questions: (a) How do clinicians with expertise approach the AAC assessment process for children with developmental disabilities? (b) Can any initial hypothesis be drawn about how SLPs approach the assessment of children with motor versus social interactive deficits? METHOD: This study used a phenomenological qualitative design. The researchers conducted 2 in-depth, semistructured interviews with 8 SLPs who specialized in AAC and self-identified as primarily working with children. RESULTS: Four major themes emerged from the data: area of assessment, method of assessment, evaluation preparation, and parent education. Each major theme contained multiple subthemes and categories within those subthemes. CONCLUSIONS: Participants discussed similar areas of assessment for both cases, indicating that some aspects of AAC assessment are universal. However, the specific aspects of what they were assessing and how they went about assessing them differed between the 2 cases. The results of the current study provide an outline of an assessment protocol for children with complex communication needs.

PMID: 28114681


AIM: Parent-reporting is needed to examine Quality of Life (QoL) of children with cerebral palsy (CP) across all severities. This study examines whether QoL changes between childhood and adolescence, and what predicts adolescent QoL. METHOD: SPARCLE is a European cohort study of children with CP, randomly sampled from population databases. Of 818 8-12-year-olds joining the study, 594 (73%) were revisited as 13-17-year-olds. The subject of this report is the 551 (316 boys, 235 girls) where the same parent reported QoL on both occasions using KIDSCREEN-52 (transformed Rasch scale, mean 50, SD 10 per domain). Associations were assessed using linear regression. RESULTS: Between childhood and adolescence, average QoL reduced in six domains (1.3-3.8 points, p<0.01) and was stable in three (Physical wellbeing, Autonomy, Social acceptance). Socio-demographic factors had little predictive value. Childhood QoL was a strong predictor of all domains of adolescent QoL. Severe impairments of motor function, IQ or communication predicted higher adolescent QoL on some domains; except that severe motor impairment predicted lower adolescent QoL on the Autonomy domain. More psychological problems and higher parenting stress in childhood and their worsening by adolescence predicted lower QoL in five and eight domains respectively; contemporaneous pain in seven domains. The final model explained 30%-40% of variance in QoL, depending on domain. INTERPRETATION: In general, impairment severity and socio-demographic factors were not predictors of lower adolescent QoL. However, pain, psychological problems and parenting stress were predictors of lower adolescent QoL in most domains. These are modifiable factors and addressing them may improve adolescent QoL.

PMID: 28110883

11. The Development of Extremely Premature Infants.

Voss W, Hobbiebrunken E, Ungermann U, Wagner M, Damm G.


BACKGROUND: Until now, there has been no comprehensive long-term study in Germany on the development of extremely premature infants up to school age. METHODS: From October 2004 to September 2008, in the German federal state of Lower Saxony, 437 infants born at a gestational age less than 28 weeks were followed up at the ages of 2 and 5 years, and some at the age of 10 years. The 5-year follow-up data were collated with the peri- and neonatological parameters and compared with the 2- and 10-year follow-up data. RESULTS: The mortality of extremely premature infants was 25.1%. Among the five-year-olds studied, 14.1% showed cognitive impairment and 17.4% had cerebral palsy. 40.4% manifested abnormalities of speech or language, 33.1% had behavioral abnormalities, and 72.5% received therapeutic interventions. Infants in whom severe brain damage was diagnosed by ultrasonography shortly after birth were more likely to develop cerebral palsy (odds ratio [OR] 38.28, 99% confidence interval [12.55; 116.80]) and to have impaired cognitive development (OR 7.36 [2.52; 21.51]). The likelihood of cognitive impairment was also higher among infants whose mothers had a lower level of education (OR 3.83 [1.68; 8.77]). 73.1% (242 out of 331) of the two-year-olds were in the same category of cognitive function at the 5-year follow-up; 82.4% (65 out of 79) of the 5-year-olds were in the same category of cognitive function at the 10-year follow-up. CONCLUSION: Many of these extremely premature infants had developmental disturbances, and many required therapeutic interventions. The risk factors revealed by this study may help identify patients who are in particular need of support, enabling targeted measures to be taken at the earliest possible stage in order to improve their cognitive and motor abilities. Nationwide, standardized follow-up at the age of 5 years would be desirable.

PMID: 28130919

Reid LB, Pagnozzi AM, Fiori S, Boyd RN, Dowson N, Rose SE.


Researchers in the field of child neurology are increasingly looking to supplement clinical trials of motor rehabilitation with neuroimaging in order to better understand the relationship between behavioural training, brain changes, and clinical improvements. Randomised controlled trials are typically accompanied by sample size calculations to detect clinical improvements but, despite the large cost of neuroimaging, not equivalent calculations for concurrently acquired imaging neuroimaging measures of changes in response to intervention. To aid in this regard, a power analysis was conducted for two measures of brain changes that may be indexed in a trial of rehabilitative therapy for cerebral palsy: cortical thickness of the impaired primary sensorimotor cortex, and fractional anisotropy of the impaired, delineated corticospinal tract. Power for measuring fractional anisotropy was assessed for both region-of-interest-seeded and fMRI-seeded diffusion tractography. Taking into account practical limitations, as well as data loss due to behavioural and image-processing issues, estimated required participant numbers were 101, 128 and 59 for cortical thickness, region-of-interest-seeded tractography, and fMRI-seeded tractography, respectively. These numbers are not adjusted for study attrition. Although these participant numbers may be out of reach of many trials, several options are available to improve statistical power, including careful preparation of participants for scanning using mock simulators, careful consideration of image processing options, and enrolment of as homogeneous a cohort as possible. This work suggests that smaller and moderate sized studies give genuine consideration to harmonising scanning protocols between groups to allow the pooling of data.

PMID: 28130065


Boyle AK, Rinaldi SF, Norman JE, Stock SJ.


Preterm birth (PTB) is the leading cause of childhood mortality in children under 5 and accounts for approximately 11% of births worldwide. Premature babies are at risk of a number of health complications, notably cerebral palsy, but also respiratory and gastrointestinal disorders. Preterm deliveries can be medically indicated/elective procedures or they can occur spontaneously. Spontaneous PTB is commonly associated with intrauterine infection/inflammation. The presence of inflammatory mediators in utero has been associated with fetal injury, particularly affecting the fetal lungs and brain. This review will outline (i) the role of inflammation in term and PTB, (ii) the effect infection/inflammation has on fetal development and (iii) recent strategies to target PTB. Further research is urgently required to develop effective methods for the prevention and treatment of PTB and above all, to reduce fetal injury.

PMID: 28122664

14. Participatory design in the development of an early therapy intervention for perinatal stroke.

Basu AP, Pearse JE, Baggaley J, Watson RM, Rapley T.


BACKGROUND: Perinatal stroke is the leading cause of unilateral (hemiparetic) cerebral palsy, with life-long personal, social and financial consequences. Translational research findings indicate that early therapy intervention has the potential for significant improvements in long-term outcome in terms of motor function. By involving families and health professionals in the development and design stage, we aimed to produce a therapy intervention which they would engage with. METHODS: Nine parents of children with hemiparesis and fourteen health professionals involved in the care of infants with perinatal stroke took part in peer review and focus groups to discuss evolving therapy materials, with revisions made iteratively. The materials and approach were also discussed at a meeting of the London Child Stroke Research Reference Group. Focus group data were coded using Normalisation Process Theory constructs to explore potential barriers and facilitators to routine uptake of the intervention. RESULTS: We developed the Early Therapy in Perinatal Stroke (eTIPS) program - a parent-delivered, home-based complex intervention addressing a current gap in practice for infants in the first 6 months of life after unilateral perinatal stroke and with the aim of improving motor outcome. Parents and health professionals saw the intervention as different from...
usual practice, and valuable (high coherence). They were keen to engage (high cognitive participation). They considered the
tasks for parents to be achievable (high collective action). They demonstrated trust in the approach and felt that parents would
undertake the recommended activities (high collective action). They saw the approach as flexible and adaptable (high reflexive
monitoring). Following suggestions made, we added a section on involving the extended family, and obtained funding for a
website and videos to supplement written materials. CONCLUSIONS: Focus groups with parents and health professionals
provided meaningful feedback to iteratively improve the intervention materials prior to embarking on a pilot study. The
intervention has a high potential to normalize and become a routine part of parents' interactions with their child following
unilateral perinatal stroke.

PMID: 28114899

15. Evidence-Based Neonatal Unit Practices and Determinants of Postnatal Corticosteroid-Use in Preterm Births below 30 Weeks GA in Europe. A Population-Based Cohort Study.
BACKGROUND: Postnatal corticosteroids (PNC) were widely used to treat and prevent bronchopulmonary dysplasia in
preterm infants until studies showed increased risk of cerebral palsy and neurodevelopmental impairment. We aimed to
describe PNC use in Europe and evaluate the determinants of their use, including neonatal characteristics and adherence to
evidence-based practices in neonatal intensive care units (NICUs). METHODS: 3917/4096 (95.6%) infants born between 24
and 29 weeks gestational age in 19 regions of 11 European countries of the EPICE cohort we included. We examined neonatal
characteristics associated with PNC use. The cohort was divided by tertiles of probability of PNC use determined by logistic
regression analysis. We also evaluated the impact of the neonatal unit's reported adherence to European recommendations for
respiratory management and a stated policy of reduced PNC use. RESULTS: PNC were prescribed for 545/3917 (13.9%)
infants (regional range 3.1-49.4%) and for 29.7% of infants in the highest risk tertile (regional range 5.4-72.4%). After
adjustment, independent predictors of PNC use were a low gestational age, small for gestational age, male sex, mechanical
ventilation, use of non-steroidal anti-inflammatory drugs to treat persistent ductus arteriosus and region. A stated NICU policy
reduced PNC use (odds ratio 0.29 [95% CI 0.17; 0.50]). CONCLUSION: PNC are frequently used in Europe, but with wide
regional variation that was unexplained by neonatal characteristics. Even for infants at highest risk for PNC use, some regions
only rarely prescribed PNC. A stated policy of reduced PNC use was associated with observed practice and is recommended.

PMID: 28114369

16. Frequency Analysis and Feature Reduction Method For Prediction of Cerebral Palsy in Young Infants.
Rahmati H, Martens H, Aamo OM, Stavdahl O, Stoen R, Adde L.
The aim of this paper is to achieve a model for prediction of cerebral palsy based on motion data of young infants. The
prediction is formulated as a classification problem to assign each of the infants to one of the healthy or with cerebral palsy
groups. Unlike formerly proposed features that are mostly defined in the time domain, this study proposes a set of features
derived from frequency analysis of infants' motions. Since cerebral palsy affects the variability of the motions, and frequency
analysis is an intuitive way of studying variability, suggested features are suitable and consistent with the nature of the
condition. In the current application, a wellknown problem, few subjects and many features, was initially encountered. In such a
case, most classifiers get trapped in a sub-optimal model and, consequently, fail to provide sufficient prediction accuracy. To
solve this problem, a feature selection method that determines features with significant predictive ability is proposed. The
feature selection method decreases the risk of false discovery and, therefore, the prediction model is more likely to be valid and
generalizable for future use. A detailed study is performed on the proposed features and the feature selection method: the
classification results confirm their applicability. Achieved sensitivity of 86%, specificity of 92% and accuracy of 91% are
comparable with state of the art clinical and expert-based methods for predicting cerebral palsy.

PMID: 28113473
17. Predictive value of General Movement Assessment for preterm infants’ development at 2 years - implementation in clinical routine in a non-academic setting.

De Bock F, Will H, Behrenbeck U, Jarczok MN, Hadders-Algra M, Philipp H.


BACKGROUND: General movements (GM) are used in academic settings to predict developmental outcome in infants born preterm. However, little is known about the implementation and predictive value of GM in non-academic settings. AIMS: The aim of this study is twofold: To document the implementation of GM assessment (GMA) in a non-academic setting and to assess its predictive value in infants born preterm. METHODS AND PROCEDURES: We documented the process of implementing GMA in a non-academic outpatient clinic. In addition, we assessed the predictive value of GMA at 1 and 3 months’ corrected age for motor and cognitive development at 2 years in 122 children born <33 weeks’ gestation. Outcome at two years was based upon the Bayley Scales of Infant Development-II (mental/psychomotor developmental index (MDI, PDI)) and a neurological examination. The infants’ odds of atypical outcome (MDI or PDI ≤70 or diagnosis CP) and the predictive accuracy of abnormal GMA were calculated in a clinical routine scenario, which used all available GM information (primarily at 3 months or at 1 month, when 3 months were not available). In addition, separate analysis was undertaken for the samples of GMA at 1 and 3 months. OUTCOMES AND RESULTS: Tips to facilitate GMA implementation are described. In our clinical routine scenario, children with definitely abnormal GM were more likely to have an atypical two-year outcome than children with normal GM (OR 13.2 (95% CI 1.56; 112.5); sensitivity 55.6%, specificity 82.1%). Definitely abnormal GM were associated with reduced MDI (-12.0, 95% CI -23.2; -0.87) and identified all children with cerebral palsy (CP) in the sample of GMA at 3 months only. CONCLUSIONS AND IMPLICATIONS: GMA can be successfully implemented in a non-academic outpatient setting. In our clinical routine scenario, GMA allowed for adequate prediction of neurodevelopment in infants born preterm, thereby allaying concerns about diagnostic accuracy in non-academic settings.

PMID: 28113095

18. Neuroregenerative potential of intravenous G-CSF and autologous peripheral blood stem cells in children with cerebral palsy: a randomized, double-blind, cross-over study.


OBJECTIVE: We performed a randomized, double-blind, cross-over study to assess the neuroregenerative potential of intravenous granulocyte colony-stimulating factor (G-CSF) followed by infusion of mobilized peripheral blood mononuclear cells (mPBMCs) in children with cerebral palsy (CP). METHODS: Children with non-severe CP were enrolled in this study. G -CSF was administered for 5 days, then mPBMCs were collected by apheresis and cryopreserved. One month later (M1), recipients were randomized to receive either mPBMCs or a placebo infusion, and these treatment groups were switched at 7 months (M7) and observed for another 6 months (M13). We assessed the efficacy of treatment by evaluating neurodevelopmental tests, as well as by brain magnetic resonance imaging-diffusion tensor imaging (MRI-DTI) and 18F-fluordeoxyglucose (FDG) brain positron emission tomography-computed tomography (PET-CT) scanning to evaluate the anatomical and functional changes in the brain. RESULTS: Fifty-seven patients aged 4.3 ± 1.9 (range 2-10) years and weighing 16.6 ± 4.9 (range 11.6-56.0) kg were enrolled in this study. The administration of G-CSF as well as the collection and reinfusion of mPBMCs were safe and tolerable. The yield of mPBMCs was comparable to that reported in studies of pediatric donors without CP and patients with nonhematologic diseases. 42.6% of the patients responded to the treatment with higher neurodevelopmental scores than would normally be expected. In addition, larger changes in neurodevelopmental test scores were observed in the 1 month after G-CSF administration (M0-M1) than during the 6 months after reinfusion with mPBMCs or placebo (M1-M7 or M7-M13). Patients who received G-CSF followed by mPBMC infusion at 7 months (T7 group) demonstrated significantly more neurodevelopmental improvement than patients who received G-CSF followed by mPBMC infusion at 1 month (T1 group). In contrast to the results of neurodevelopmental tests, the results of MRI-DTI at the end of this study showed greater improvement in the T1 group. Although we observed metabolic changes to the cerebellum, thalamus and cerebral cortex in the 18F-FDG brain PET-CT scans, there were no significant differences in such changes between the mPBMC and placebo group or between the T1 and T7 group. CONCLUSIONS: Neurodevelopmental improvement was seen in response to intravenous G-CSF followed by mPBMC reinfusion, particularly to the G-CSF alone even without mPBMC reinfusion. Further studies using a larger number of mPBMCs for the infusion which could be collected by repeated cycles of apheresis or using repeated cycles of G-CSF alone, are needed to clarify the effect of mPBMC reinfusion or G-CSF alone (Trial registration: ClinicalTrials.gov, NCT02983708. Registered 5 December, 2016, retrospectively registered).

PMID: 28109298