1. BRAZILIAN VERSION OF THE SHRINERS HOSPITAL UPPER EXTREMITY EVALUATION (SHUEE): TRANSLATION, CULTURAL ADAPTATION, AND EVALUATION OF PSYCHOMETRIC PROPERTIES. [Article in English, Portuguese]
Nicolini-Panisson RD, Tedesco AP, Davids JR, Wagner LV, Mattiello R, Donadio MVF.


OBJECTIVE: To validate the upper limb assessments tool, Shriners Hospital Upper Extremity Evaluation (SHUEE), for individuals with hemiplegic cerebral palsy in the Brazilian population. METHODS: Validation study to translate and culturally adapt the Manual and the instrument. The psychometric properties evaluated were reliability and convergent validity. Reliability was determined by internal consistency (Cronbach's $\alpha$ coefficient), ceiling and floor effect, sensitivity to changes, and intra- and interobserver agreement. Convergent validity was performed using the Pediatric Motor Activity Log, the self-care scale of the Pediatric Evaluation of Disability Inventory, and the Manual Ability Classification System. RESULTS: We evaluated 21 individuals with hemiplegic cerebral palsy, with a mean age of 8.7±4.0 years. After the instrument was translated, there was no need for cultural adaptation. The total Cronbach's $\alpha$ coefficient was 0.887 (95% confidence interval [95%CI] 0.745-0.970). We calculated sensitivity to changes in five subjects who underwent treatment with Botulinum Toxin Type A and physical therapy, with a significant difference between pre- and post-treatment evaluations in the Spontaneous Functional Analysis and Dynamic Positional Analysis. Convergent validity showed a significant correlation of the Spontaneous Functional Analysis and Dynamic Positional Analysis with the scales evaluated. All items of SHUEE presented high intra- and interobserver agreement. CONCLUSIONS: The results revealed that the Brazilian version of the SHUEE demonstrated good reliability and convergent validity, suggesting that it is an adequate and reliable tool for individuals with hemiplegic cerebral palsy in the Brazilian population.

PMID: 32374805

George KA, Damiano DL, Kim Y, Bulea TC.


Background: Rehabilitation in cerebral palsy (CP) seeks to harness neuroplasticity to improve movement, including walking, yet cortical activation underlying gait is not well understood. Methods: We used electroencephalography (EEG) to compare motor related cortical activity, measured by mu rhythm, during quiet standing and treadmill walking in 10 children with unilateral CP and 10 age- and sex-matched children with typical development (TD). Peak mu band frequency, mu rhythm desynchronization (MRD), and gait related intra- and inter-hemispheric coherence were examined. Results: MRD during
walking was observed bilaterally over motor cortex in both cohorts but peak mu band frequency showing MRD was significantly lower in CP compared to TD. Coherence during quiet standing between motor and frontal regions was significantly higher in the non-dominant compared to dominant hemisphere in CP with no hemispheric differences in TD.

Conclusions: EEG-based measures should be further investigated as clinical biomarkers for atypical motor development and to assess rehabilitation effectiveness.

PMID: 32372674

Desailly E, Badina A, Khouri N.


INTRODUCTION: Femoral derotation osteotomy (FDO) is a treatment option in children and adolescents with cerebral palsy who have transverse plane deviations in their lower limbs. When the transverse kinematic deviations are asymmetric, the osteotomy indication can be unilateral. HYPOTHESIS: Unilateral FDO has a kinematic effect on ipsilateral transverse plane deviations along with those of the pelvis and contralateral side. MATERIALS AND METHODS: Among the 170 diplegic children that our team has operated on, 34 underwent unilateral FDO. Their mean age was 12.5±2.7 years; 12 were GMFCS level I and 22 were level II. The kinematic changes 18 months after surgery were evaluated with a paired Student's t test and correlations were determined with the Spearman test (p<0.05). The mean preoperative femoral anteversion was 45°±8°. In terms of kinematics, on the operated side, the children had a mean internal hip rotation of 26°±7°, external pelvis rotation of -8°±6° and inward foot progression angle of 8°±12°. RESULTS: The anteversion was corrected surgically by -28°±5°. Postoperatively, the ipsilateral hip rotation (10°±10°), pelvis rotation (-2°±5°) and foot rotation (6°±12°) were significantly improved. No correlations were identified between the resulting kinematic parameters and surgical correction. The five feet that had inward rotation (13°±9°) were improved to (-5°±7°). DISCUSSION: Unilateral FDO of the hip in patients with asymmetry not only reduces the internal rotation of the operated hip, it also normalizes the rotation of the pelvis and both feet. However, these improvements are not directly related to the amount of surgical correction. LEVEL OF EVIDENCE: IV: case series.

PMID: 32360555

Park EY.


BACKGROUND: The prognosis of gross motor function is a major concern for therapy and intervention in children with cerebral palsy (CP). The classification system for gross motor function, the Gross Motor Function Classification System (GMFCS), is actively studied because it could be useful in the communication between professionals and families. This study aimed to verify the stability of GMFCS over 2 years in children with CP aged 2-12 years. METHODS: The GMFCS level of 100 children with CP who underwent rehabilitation therapy in hospitals or who attended special elementary schools in South Korea were collected in the study. The agreements across three measurement points were analyzed in these children. RESULTS: The weighted kappa coefficients were statistically significant (p < .05). The coefficients ranged from 0.690 to 0.789 in children with CP aged 2-12 years. The lowest coefficient of 0.557 was observed in children with CP aged 2-4 years between the first and third measurement points. CONCLUSIONS: The results provided evidence of GMFCS stability for the first year and change of the GMFCS during the two-year study period in children aged 2-4 years. Moreover, the findings indicate that the stability of GMFCS varies with time, duration, and age. It is recommended that GMFCS assessments be performed periodically, which are even more necessary for children with CP aged 2-4 years.

PMID: 32375677

Botulinum NeuroToxin-A (BoNT-A) injections to the medial gastrocnemius (MG) and lower-leg casts are commonly combined to treat ankle equinus in children with spastic cerebral palsy (CP). However, the decomposed treatment effects on muscle or tendon structure, stretch reflexes, and joint are unknown. In this study, BoNT-A injections to the MG and casting of the lower legs were applied separately to gain insight into the working mechanisms of the isolated treatments on joint, muscle, and tendon levels. Thirty-one children with spastic CP (GMFCS I-III, age 7.4 ± 2.6 years) received either two weeks of lower-leg casts or MG BoNT-A injections. During full range of motion slow and fast passive ankle rotations, joint resistance and MG stretch reflexes were measured. MG muscle and tendon lengths were assessed at resting and at maximum dorsiflexion ankle angles using 3D-freehand ultrasound. Treatment effects were compared using non-parametric statistics. Associations between the effects on joint and muscle or tendon levels were performed using Spearman correlation coefficients (p < 0.05). Increased joint resistance, measured during slow ankle rotations, was not significantly reduced after either treatment. Additional joint resistance assessed during fast rotations only reduced in the BoNT-A group (-37.6%, p = 0.013, effect size = 0.47), accompanied by a reduction in MG stretch reflexes (-70.7%, p = 0.003, effect size = 0.56). BoNT-A increased the muscle length measured at the resting ankle angle (6.9%, p = 0.013, effect size = 0.53). Joint angles shifted toward greater dorsiflexion after casting (32.4%, p = 0.004, effect size = 0.56), accompanied by increases in tendon length (5.7%, p = 0.039, effect size = 0.57; r = 0.40). No associations between the changes in muscle or tendon lengths and the changes in the stretch reflexes were found. We conclude that intramuscular BoNT-A injections reduced stretch reflexes in the MG accompanied by an increase in resting muscle belly length, whereas casting resulted in increased dorsiflexion without any changes to the muscle length. This supports the need for further investigation on the effect of the combined treatments and the development of treatments that more effectively lengthen the muscle.

PMID: 32373040

6. SPIDER as A Rehabilitation Tool for Patients with Neurological Disabilities: The Preliminary Research. Glowinski S, Blazejewski A.


(1) Background and purpose: SPIDER (Strengthening Program for Intensive Developmental Exercises and activities for Reaching health capability) is dedicated for patients suffering from Cerebral Palsy, Sclerosis Multiplex, Spinal Bifida, Spinal Muscular Atrophy and strokes. Authors proposed a computer model for the evaluation patient's condition and the rehabilitation progress. (2) Methods: The 2-year-old and 76-year-old patients with neurological problems, who underwent individual therapy included balancing and coordination practising with SPIDER device. The model comparing the forces, which act during the therapy process, such as the expander and gravity forces, was worked out using Matlab software. (3) Results: The model allowed controlling the changes into the patients centre of gravity forces continuous adjustment and postural stability during any patient's movement. After rehabilitation sessions, lasted for 28 days during which patients received the progress information and the therapist got the numeric data, regarding the period of the therapy. (4) Conclusions: The first patient was able to move, dramatically improved the ability to balance and coordination. The second one presented change in gait, improvement in mobility, motor function and decreased fall risk. The proposed computer model gives information about the forces acting to the patient body. The physiotherapist can evaluate the progress of patient verticalization and receive information, in the form of numbers and charts.

PMID: 32365884

Mendizábal Alonso P.


INTRODUCTION: Cerebral palsy is produced by nonprogressive injury to the developing brain. This lesion produces life-long motor impairments, disturbances in perception, speech, communication, cognition and competence. Physiotherapy is an
important part of treatment, and may include hippotherapy, which uses the movement of the horse to stimulate the sensorial, neuromotor and cognitive systems to obtain functional results. METHODS: We performed a literature search using distinct databases and the following Keywords: "hippotherapy"; "cerebral palsy"; "children"; "treatment" and "physiotherapy". After application of the inclusion and exclusion criteria; elimination of duplicated tests; and critical appraisal of the retrieved texts; 22 articles were finally selected for the review. CONCLUSION: Hippotherapy is used by physiotherapy in the treatment of cerebral palsy. In this therapy, the horse's movement is purposefully manipulated to stimulate the patient's sensitive, neuromotor and cognitive systems and promote functional goals. Among the interventions used, the most recommend by the authors is the postural alignment, although there is no single standard of care, but the treatment is individually-tailored to the needs of each patient with cerebral palsy.

PMID: 32370834

8. Severe Agitation in a Teenager With Spastic Cerebral Palsy: A Clinical Challenge.
Greenky D, Khan NS.

Neuroleptic malignant syndrome is a challenging diagnosis because it mimics many other conditions. We present a case of a 16-year-old boy with spastic cerebral palsy who presented with severe agitation, hyperthermia, and autonomic dysfunction. He arrived to a community pediatric hospital without a caregiver to provide a detailed history, which further complicated his management.

PMID: 32384395

9. [Effectiveness of robotic assistance for gait training in children with cerebral palsy. a systematic review]. [Article in Spanish]
Colomera JA, Nahuelhual P.

INTRODUCTION: In recent years, the use of gait training using robotic assistance systems has progressively increased in the paediatric population with cerebral palsy. OBJECTIVE: To systematically assess the effects of robotic assistance for gait training compared with physical rehabilitation therapy in children with cerebral palsy (CP), based on the International Classification of Functioning, Health and Disability (ICF). MATERIALS AND METHODS: A systematic review was carried out according to the recommendations of the Cochrane Collaboration. We included randomised or quasi-randomised clinical trials that analysed children with CP classified according to The Gross Motor Function Classification System (GMFCS) I-III. The search was carried out in PubMed, PEDro, CENTRAL, CINALH, Cochrane, Embase, Europe PMC, LILACS and Science Direct. The selection and extraction of data from the studies was carried out by two independent researchers. Disagreements were resolved by consensus. A descriptive analysis of the selected studies was performed. Assessment of risk of bias was performed with the Cochrane Collaboration tool. RESULTS: Four studies met the eligibility criteria. Most of the temporal-spatial, kinetic and kinematic parameters of gait were evaluated, all corresponding to the activity component of the ICF. CONCLUSIONS: Due to the methodological variability of the studies, it is not possible to determine whether robot-assisted gait training is effective for treatment in children with CP.

PMID: 32370825

10. [Benefits of robotics in gait rehabilitation in cerebral palsy: A systematic review].[Article in Spanish]
Lobato Garcia L, González González Y, Da Cuña Carrera I, Alonso Calvete A.
BACKGROUND AND AIM: Cerebral palsy is the most common motor disability in childhood, with an estimated incidence of two out of every 1,000 live births. The impairment mostly affects gait. The aim of rehabilitation programmes is to enhance independence in affected individuals, especially mobility. To do this, robot-assisted gait rehabilitation programmes have been developed. Therefore, this study aimed to identify the benefits of robotics in gait rehabilitation in cerebral palsy. MATERIAL AND METHODS: We performed a literature search using the MeSH terms «cerebral palsy», «robotics» and «gait». RESULTS: After applying the selection criteria, we obtained 10 research studies and three protocols analysing the benefits of robotics in cerebral palsy and demonstrating that their use provides major advantages.

PMID: 32370827


Investigating muscle activity and coactivation with surface electromyography (sEMG) gives insight into pathological muscle function during activities like walking in people with neuromuscular impairments, such as children with cerebral palsy (CP). There is large variation in the amount of coactivation reported during walking in children with CP, possibly due to the inconsistent handling of sEMG and in calculating the coactivation index. The aim of this study was to evaluate how different approaches of handling sEMG may affect the interpretation of muscle activity and coactivation, by looking at both absolute and normalized sEMG. Twenty-three ambulatory children with CP and 11 typically developing (TD) children participated. We conducted a three-dimensional gait analysis (3DGA) with concurrent sEMG measurements of tibialis anterior, soleus, gastrocnemius medialis, rectus femoris, and hamstring medialis. They walked barefoot at a self-selected, comfortable speed back and forth a 7-m walkway. The gait cycle extracted from the 3DGA was divided into six phases, and for each phase, root mean square sEMG amplitude was calculated (sEMG-RMS-abs), and also normalized to peak amplitude of the linear envelope (50-ms running RMS window) during the gait cycle (sEMG-RMS-norm). The coactivation index was calculated using sEMG-RMS-abs and sEMG-RMS-norm values and by using two different indices. Differences between TD children's legs and the affected legs of children with CP were tested with a mixed model. The between-subject muscle activity variability was more evenly distributed using sEMG-RMS-norm; however, potential physiological variability was eliminated as a result of normalization. Differences between groups in one gait phase using sEMG-RMS-abs showed opposite differences in another phase using sEMG-RMS-norm for three of the five muscles investigated. The CP group showed an increased coactivation index in two out of three muscle pairs using sEMG-RMS-abs and in all three muscle pairs using sEMG-RMS-norm. These results were independent of index calculation method. Moreover, the increased coactivation indices could be explained by either reduced agonist activity or increased antagonist activity. Thus, differences in muscle activity and coactivation index between the groups change after normalization. However, because we do not know the truth, we cannot conclude whether to normalize and recommend incorporating both.

PMID: 32362862


PMID: 32384364

AIM: To link data from a large maternal perinatal trial with the Australian Cerebral Palsy Register (ACPR) to identify children with cerebral palsy (CP). METHOD: Deidentified data from the Australasian Collaborative Trial of Magnesium Sulphate (ACTOMgSO4) and the ACPR were linked. Children born from 1996 to 2000 at Australian hospitals who survived and had 2-year paediatric assessments were included. Children identified with CP in: (1) both the ACTOMgSO4 (2y) and the ACPR (5y), (2) the ACTOMgSO4 only, and (3) the ACPR only were compared. RESULTS: We included 913 children (492 males, 421 females; mean gestational age at birth 27.8wks [standard deviation 2.1wks]; range 23.0-40.0wks). Eighty-four children received a CP diagnosis: 35 by the ACTOMgSO4 and the ACPR, 29 by the ACTOMgSO4 only, and 20 by the ACPR only. The ACTOMgSO4 diagnosed 76.2% (95% confidence interval [CI] 65.9-84.1) and the ACPR identified 65.5% (95% CI 54.7-74.9). Children born in states/territories with long-standing versus more recently established registers were more likely to be included on the ACPR (p<0.05). INTERPRETATION: Linking deidentified perinatal trial data with the ACPR was achieved. Limitations of both strategies for identifying children with CP in this era (late 1990s and early 2000s) probably explain many of the differences observed, and inform future linkage studies and evaluations of CP-preventive interventions.

PMID: 32383806


AIM: The aim was to identify the prevalence of long-lasting pain among children with cerebral palsy (CP) and to investigate the association between pain and participation in physical leisure activities. METHODS: This is a cross-sectional study based on data from the National Danish Clinical Quality Database of children with CP. The study population consisted of 960 children aged 2-11 years across all Gross Motor Function Classification System (GMFCS) levels. Data were collected at children's regular clinical visits in 2016 or 2017. Information about pain and participation in physical leisure activities were obtained. The association was estimated as odds ratios (OR) and 95% confidence intervals (95% CI) by logistic regression adjusted for age and sex. RESULTS: We included data from 817 children (59% boys) median age six years, 52% classified as GMFCS-level I. A total of 36% reported pain and the most frequent pain locations were hips, feet and knees. Children reporting pain had lower odds for participation in physical leisure activities (OR 0.71, 95% CI 0.53-0.96). CONCLUSION: A large proportion of children with CP reported pain. There is an indication that long-lasting pain influences participation in physical leisure activities. Pain relieving interventions are important to decrease pain-related suffering and facilitate participation.

PMID: 32374451

15. Early identification of infants at risk of cerebral palsy: developing the use of general movement assessment in routine clinical practice in a tertiary neonatal unit in New Zealand.
Sandle M, Sheppard A, Fletcher AA, Berry M, DeVries N.


BACKGROUND: Preterm infants have a high risk of neurodevelopmental disability, including cerebral palsy (CP). Often, CP is not diagnosed until after 12 months, leading to delay in targeted interventions. The General Movements assessment (GM) evaluates the spontaneous movements of high-risk infants from birth to 20 weeks corrected postnatal age (CPA), and accurately predicts the risk of CP. This allows for earlier diagnosis and intervention, potentially changing the trajectory of disability, yet routine use of GM is not well established in New Zealand. AIM: To describe the process of setting up GM in a tertiary neonatal unit. METHODS: We reviewed the process and progress made to date setting up GM in our service. RESULTS: Challenges and potential solutions for the implementation of GM were identified. Key areas of development included staff training and support, IT services, resources, medical documentation, inter-departmental communication and establishing clinical pathways. CONCLUSION: GM has become successfully integrated into the assessment of high-risk infants in our neonatal unit, with the aim to provide valuable information to health professionals and families to optimise intervention and improve outcomes. Efforts will continue to ensure there is robust and sustainable system for using GM in our service.
Dieleman LM, Soenens B, Prinzie P, De Clercq L, Ortibus E, De Pauw SSW.


The purpose of this study was to advance the current understanding of the daily dynamics that are involved in raising a child with Cerebral Palsy (CP). Specifically, we examined the role of mindful parenting and of day-to-day variation in parents' psychological needs and child behavior in explaining day-to-day variation in parents' autonomy-supportive, psychologically controlling, and responsive parenting behavior. Parents (N = 58) of children with CP (Mage = 12.68 years) participated in a 7-day diary study. Multilevel analyses indicated that parents' autonomy-supportive, psychologically controlling, and responsive behaviors fluctuate considerably between days. Further, daily fluctuations in both child behavior and parents' own psychological needs were found to be associated with this daily variability in parenting. In addition, interindividual differences in mindful parenting were associated positively with parents' responsiveness and negatively with psychologically controlling parenting across the week. These findings point towards the changeability of parenting behavior among parents of a child with CP and suggest that interventions targeting parenting behavior in the context of CP will be most effective when taking into account both the parents' and the child's functioning.

PMID: 32381132

17. Longitudinal Trajectories and Reference Percentiles for Participation in Family and Recreational Activities of Children with Cerebral Palsy.
Chiarello LA, Palisano RJ, Avery L, Hanna S; On Track Study Team.


Aim: To create longitudinal trajectories and reference percentiles for frequency of participation in family and recreational activities for children with cerebral palsy (CP) by Gross Motor Function Classification System (GMFCS) level.Methods: 708 children with CP 18-months to 12-years of age and their families participated in two to five assessments using the GMFCS and Child Engagement in Daily Life Measure. Data were analyzed using mixed-effects models and quantile regression. Results: Longitudinal trajectories depict the relatively stable level of frequency of participation with considerable individual variability. Average change in the frequency of participation scores of children from 2-12 years of age by GMFCS level varied from 3.7 (GMFCS level I) to -9.0 points (GMFCS level V). A system to interpret the magnitude of change in percentiles over time is presented. Conclusions: Longitudinal trajectories and reference percentiles can inform therapists and families for collaboratively designing services and monitoring performance to support children's participation in family and recreational activities.

PMID: 32363980

18. The use of complementary and alternative medicine treatments by mothers of children with developmental disabilities.
Dr Sener DK, Dr Karaca A.


This study aims to determine the rates of complementary and alternative medicine methods used by mothers of children with developmental disabilities, reasons for using methods and comparison of methods according to diagnosis groups. The cohort in this cross-sectional and correlational study consisted of the mothers of 390 students with developmental disabilities. 77.2% of the mothers reported using at least one complementary and alternative medicine treatment. The highest level of use was found in the groups of mothers of children with cerebral palsy (100%) and autism spectrum disorder (88.5%), respectively. The most
commonly used treatments were biological therapies consisting of special diets and multivitamins, manipulative and body-based methods including massage and exercise, and mind-body interventions such as prayer, wearing amulets and seeking help from a Muslim preacher (hodja). However, mothers never used alternative medicine treatments such as homeopathy, acupuncture, or Ayurveda, nor did they use energy-based healing techniques such as reiki, tai chi, yoga, kinesiology, or neurofeedback exercises. Healthcare professionals, especially nurses as health care team members, should be knowledgeable and careful about the benefits, side effects, administration methods, and contraindications of complementary and alternative medicine treatments. This article is protected by copyright. All rights reserved.

PMID: 32362016

19. Neurodevelopmental impairment at three years of age after fetoscopic laser surgery for twin-to-twin transfusion syndrome.


BACKGROUND: Data on neurodevelopmental outcomes of children surviving after fetoscopic laser surgery (FLS) for twin-to-twin transfusion syndrome (TTTS) are scarce. METHODS: We retrospectively investigated children surviving after FLS for TTTS at 16-26 weeks’ gestation between 2003-2014. Children were evaluated by standardized neurologic examinations using the Kyoto Scale 2001 at a corrected age of 3 years ±6 months. Neurodevelopmental impairment (NDI) was defined as cerebral palsy (CP), bilateral blindness, bilateral deafness or a developmental quotient (DQ) < 70 points. Brain magnetic resonance imaging (MRI) was performed at term-equivalent age. RESULTS: A total of 188 children from 110 twin pregnancies were evaluated. NDI was detected in 16/188 (8.5%) children, including 6 cases of CP (3.2%). No children had bilateral blindness or deafness. An earlier gestational age at delivery was associated with a higher incidence of NDI (P < 0.001). Abnormal brain MRI findings were detected in 9/16 (56%) of children with NDI, including 6/6 (100%) with CP.

CONCLUSION: The incidence of NDI in children following FLS at 3 years old was 8.5%. Prematurity is a strong risk factor for NDI. Brain MRI may predict the development of CP. This article is protected by copyright. All rights reserved.

PMID: 32362029

20. Prolonged astrocyte-derived erythropoietin expression attenuates neuronal damage under hypothermic conditions.
Toriuchi K, Kakita H, Tamura T, Takeshita S, Yamada Y, Aoyama M.


BACKGROUND: Hypoxic-ischemic encephalopathy (HIE) has a high morbidity rate and involves severe neurologic deficits, including cerebral palsy. Therapeutic hypothermia (TH) has been shown to decrease the mortality rate and provide neuroprotection in infants with HIE. However, death and disability rates in HIE infants treated with TH remain high. Although the cellular mechanism of the neuroprotective effect of TH remains unclear, astrocytic erythropoietin (EPO) is known to be a key mediator of neuroprotection under hypoxic conditions. In the present study, we investigated the hypothermia effect on EPO expression in astrocytes and determined whether hypothermia attenuates neuronal damage via EPO signaling. METHODS: Astrocytes derived from rat cerebral cortex were cultured under oxygen/glucose deprivation (OGD). The expression of EPO and hypoxia-inducible factor (HIF), a transcription factor of EPO, was assessed. After OGD, astrocytes were cultured under normothermic (37 °C) or hypothermic (33.5 °C) conditions, and then EPO and HIF expression was assessed. After OGD, rat cortical neurons were cultured in astrocyte-conditioned medium (ACM) derived from the hypothermic group, and neuronal apoptosis was evaluated. RESULTS: OGD induced EPO mRNA and protein expression, although at lower levels than hypoxia alone. HIF-1α and HIF-2α protein expression increased under hypoxia alone and OGD, although OGD increased HIF-2α protein expression less than hypoxia alone. EPO gene and protein expression after OGD was significantly higher under hypothermia. Moreover, expression of HIF-1α and HIF-2α protein was enhanced under hypothermia. In the presence of ACM derived from hypothermic astrocytes following OGD, the number of cleaved caspase 3 and TdT-mediated dUTP nick-end labeling-positive apoptotic neurons was lower than in the presence of ACM from normothermic astrocytes following OGD. Blockade of EPO signaling using anti-EPO neutralization antibody attenuated the anti-apoptotic effect of ACM derived from
hypothermic astrocytes following OGD. CONCLUSIONS: Hypothermia after OGD stabilized HIF-EPO signaling in astrocytes, and upregulated EPO expression could suppress neuronal apoptosis. Investigating the neuroprotective effect of EPO from astrocytes under hypothermic conditions may contribute to the development of novel neuroprotection-based therapies for HIE.

PMID: 32359362