Cerebral palsy research news

Monday 7 September 2020

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Interventions and Management

1. Upper Extremity Muscle Strength in Children With Unilateral Spastic Cerebral Palsy: A Bilateral Problem?
Koen J F M Dekkers, Eugene A A Rameckers, Rob J E M Smeets, Andrew M Gordon, Lucianne A W M Speth, Claudio L Ferre, Yvonne J M Janssen-Potten

Phys Ther. 2020 Aug 28;pzaa155. doi: 10.1093/ptj/pzaa155. Online ahead of print.

Objective: The objective was to investigate whether muscle strength in the nonaffected and affected upper extremities (UEs) in children (7-12 years) with unilateral spastic cerebral palsy (USCP) differs from that in children with typical development (TD). Methods: A cross-sectional study design was used. Isometric arm strength (wrist flexion, wrist extension with flexed and extended fingers, elbow flexion/extension) was assessed in 72 children (mean age = 9.3 [SD = 1.9] years) with USCP, and isometric grip/pinch strength was assessed in 86 children (mean age = 9.3 [SD = 1.8] years) with USCP. Arm/grip/pinch strength was assessed in 120 children (mean age = 9.5 [SD = 1.7] years) with TD. Arm strength was measured with a hand-held dynamometer, and grip/pinch strength was measured with a calibrated, modified (digitized) grip dynamometer and a pinch meter. The nonaffected UE of children with USCP was compared with the preferred UE of children with TD, because both sides represent the preferred UE. The affected UE was compared with the nonpreferred UE of children with TD, as both sides represent the nonpreferred UE. Results: In all measurements except for grip strength of the preferred UE, children with USCP were weaker than children with TD. Conclusions: In children with USCP, muscle strength weakness exists in both UEs. Impact: When unimanual or bimanual ability limitations are present in children with unilateral cerebral palsy, investigation of the muscle strength of the nonaffected UE should be part of the assessment.

PMID: 32860701

2. Upper Extremity Tendon Transfers: A Brief Review of History, Common Applications, and Technical Tips
Jason Gardenier, Rohit Garg, Chaitanya Mudgal

Indian J Plast Surg. 2020 Aug;53(2):177-190. doi: 10.1055/s-0040-1716456. Epub 2020 Aug 29.

Background Tendon transfer in the upper extremity represents a powerful tool in the armamentarium of a reconstructive surgeon in the setting of irreparable nerve injury or the anatomic loss of key portions of the muscle-tendon unit. The concept uses the redundancy/expendability of tendons by utilizing a nonessential tendon to restore the function of a lost or nonfunctional muscle-tendon unit of the upper extremity. This article does not aim to perform a comprehensive review of tendon transfers. Instead it is meant to familiarize the reader with salient historical features, common applications in the upper limb, and provide the reader with some technical tips, which may facilitate a successful tendon transfer. Learning Objectives (1) Familiarize the reader with some aspects of tendon transfer history. (2) Identify principles of tendon transfers. (3) Identify important preoperative considerations. (4) Understand the physiology of the muscle-tendon unit and the Blix curve. (5) Identify strategies for setting tension during a tendon transfer and rehabilitation strategies. Design This study was designed to

review the relevant current literature and provide an expert opinion. Conclusions Tendon transfers have evolved from polio to tetraplegia to war and represent an extremely powerful technique to correct neurologic and musculotendinous deficits in a variety of patients affected by trauma, peripheral nerve palsies, cerebral palsy, stroke, and inflammatory arthritis. In the contemporary setting, these very same principles have also been very successfully applied to vascularized composite allotransplantation in the upper limb.

PMID: 32884184

3. Surgical site infections in pediatric spinal surgery after implementation of a quality assurance program
Bradley Hammoor, Hiroko Matsumoto, Gerard Marciano, Lucas Dziesinski, Kevin Wang, Benjamin D Roye, David P Roye, Michael G Vitale

Spine Deform. 2020 Sep 1. doi: 10.1007/s43390-020-00192-4. Online ahead of print.

Objective: To assess the effectiveness of two infection-reducing programs in mitigating the incidence of post-operative surgical site infections (SSI) in pediatric patients after spinal deformity surgery at our institution. Infections following spinal deformity surgery are associated with higher morbidity as well as significantly increased healthcare costs. SSI in patients with neuromuscular etiologies is especially high, exceeding 8 percent for myelodysplasia patients and 6 percent for cerebral palsy patients. Methods: Manual chart review was conducted for 1934 pediatric spine procedures in 1200 patients at our institution between 2008 and 2018. Patients between the ages of 0 and 21 having any spinal surgical procedure including lengthening of growing rods were included. Results: Institution of two separate infection-reducing programs reduced risk of SSI in this population by 65.4%, when adjusted for age and number of instrumentation levels (risk ratio [RR] = 0.3, 95% confidence interval [CI] = 0.2; 0.6, p = 0.001). Patients undergoing Initial Instrumentation demonstrated 68.8% less risk of SSI compared to those who had other types of surgical procedures, after adjusting for age and the number of level instrumented (RR = 0.3, 95% CI 0.2; .6, p = 0.002). It was observed that the effect of each of these infection-reducing programs diminished with time. This effect was also observed with prior programs implemented at our institution. Conclusion: The incidence of SSI decreased following the implementation of two infection-reducing programs especially in patients undergoing Initial Instrumentation procedures. However, time-series analysis suggests these programs may have maximal effect immediately following institution that diminishes with time. Level of evidence: Level III.

PMID: 32875547

4. Does screw position matter for guided growth in cerebral palsy hips?
Po-Jen Hsu, Kuan-Wen Wu, Chia-Che Lee, Sheng-Chieh Lin, Ken N Kuo, Ting-Ming Wang

Bone Joint J. 2020 Sep;102-B(9):1242-1247. doi: 10.1302/0301-620X.102B9.BJJ-2020-0340.R1.

Aims: Guided growth has been used to treat coxa valga for cerebral palsy (CP) children. However, there has been no study on the optimal position of screw application. In this paper we have investigated the influence of screw position on the outcomes of guided growth. Methods: We retrospectively analyzed 61 hips in 32 CP children who underwent proximal femoral hemi epiphysiodesis between July 2012 and September 2017. The hips were divided into two groups according to the transphyseal position of the screw in the coronal plane: across medial quarter (Group 1) or middle quarter (Group 2) of the medial half of the physis. We compared pre- and postoperative radiographs in head-shaft angle (HSA), Reimer's migration percentage (MP), acetabular index (AI), and femoral anteversion angle (FAVA), as well as incidences of the physis growing-off the screw within two years. Linear and Cox regression analysis were conducted to identify factors related to HSA correction and risk of the physis growing-off the screw. Results: A total of 37 hips in Group 1 and 24 hips in Group 2 were compared. Group 1 showed a more substantial decrease in the HSA (p = 0.003) and the MP (p = 0.032). Both groups had significant and similar improvements in the AI (p = 0.809) and the FAVA (p = 0.304). Group 1 presented a higher incidence of the physis growing-off the screw (p = 0.038). Results of the regression analysis indicated that the eccentricity of screw position correlated with HSA correction and increases the risk of the physis growing-off the screw. Conclusion: Guided growth is effective in improving coxa valga and excessive femoral anteversion in CP children. For younger children, despite compromised efficacy of varus correction, we recommend a more centered screw position, at least across the middle quarter of the medial physis, to avoid early revision. Cite this article: Bone Joint J 2020;102-B(9):1242-1247.

PMID: 32862682

5. Suspension of Hip Surveillance for Children with Cerebral Palsy During the COVID-19 Outbreak: The Benefit of Hip Surveillance Does Not Outweigh the Risk of Infection
Stacey Miller, Jeffrey Bone, Kishore Mulpuri

Review Indian J Orthop. 2020 Aug 28;1-3. doi: 10.1007/s43465-020-00236-x. Online ahead of print.

PMID: 32873988

6. [Therapeutic effect of scalp acupuncture combined with rehabilitation training on balance dysfunction in children with spastic hemiplegia][Article in Chinese]
Wei Luo, Pao-Qiu Wang, Chun-Lei Liu, Chao Huang, Yong Yang, Yi-Mei Wang

Zhen Ci Yan Jiu. 2020 Aug 25;45(8):662-6. doi: 10.13702/j.1000-0607.190461.

Objective: To investigate the therapeutic effect of scalp acupuncture and rehabilitation training on balance dysfunction in children with spasmodic hemiplegia so as to provide the reference to the optimization of treatment scheme. Methods: A total of 60 children with spastic hemiplegia were divided into a routine group and a scalp acupuncture group, 30 cases in each one according to random number table. In the routine group, the rehabilitation training was provided, including exercise training, balance training, spasmotherapy apparatus, electromyography biofeedback apparatus and orthoses. In the scalp acupuncture group, on the base of the treatment as the routine group, scalp acupuncture was supplemented at motor area, foot motor sensory area, equilibrium area and parietal temporal anterior oblique line. Separately, before the treatment, after 3 months treatment and after 6 months treatment, the dimension D and E of the gross motor function measure-88 (GMFM-88) and Berg balance scale (BBS) were adopted to evaluate balance related motor functions and equilibrium function. The differences in the above 3 indicators at different time stages were compared in children between the two groups. Results: Compared with the score before the treatment, BBS score was obviously increased after 3 and 6 months treatment in the patients of the two groups respectively ($P<0.05$). The score in the dimension D and E after 6-month treatment was increased significantly as compared with the score before treatment and after 3-month treatment in the same group respectively ($P<0.05$). Compared with the routine group, the score of dimension D and E of GMFM-88 as well as BBS score were all increased obviously in the scalp acupuncture group after 3 and 6 months treatment ($P<0.05$). Conclusion: On the base of routine rehabilitation training, scalp acupuncture can improve balance function of children with spastic hemiplegia better.

PMID: 32869578

7. Design, Validity, and Reliability of a New Test, Based on an Inertial Measurement Unit System, for Measuring Cervical Posture and Motor Control in Children with Cerebral Palsy
Cristina Carmona-Pérez, Alberto Pérez-Ruiz, Juan L Garrido-Castro, Francisco Torres Vidal, Sandra Alcaraz-Clariana, Lourdes García-Luque, Daiana Priscila Rodrigues-de-Souza, Francisco Alburquerque-Sendín

Diagnostics (Basel). 2020 Sep 1;10(9):E661. doi: 10.3390/diagnostics10090661.

Objective: The aim of this study was to design and propose a new test based on inertial measurement unit (IMU) technology, for measuring cervical posture and motor control in children with cerebral palsy (CP) and to evaluate its validity and reliability. Methods: Twenty-four individuals with CP (4-14 years) and 24 gender- and age-matched controls were evaluated with a new test based on IMU technology to identify and measure any movement in the three spatial planes while the individual is seated watching a two-minute video. An ellipse was obtained encompassing 95% of the flexion/extension and rotation movements in the sagittal and transversal planes. The protocol was repeated on two occasions separated by 3 to 5 days. Construct and concurrent validity were assessed by determining the discriminant capacity of the new test and by identifying associations between functional measures and the new test outcomes. Relative reliability was determined using the intraclass correlation coefficient (ICC) for test-retest data. Absolute reliability was obtained by the standard error of measurement (SEM) and the Minimum Detectable Change at a 90% confidence level (MDC90). Results: The discriminant capacity of the area and both dimensions of the new test was high (Area Under the Curve ≈ 0.8), and consistent multiple regression models were identified to explain functional measures with new test results and sociodemographic data. A consistent trend of ICCs higher than 0.8 was identified for CP individuals. Finally, the SEM can be considered low in both groups, although the high variability among

individuals determined some high MDC90 values, mainly in the CP group. Conclusions: The new test, based on IMU data, is valid and reliable for evaluating posture and motor control in children with CP.

PMID: 32882885

8. Comparison of the Results of Primary Versus Repeat Hamstrings Surgical Lengthening in Cerebral Palsy
Mauro C de Morais Filho, Francesco C Blumetti, Marcelo H Fujino, Marcelo M Matias, Cátia M Kawamura, José Augusto F Lopes

J Pediatr Orthop. 2020 Aug 28. doi: 10.1097/BPO.0000000000001675. Online ahead of print.

PMID: 32868516

9. Toward a hybrid exoskeleton for crouch gait in children with cerebral palsy: neuromuscular electrical stimulation for improved knee extension
Blynn L Shideler, Thomas C Bulea, Ji Chen, Christopher J Stanley, Andrew J Gravunder, Diane L Damiano

J Neuroeng Rehabil. 2020 Sep 3;17(1):121. doi: 10.1186/s12984-020-00738-7.

Background: Neuromuscular Electrical Stimulation (NMES) has been utilized for many years in cerebral palsy (CP) with limited success despite its inherent potential for improving muscle size and/or strength, inhibiting or reducing spasticity, and enhancing motor performance during functional activities such as gait. While surface NMES has been shown to successfully improve foot drop in CP and stroke, correction of more complex gait abnormalities in CP such as flexed knee (crouch) gait remains challenging due to the level of stimulation needed for the quadriceps muscles that must be balanced with patient tolerability and the ability to deliver NMES assistance at precise times within a gait cycle. Methods: This paper outlines the design and evaluation of a custom, noninvasive NMES system that can trigger and adjust electrical stimulation in real-time. Further, this study demonstrates feasibility of one possible application for this digitally-controlled NMES system as a component of a pediatric robotic exoskeleton to provide on-demand stimulation to leg muscles within specific phases of the gait cycle for those with CP and other neurological disorders who still have lower limb sensation and volitional control. A graphical user interface was developed to digitally set stimulation parameters (amplitude, pulse width, and frequency), timing, and intensity during walking. Benchtop testing characterized system delay and power output. System performance was investigated during a single session that consisted of four overground walking conditions in a 15-year-old male with bilateral spastic CP, GMFCS Level III: (1) his current Ankle-Foot Orthosis (AFO); (2) unassisted Exoskeleton; (3) NMES of the vastus lateralis; and (4) NMES of the vastus lateralis and rectus femoris. We hypothesized in this participant with crouch gait that NMES triggered with low latency to knee extensor muscles during stance would have a modest but positive effect on knee extension during stance. Results: The system delivers four channels of NMES with average delays of 16.5 ± 13.5 ms. Walking results show NMES to the vastus lateralis and rectus femoris during stance immediately improved mean peak knee extension during mid-stance ($p = 0.003$*) and total knee excursion ($p = 0.009$*) in the more affected leg. The electrical design, microcontroller software and graphical user interface developed here are included as open source material to facilitate additional research into digitally-controlled surface stimulation (github.com/NIHFAB/NMES). Conclusions: The custom, digitally-controlled NMES system can reliably trigger electrical stimulation with low latency. Precisely timed delivery of electrical stimulation to the quadriceps is a promising treatment for crouch. Our ultimate goal is to synchronize NMES with robotic knee extension assistance to create a hybrid NMES-exoskeleton device for gait rehabilitation in children with flexed knee gait from CP as well as from other pediatric disorders. Trial registration: clinicaltrials.gov, ID: NCT01961557 . Registered 11 October 2013; Last Updated 27 January 2020.

PMID: 32883297

10. Calf lengthening may improve knee recurvatum in specific children with spastic diplegic cerebral palsy
Jeremy Bauer, K Patrick Do, Jing Feng, Michael Aiona

J Child Orthop. 2020 Aug 1;14(4):353-357. doi: 10.1302/1863-2548.14.200092.

Purpose: Knee hyperextension in stance is a difficult condition to treat in children with spastic diplegic cerebral palsy (CP). In children with passive knee hyperextension, the presence of contracture or spasticity of the calf leads to knee hyperextension in stance phase. We hypothesize surgical treatment of the contracture of the calf will lead to less knee hyperextension. Methods: We performed a retrospective review of children who were evaluated in our movement laboratory over 23 years with a diagnosis of CP Gross Motor Function Classification System I, II or III. We selected children who had passive knee hyperextension on exam and who underwent calf lengthening surgery. Children were divided into two groups: early recurvatum (ER) (n = 20) and late recurvatum (LR) (n = 14). Results: There was no difference in the preoperative passive knee extension among the groups or the surgeries performed. For children who had passive knee hyperextension, calf lengthening improved static dorsiflexion with knee flexion on clinical exam by 9.3° in the ER group, 9.6° in the LR group as well as dorsiflexion with knee extension on clinical exam by 9.5° in the ER group and 6.4° in the LR group. The kinematic data showed that the ER group improved their knee hyperextension by 11° ($p < 0.001$), whereas the LR group did not significantly change their stance phase knee position. Conclusion: Children with passive knee hyperextension who have a calf contracture and walk in knee hyperextension in the first half of stance phase may improve after calf lengthening.Level of Evidence: III.

PMID: 32874371

11. A Systematic Review of Total Knee Arthroplasty in Neurologic Conditions: Survivorship, Complications, and Surgical Considerations
Eoghan Pomeroy, Christopher Fenelon, Evelyn P Murphy, Peter F Staunton, Fiachra E Rowan, May S Cleary

J Arthroplasty. 2020 Aug 8;S0883-5403(20)30887-1. doi: 10.1016/j.arth.2020.08.008. Online ahead of print.

Background: Patients with neurologic disorders present a unique set of challenges for knee surgeons because of contractures, muscle weakness, spasticity, and ligament instability. The primary purpose of this review was to report the outcomes of total knee arthroplasty (TKA) in these patients, including survivorship, complications, and surgical considerations. Methods: We performed a systematic review of articles using PubMed, Cochrane Central, EMBASE, and Google Scholar. All studies reporting outcomes of TKA in patients with Parkinson disease, multiple sclerosis, poliomyelitis, Charcot joint, spina bifida, stroke, and cerebral palsy were included. Results: In total 38 studies were included: 22 studies (461 patients) reported patient-reported outcome measures and 24 studies (510 patients) reported survivorship. All 38 studies reported complication rates. TKA resulted in an improvement in functional outcome in all series. Complication rate was higher in patients with neurologic conditions. Of studies reporting survivorship, mean follow-up ranged from 1 to 12 years with survivorship from 66% to 100%. All levels of implant constraint were reported without consensus. Limited rehabilitative data exist. Conclusion: TKA in patients with neurologic disorders improves symptoms and function but carries significant risk. This review helps surgeons preoperatively counsel their patients in an informed manner. Careful planning, perioperative care, and appropriate implant selection may mitigate risk of complication.

PMID: 32873450

12. Interventions and lower-limb macroscopic muscle morphology in children with spastic cerebral palsy: a scoping review
Fenna Walhain, Kaat Desloovere, Marlies Declerck, Anja Van Campenhout, Lynn Bar-On

Review Dev Med Child Neurol. 2020 Sep 2. doi: 10.1111/dmcn.14652. Online ahead of print.

Aims: To identify and map studies that have assessed the effect of interventions on lower-limb macroscopic muscle-tendon morphology in children with spastic cerebral palsy (CP). Method: We conducted a literature search of studies that included pre- and post-treatment measurements of lower-limb macroscopic muscle-tendon morphology in children with spastic CP. Study quality was evaluated and significant intervention effects and effect sizes were extracted. Results: Twenty-eight articles were identified. They covered seven different interventions including stretching, botulinum neurotoxin A (BoNT-A), strengthening, electrical stimulation, whole-body vibration, balance training, and orthopaedic surgery. Study quality ranged from poor (14 out of 28 studies) to good (2 out of 28). Study samples were small (n=4-32) and studies were variable regarding which muscles and macroscopic morphological parameters were assessed. Inconsistent effects after intervention (thickness and cross-sectional area for strengthening, volume for BoNT-A), no effect (belly length for stretching), and small effect sizes were reported. Interpretation: Intervention studies reporting macroscopic muscle-tendon remodelling after interventions are limited and heterogeneous, making it difficult to generalize results. Studies that include control groups and standardized assessment protocols are needed to improve study quality and data synthesis. Lack or inconclusive effects at the macroscopic level could

indicate that the effects of interventions should also be evaluated at the microscopic level. What this paper adds: Muscle-targeted interventions to remodel muscle morphology are not well understood. Studies reporting macroscopic muscle remodelling following interventions are limited and heterogeneous. Passive stretching may preserve but does not increase muscle length. The effects of isolated botulinum neurotoxin A injections on muscle volume are inconsistent. Isolated strengthening shows no consistent increase in muscle volume or thickness.

PMID: 32876960

13. Effectiveness of instrumented gait analysis in interdisciplinary interventions on parents' perception of family-centered service and on gross motor function in children with cerebral palsy: a randomized controlled trial
Christina Esmann Fonvig, Helle Mätzke Rasmussen, Søren Overgaard, Anders Holsgaard-Larsen

BMC Pediatr. 2020 Sep 1;20(1):411. doi: 10.1186/s12887-020-02315-2.

Background: Children with cerebral palsy often exhibit an altered gait pattern; however, it is uncertain whether the use of an instrumented gait analysis in interdisciplinary interventions affects the perceived experience of family-centered service (FCS) and/or gross motor function. The aim of this study is to investigate whether individually tailored interdisciplinary interventions, based on an instrumented gait analysis report, has a superior effectiveness on perceived FCS and gross motor function in children with cerebral palsy, compared to 'care as usual' without the use of instrumented gait analysis. Furthermore, to investigate potential associations between perceived FCS and gross motor function improvement with the goal of improving future therapy on gross motor function. Method: This is a sequel analysis on tertiary outcome measures from a prospective, single blind, randomized, parallel group study including two groups of 30 children aged 5-8 years with spastic cerebral palsy at Gross Motor Function Classification System levels I-II (n = 60). The intervention group underwent a three-dimensional gait analysis, from which a clinical report was written with recommendations on interdisciplinary interventions, such as physical therapy, orthopedic surgery, orthotics or spasticity management. To assess effectiveness on perceived FCS and gross motor function, at baseline, 26 weeks and 52 weeks, the five domains in the Measure of Processes of Care (MPOC-20) (Enabling and partnership, Providing general information, Providing specific information about the child, Respectful and supportive service, and Coordinated and comprehensive care) and the Gross Motor Function Measurement (GMFM-66) were used as outcome measures. Results: No significant differences in between-group change scores in any of the five MPOC-20 domains were observed (p = 0.40-0.97). In favor of the intervention group a significantly higher between-group change score in GMFM-66 (mean difference: 3.05 [95%CI: 1.12-4.98], p = 0.003) after 52 weeks was observed. Conclusion: The addition of an instrumented gait analysis report to 'care as usual' did not improve the parents' perceptions of FCS in treatment of children with cerebral palsy. However, superior improvement in the GMFM-66 was observed in the intervention group, suggesting meaningful gross motor function improvement. Trial registration: Clinical Trials, NCT02160457 . Registered June 10th 2014.

PMID: 32873289

14. Toe walking in children with cerebral palsy: a possible functional role for the plantar flexors
Christian Beyaert, Jonathan Pierret, Rajul Vasa, Jean Paysant, Sébastien Caudron

J Neurophysiol. 2020 Sep 2. doi: 10.1152/jn.00717.2019. Online ahead of print.

Equinus and toe walking are common locomotor disorders in children with cerebral palsy (CP) walking barefoot or with normal shoes. We hypothesized that, regardless of the type of footwear, the plantar flexors do not cause early equinus upon initial foot contact, but decelerate ankle dorsiflexion during weight acceptance (WA). This latter action promoted by early flat-foot contact is hypothesized to be functional. Hence, we performed an instrumented gait analysis of 12 children with CP (Gross Motor Function Classification System class: I or II; mean age: 7.2 years) and 11 age-matched typically developing children. The participants walked either barefoot, with unmodified footwear (4° positive-heel shoes) or with 10° negative-heel shoes (NHSs). In both groups, wearing NHSs was associated with greater ankle dorsiflexion upon initial foot contact, and greater tibialis anterior activity (but no difference in soleus activity) during the swing phase. However, the footwear condition did not influence the direction and amplitude of the first ankle movement during WA and the associated peak negative ankle power. Regardless of the footwear condition, the CP group displayed (i) early flattening of the foot and ample dorsiflexion (decelerated by the plantar flexors) during WA, and (ii) low tibialis anterior and soleus activities during the second half of the swing phase (contributing to passive equinus upon foot strike). In children with CP, the early action of plantar flexors (which typically decelerate the forward progression of the center of mass) may be a compensatory mechanism that contributes to the WA's role in controlling balance during gait.

PMID: 32877265

15. Does the Type of Toeing Affect Balance in Children With Diplegic Cerebral Palsy? An Observational Cross-sectional Study
Heba G Abd El Aziz, Ayman H El Khatib, Hamada A Hamada

J Chiropr Med. 2019 Sep;18(3):229-235. doi: 10.1016/j.jcm.2019.01.005. Epub 2020 Aug 21.

Objective: The purpose of the study was to find out effect of toeing on balance in children with diplegic cerebral palsy. Methods: An observational study was conducted. Thirty children with spastic diplegic cerebral palsy, aged 5 to 8 years, participated in this study. They were classified into 2 groups: group A was children with out-toeing, and group B was children with in-toeing. Foot progression angle was measured by using dynamic footprint, and balance was evaluated using Biodex Balance System equipment. The outcome of interest was postural control (overall stability, anteroposterior stability, and mediolateral stability). Results: Statistical analysis revealed a significant difference for the tested variables of interest between the 2 tested groups. Multiple pairwise comparison tests revealed that there was significantly better overall stability, anteroposterior stability, and mediolateral stability ($P < .05$) in group A. Conclusion: It can be concluded that children with out-toeing have higher balance and stability than children with in-toeing.

PMID: 32874163

16. Dystonia and choreoathetosis presence and severity in relation to powered wheelchair mobility performance in children and youth with dyskinetic cerebral palsy
Saranda Bekteshi, Marco Konings, Ioana Gabriela Nica, Sotirios Gakopoulos, Jean-Marie Aerts, Hans Hallez, Elegast Monbaliu

Eur J Paediatr Neurol. 2020 Aug 22;S1090-3798(20)30163-X. doi: 10.1016/j.ejpn.2020.08.002. Online ahead of print.

Introduction: Power wheelchairs (PW) with head/foot steering systems are used as an alternative to joysticks in children with severe dyskinetic cerebral palsy (DCP). Mobility training programs are unstandardized to date, and insight on dystonia, choreoathetosis, and mobility performance may lead to greater independent mobility. Objective: To map the presence and severity of dystonia and choreoathetosis during PW mobility in DCP and their relation with mobility performance. Methods: Ten participants with DCP performed four PW mobility tasks using a head/foot steering system. Dystonia and choreoathetosis in the neck and arm regions were evaluated using the Dyskinesia Impairment Mobility Scale (DIMS). PW mobility performance was assessed using time-on-task and the number of errors during performance. The Wilcoxon-signed rank test and the Spearman's correlation coefficients were used to explore differences and correlations. Results: Median levels of dystonia (83.6%) were significantly higher ($p < 0.01$) than median levels of choreoathetosis (34.4%). Positive significant correlations were found between the Arm Proximal DIMS and the PW mobility experience ($rs=-0.92$, $p < 0.001$), and between the Arm Distal DIMS and the number of errors ($rs = 0.66$, $p = 0.039$) during mobility performance. Conclusions: Dystonia is more present and severe during PW mobility than choreoathetosis. The hypertonic hallmark of dystonia may mask the hyperkinetic hallmark of choreoathetosis, resulting in lower median levels. Results may suggest that with an increase in driving experience, children with DCP adopt deliberate strategies to minimize the negative impact of arm overflow movements on mobility performance, however, future research with bigger sample size and additional outcome measures is strongly encouraged.

PMID: 32868197

17. High clinician- and patient-reported satisfaction with individualized onabotulinumtoxinA treatment for spasticity across several etiologies from the ASPIRE study
Gerard E Francisco, Daniel S Bandari, Ganesh Bavikatte, Wolfgang H Jost, Emily McCusker, Joan Largent, Aleksej Zuzek, Alberto Esquenazi

Toxicon X. 2020 Jun 6;7:100040. doi: 10.1016/j.toxcx.2020.100040. eCollection 2020 Sep.

Etiology-specific onabotulinumtoxinA utilization to manage spasticity is largely unknown. In this 1-year interim analysis, we evaluated real-world onabotulinumtoxinA utilization and effectiveness across several etiologies from the Adult Spasticity International Registry (ASPIRE) study. ASPIRE is a multicenter, prospective, observational registry (NCT01930786) examining stroke, multiple sclerosis [MS], cerebral palsy [CP], traumatic brain injury [TBI], and spinal cord injury [SCI] patients with spasticity treated with onabotulinumtoxinA at the clinician's discretion. Assessments included onabotulinumtoxinA utilization (each session), clinician (subsequent session)/patient (5±1 weeks post-treatment) satisfaction, and the Disability Assessment Scale (DAS; subsequent session). 730 patients received ≥1 onabotulinumtoxinA treatment, with 37% naïve to botulinum toxin(s) for spasticity. The most common etiology was stroke (n=411, 56%), followed by MS (N=119, 16%), CP (N=77, 11%), TBI (N=45, 6%), and SCI (N=42, 6%). The total body mean cumulative dose (±SD) of onabotulinumtoxinA per session ranged from 296 U (±145) in CP to 406 U (±152) in TBI. The most commonly treated upper limb presentations were clenched fist (stroke, MS, and SCI), flexed wrist (CP), and flexed elbow (TBI). Equinovarus foot was the most commonly treated lower limb presentation in all etiologies. Stroke patients showed improved DAS scores for nearly all subscales in both limbs, indicative of improved global function. All etiologies showed improved lower limb mobility DAS scores. Across all sessions, clinicians (range: 87.4% [SCI]-94.2% [CP]) and patients (range: 67.6% [TBI]-89.7% [SCI]) reported extreme satisfaction/satisfaction that onabotulinumtoxinA helped manage spasticity, and clinicians (range: 94.6% [TBI]-98.8% [CP]) and patients (range: 88.4% [stroke]-91.2% [TBI]) would definitely/probably continue treatment. Treatment-related adverse events (TRAEs) and treatment-related serious adverse events (TRSAEs) were reported as follows: stroke: 10 TRAEs (2.2% patients), 3 TRSAEs (0.5%); MS: 5 TRAEs (4.2%), 0 TRSAEs; CP: 0 TRAEs, 0 TRSAEs; TBI: 1 TRAEs (2.2%), 0 TRSAEs; SCI: 0 TRAEs, 0 TRSAEs. No new safety signals were identified. High clinician- and patient-reported satisfaction were observed following individualized onabotulinumtoxinA treatment, as well as improved global function. Interim results from ASPIRE demonstrate etiology-specific similarities and differences in clinical approaches to manage spasticity.

PMID: 32875289

18. Pharmacological Management of Spasticity in Children With Cerebral Palsy
Mary Reilly, Kayley Liuzzo, Allison B Blackmer

J Pediatr Health Care. Sep-Oct 2020;34(5):495-509. doi: 10.1016/j.pedhc.2020.04.010.

Cerebral palsy (CP), a nonprogressive disease of the central nervous system, is the most common motor disability in childhood. Patients with CP often have a multitude of associated comorbidities, including impact on muscle tone. There are four main types of CP, with spastic as the most commonly diagnosed. Reduction in spasticity is important because it can affect not only the patient's quality of life, functional abilities, and well-being but also the lives of caregivers. The American Academy of Neurology and Child Neurology Society released a practice parameter regarding the pharmacological management of CP-related spasticity in 2010. Since then, data have been published evaluating the safety and efficacy of oral and parenteral medications to manage spasticity. This continuing education review evaluates the available safety and efficacy evidence for oral and parenteral pharmacological agents used to reduce spasticity in children with CP and provides a reference for practitioners managing these patients.

PMID: 32861428

19. Exploring the association of predisposing factors of Cerebral Palsy and developmental defects of enamel: a case-control study
B R Nogueira, A M Silva, T de Castelo Branco Araújo, M C Ferreira, R F Mendes, R R Prado Júnior

Eur Arch Paediatr Dent. 2020 Aug 29. doi: 10.1007/s40368-020-00558-2. Online ahead of print.

Aim: To evaluate the occurrence of developmental defects of enamel (DDE) in children and adolescents with Cerebral Palsy (CP) and to analyze the effect of common factors in the etiology of CP on the occurrence of DDE. Methods: A case-control study was carried out using the modified DDE index to classify enamel defects. The study group (SG) consisted of 45 participants with CP aged between three and 14 years. The control group (CG) consisted of 88 normotypical schoolchildren, paired by gender and age group. Caregivers answered a questionnaire on their socioeconomic status and medical history. The Chi-square tests, bivariate and multivariate analysis were performed (level significance < 0.05). Results: The occurrence of

DDE in SG and CG was 60% and 64.8%, respectively (p value = 0.726). The most frequent defect observed in SG was diffuse opacity (44.4%), followed by demarcated opacity (26.7%) and enamel hypoplasia (2.2%). No difference was observed in the defect's distribution among both groups (p value = 0.083). For SG, the bivariate analysis revealed a statically significant association between the presence of DDE and age group 7-14 years old and maternal schooling below 11 years. After adjusting for confounding variables, age, family income and maternal schooling were not associated with DDE. Conclusion: In conclusion, the occurrence of DDE was high and similar in both groups. The pre, peri or post-natal factors associated with CP were not significant for the presence of DDE.

PMID: 32860616

20. Prenatal Tobacco Exposure and Childhood Neurodevelopment among Infants Born Prematurely
Lindsay S Robbins, Christina T Blanchard, Rachel G Sinkey, Stacy L Harris, Alan T Tita, Lorie M Harper

Am J Perinatol. 2020 Aug 30. doi: 10.1055/s-0040-1715845. Online ahead of print.

Objective: Nicotine is an established neuroteratogen, and prenatal tobacco exposure alters the structure of the developing nervous system. An association between prenatal tobacco exposure and impaired neurologic function is less well established. We examine the association between prenatal tobacco exposure and childhood neurodevelopment among infants born preterm. Study design: Secondary analysis of a multicenter randomized controlled trial assessing the benefits of magnesium sulfate for the prevention of cerebral palsy in preterm infants. Women were included if they delivered a singleton and nonanomalous infant before 37 weeks. Exposure was any self-reported prenatal tobacco use. Primary outcome was the original trial composite outcome of moderate or severe cerebral palsy at 2 years of age, or stillbirth, or infant death by 1 year of age. Secondary outcomes included components of the composite and mild cerebral palsy at 2 years, Bayley Scales of Infant Development II motor and mental scores, death before two years, and use of auditory aids or corrective lenses. Multivariable logistic regression models were performed to estimate adjusted odds ratios (aOR) with 95% confidence intervals. Results: Of 1,826 women included, 503 (27.5%) used tobacco. Tobacco users were more likely to be older, unmarried, and white; have a prior preterm birth; have received no prenatal care; and to use illicit drugs or alcohol. Gestational age at delivery, betamethasone exposure, and magnesium exposure were not different between groups. There were no differences in the composite primary outcome or in rates of cerebral palsy by tobacco use. Moderate developmental delay was more common among tobacco exposed in bivariate but not adjusted analysis (20.5 vs. 15.9%, p = 0.035). In adjusted analysis, tobacco exposure was associated with increased use of corrective lenses (5.0 vs. 2.9%, aOR: 2.28, 95% confidence interval: 1.28-4.07). Conclusion: Prenatal tobacco exposure is not associated with neurodevelopmental impairment in infants born preterm. However, tobacco exposure may be associated with impaired vision.

PMID: 32862421

21. Functioning, participation, and quality of life in children with intellectual disability: an observational study
Katrina Williams, Peter Jacoby, Andrew Whitehouse, Rachel Kim, Amy Epstein, Nada Murphy, Sue Reid, Helen Leonard, Dinah Reddihough, Jenny Downs

Dev Med Child Neurol. 2020 Aug 30. doi: 10.1111/dmcn.14657. Online ahead of print.

Aims: To investigate associations between functioning, community participation, and quality of life (QoL) and identify whether participation mediates the effects of functioning on QoL. Method: The caregivers of 435 children (211 females, 224 males; mean age 12y; SD 3y 11mo; age range 5-18y) with intellectual disability and autism spectrum disorder, cerebral palsy, Down syndrome, or Rett syndrome reported on their child's functioning (dependence for managing personal needs, mobility, communication, eye contact when speaking), frequency of participation, and QoL. Linear regression and mediation analyses were used to evaluate the relationships between child functioning, participation, and QoL. Results: Children with greater dependency for managing personal needs and limited eye contact when speaking experienced poorer QoL. Less impaired functioning was associated with more frequent participation, which, in turn, was associated with a 3-point gain in QoL for each additional point in frequency of participation (coefficient=2.67, 95% confidence interval 1.56-3.78). The effect of impaired functioning on QoL was partially mediated by participation in children with greater dependency in managing personal needs and those with mildly impaired communication. Interpretation: Greater levels of impairments with poorer functioning, notably a high level of dependence, were associated with poorer QoL. Poorer QoL can be partly explained by less frequent community participation.

PMID: 32862445

22. Family functioning and strengths in families raising a child with cerebral palsy
Assimina Tsibidaki

Res Dev Disabil. 2020 Aug 30;106:103767. doi: 10.1016/j.ridd.2020.103767. Online ahead of print.

Cerebral palsy (CP) is a serious disorder that has serious consequences on the functioning of children and their families. This study explores family functioning (adaptation, cohesion and family type) and strengths (pride, accord and whole) in Greek and Italian families raising a child with CP and their interaction. Participants were 120 parents of a biological child with CP. Data collection used a self-report questionnaire, the Family Adaptability and Cohesion Evaluation Scale (FACES-III) and the Family Strengths Inventory. According to the findings, parents (in both countries) estimate and wish their family to be in the balanced range which represents healthy family functioning according to the revised edition of the Olson Circumplex Model. Finally, they share a high sense of family strengths, which is mainly displayed in the high sense of pride and accord.

PMID: 32877831

23. Health service use among adults with cerebral palsy: a mixed methods systematic review protocol
Manjula Manikandan, Aisling Walsh, Claire Kerr, Michael Walsh, Jennifer M Ryan

BMJ Open. 2020 Aug 30;10(8):e035892. doi: 10.1136/bmjopen-2019-035892.

Introduction: Cerebral palsy (CP) is a neurodisability that primarily results in motor impairments and activity limitations, but is often associated with epilepsy and disturbances of sensation, perception, cognition, behaviour and speech. Most children with CP survive well into adulthood. Adults with CP experience increased risk of age-related chronic conditions such as arthritis, stroke, cardiorespiratory and mental health conditions in addition to the ongoing disabilities experienced from childhood. Therefore, adults with CP often require extensive health services. However, health service use among adults with CP has not been well documented. This mixed method review aims to identify, appraise and synthesise quantitative and qualitative literature examining health service use among adults with CP. Methods and analysis: The mixed method systematic review will be conducted in accordance with the Joanna Briggs Institute (JBI) methodology. A systematic search of MEDLINE (Ovid), CINAHL, Embase, PsycINFO and Cochrane Library from inception to March 2020 will be conducted. Quantitative observational studies, qualitative studies and mixed method studies examining health service use among adults with CP (≥18 years) will be included. Outcomes of interest are the proportion of adults using health services frequency of use and experiences of health services from the perspectives of adults with CP, caregivers and health service providers. Two reviewers will independently screen titles, abstracts and full-texts, extract data and assess the quality of included studies using JBI instruments. Where possible a pooled analysis and aggregation of findings will be performed for quantitative and qualitative data, respectively, and Grading of Recommendations Assessment, Development and Evaluation (GRADE)/GRADE-CERQual (Confidence in Evidence from Reviews of Qualitative research) employed. Quantitative and qualitative findings will be integrated using a triangulation approach at the synthesis stage. A narrative synthesis will be carried out where this is not possible. Ethics and dissemination: Ethical approval is not required for this review. The findings will be disseminated through a peer-reviewed journal and conferences. Prospero registration number: CRD42020155 380.

PMID: 32868352

24. Transition From Pediatric to Adult Care for Young Adults With Chronic Respiratory Disease
L Denise Willis

Review Respir Care. 2020 Sep 1;respcare.08260. doi: 10.4187/respcare.08260. Online ahead of print.

Advances in medicine and technology have led to improved survival rates of children with chronic respiratory disease such as cystic fibrosis, neuromuscular disease, and ventilator dependence. Survival into adulthood has created the need for adult specialists for conditions originating in childhood. Transition from pediatric to adult health care is a process that requires

advanced planning and preparation and is not a one-time transfer event. Transition should be standard practice, but many children with special health care do not experience successful transition outcomes. Barriers to successful transition include lack of a standardized process, inadequate planning, and poor communication. Adverse outcomes have occurred in cases of abrupt or haphazard transfers. A successful transition process includes early introduction and ongoing discussion that engages the adolescent to plan and prepare for the eventual transfer of care. Care responsibilities should be gradually shifted from the parent to the adolescent in a manner appropriate for the adolescent's age and developmental status. Good communication and collaboration between pediatric and adult care teams is crucial to ensure a smooth transfer of care. Incorporating the 6 core elements of transition can be helpful in developing a successful transition program. This narrative review summarizes the literature for health care transition from pediatric to adult care including the rationale, barriers, factors associated with successful transition, and special considerations. The intent of this review is to increase clinician awareness of health care transitions and the components necessary for an effective transfer of young adults with chronic respiratory disease. Understanding the transition process is an important consideration for both pediatric and adult clinicians, including respiratory therapists.

PMID: 32873753

25. New perspectives on person-centered care: an affordance-based account
Juan Toro, Kristian Martiny

Med Health Care Philos. 2020 Sep 4. doi: 10.1007/s11019-020-09977-w. Online ahead of print.

Despite the growing interest and supporting evidence for person-centered care (PCC), there is still a fundamental disagreement about what makes healthcare person-centered. In this article, we define PCC as operating with three fundamental conditions: personal, participatory and holistic. To further understand these concepts, we develop a framework based on the theory of affordances, which we apply to the healthcare case of rehabilitation and a concrete experiment on social interactions between persons with cerebral palsy and physio- and occupational therapists. Based on the application of the theory, we argue that in order for healthcare to be considered as PCC, professionals need to adopt a personalistic attitude in their care, defined (at the how-level) in terms of mutual affordances: how the professional and the person of care acknowledges each other as a person in an interaction. In opposition, we define (at the what level) the functionalistic attitude in terms of object affordances, those related to a concrete goal. We show that PCC requires a balance of personalistic and functionalistic attitudes, since this contributes to a participatory and holistic conception of, and interaction with, the person of care.

PMID: 32886295

26. Risk factors for cerebral palsy in neonates due to placental abruption
Kiyotake Ichizuka, Satoshi Toyokawa, Tsuyomu Ikenoue, Shoji Satoh, Junichi Hasegawa, Tomoaki Ikeda, Nanako Tamiya, Akihito Nakai, Keiya Fujimori, Tsugio Maeda, Naohiro Kanayama, Hideaki Masuzaki, Mitsutoshi Iwashita, Hideaki Suzuki, Satoru Takeda

J Obstet Gynaecol Res. 2020 Sep 3. doi: 10.1111/jog.14447. Online ahead of print.

Aim: This study aimed to identify risk factors for the onset of cerebral palsy (CP) in neonates due to placental abruption and investigate their characteristics. Methods: A retrospective case-control study was conducted using a nationwide registry from Japan. The study population included pregnant women (n = 122) who delivered an infant with CP between 2009 and 2015, where placental abruption was identified as the single cause of CP. The control group consisted of pregnant women with placental abruption, who delivered an infant without CP and were managed from 2013 to 2014. They were randomly identified from the prenatal database of the Japan Society of Obstetrics and Gynecology (JSOG-DB; n = 1214). Risk factors were investigated using multivariate analysis. Results: Alcohol consumption (3.38, 2.01-5.68) (odds ratio, 95% confidence interval), smoking during pregnancy (3.50, 1.32-9.25), number of deliveries (1.28, 1.05-1.56), polyhydramnios (5.60, 1.37-22.6), oral administration of ritodrine hydrochloride (2.09, 1.22-3.57) and hypertensive disorders in pregnancy (2.25, 1.27-4.07) were significant risk factors. In contrast, intravenous administration of oxytocin (odds ratio, 95% confidence interval: 0.22, 0.09-0.58) and magnesium sulfate (0.122, 0.02-0.89) attenuated risk. Conclusion: Alcohol consumption, smoking during pregnancy, number of deliveries, polyhydramnios, oral administration of ritodrine hydrochloride and hypertensive disorders in pregnancy were identified as risk factors for CP following placental abruption. Regarding alcohol consumption and smoking during pregnancy, the results suggest the importance of educational activities targeting pregnant women to increase their awareness of

placental abruption.

PMID: 32885550

27. Molecular and Therapeutic Aspects of Hyperbaric Oxygen Therapy in Neurological Conditions
Inbar Fischer, Boaz Barak

Review Biomolecules. 2020 Aug 27;10(9):E1247. doi: 10.3390/biom10091247.

In hyperbaric oxygen therapy (HBOT), the subject is placed in a chamber containing 100% oxygen gas at a pressure of more than one atmosphere absolute. This treatment is used to hasten tissue recovery and improve its physiological aspects, by providing an increased supply of oxygen to the damaged tissue. In this review, we discuss the consequences of hypoxia, as well as the molecular and physiological processes that occur in subjects exposed to HBOT. We discuss the efficacy of HBOT in treating neurological conditions and neurodevelopmental disorders in both humans and animal models. We summarize by discussing the challenges in this field, and explore future directions that will allow the scientific community to better understand the molecular aspects and applications of HBOT for a wide variety of neurological conditions.

PMID: 32867291

28. Infant outcome after active management of early-onset fetal growth restriction with absent or reverse umbilical artery blood flow
E Morsing, J Brodszki, A Thuring, K Maršál

Ultrasound Obstet Gynecol. 2020 Aug 30. doi: 10.1002/uog.23101. Online ahead of print.

Objective: To describe in a retrospective cohort study the short-term and long-term outcomes of all infants with early-onset fetal growth restriction (FGR) and umbilical artery absent (AEDF) or reverse (REDF) end-diastolic flow, delivered before 30 gestational weeks and actively managed at the level 3 perinatal unit in Lund, Sweden between 1998 and 2015. Methods: Outcomes of 139 fetuses with birthweight (BW) small-for-gestational age and ARED flow (FGR group; 26% twins) were compared with those of all infants with BW appropriate-for-gestational age (AGA group; n=946; 28% twins). In the FGR group, the main indication for delivery was the Doppler finding of ARED flow in the umbilical artery. Results: FGR infants had a median BW 630 g (range 340-1165) and gestational age at birth 187 days (164-209) as compared to the AGA group with 950 g (470-2194) and 185 days (154-209), respectively. Perinatal mortality did not differ between the two groups (5% and 5.4% in the FGR and AGA group, respectively). All 7 intrauterine deaths in the FGR group occurred before 26 weeks of gestation. Severe intraventricular hemorrhages were less frequent, and bronchopulmonary dysplasia and septicemia more frequent in the FGR group than in the AGA group ($p=0.008$, $p<0.001$ and $p=0.006$, respectively). The survival rate at 2 years (83% of liveborn infants) and rate of cerebral palsy (7%) in the FGR group did not differ from those of AGA group (82% and 8%, respectively). Survival without neurodevelopmental impairment was higher in the AGA group (83%) than in the FGR group (62%) ($p<0.001$). Within the FGR group, the outcomes between twins and singletons, and between fetuses with AEDF and REDF were similar. Conclusions: Infants born very preterm after severe FGR had similar survival as AGA infants of corresponding gestational age, however, they were at higher risk of neurodevelopmental impairment, the risk being most pronounced following birth before 25 gestational weeks. Gestational age remains an important factor associated with the prognosis of early-onset FGR, nevertheless, the present results support a hypothesis to be prospectively tested that fetuses with umbilical artery ARED flow may benefit from early intervention rather than expectancy and that umbilical artery Doppler findings could be a part of the clinical protocols also in very early gestational weeks.

PMID: 32862450

29. Earlier and improved screening for impending fetal compromise
Mark I Evans, David W Britt, Robert D Eden, Shara M Evans, Barry S Schifrin

J Matern Fetal Neonatal Med. 2020 Sep 1;1-9. doi: 10.1080/14767058.2020.1811670. Online ahead of print.

Objective: The use of pH and base excess (FSSPHBE) from fetal scalp sampling (FSS) was abandoned when cardiotocography (CTG) was believed to be sufficiently accurate to direct patient management. We sought to understand the fetus' tolerance to stress in the 1st stage of labor and to develop a better and earlier screening test for its risk for developing acidosis. To do so, we investigated sequential changes in fetal pH and BE obtained from FSS in the 1st stage of labor as part of a research protocol from the 1970s. We then examined the utility of multiple of the median (MoM's) conversion of BE and pH values, and the capacity of Fetal Reserve Index (FRI) scores to be a proxy for such changes. We then sought to examine the predictive capacity of 1st stage FRI and its change over the course of the first stage of labor for the subsequent development of acidosis risk in the 2nd stage of labor. Methods: Using a retrospective research database evaluation, we evaluated FSSPHBE data from 475 high-risk parturients monitored in labor and their neonates for 1 h postpartum. We categorized specimens according to cervical dilatation (CxD) at the time of FSSPHBE and developed non-parametric, multiples of the median (MOMs) assessments. FRI scores and their change over time were used as predictors of FSSPHBE. Our main outcome measures were the changes in BE and pH at different cervical dilatations (CxD) and acidosis risk in the early 2nd stage of labor. Results: FSSPHBE worsens over the course of the 1st stage. The implications of any given BE are very different depending upon CxD. At 9 cm, -8 Mmol/L is 1.1 MOM; at 3 cm, it would be 2.0 MOM. The FRI level and its trajectory provide a 1st stage screening tool for acidosis risk in the second stage. Conclusions: Fetal acid-base balance ("reserve") deteriorates beginning early in the 1st stage of labor, irrespective of whether the fetus reaches a critical threshold of concern for actual acidosis. The use of MoM's logic improves appreciation of such information. The FRI and its trajectory reasonably approximate the trajectory of the FSSPHBE and appears to be a suitable screening test for early deterioration and for earlier interventions to keep the fetus out of trouble rather than wait until high risk status develops.

PMID: 32873102

30. Molecular Basis of Sex Difference in Neuroprotection induced by Hypoxia Preconditioning in Zebrafish
Tapatee Das, Kalyani Soren, Mounica Yerasi, Avijeet Kamle, Arvind Kumar, Sumana Chakravarty

Mol Neurobiol. 2020 Aug 29. doi: 10.1007/s12035-020-02091-1. Online ahead of print.

Hypoxia, the major cause of ischemic injury, leads to debilitating disease in infants via birth asphyxia and cerebral palsy, whereas in adults via heart attack and stroke. A widespread, natural protective phenomenon termed 'hypoxic preconditioning' (PH) occurs when prior exposures to hypoxia eventually result in robust hypoxia resistance. Accordingly, we have developed and optimized a novel model of hypoxic preconditioning in adult zebrafish to mimic the tolerance of mini stroke(s) in human, which appears to protect against the severe damage inflicted by a major stroke event. Here, we observed a remarkable difference in the progression pattern of neuroprotection between preconditioning hypoxia followed by acute hypoxia (PH) group, and acute hypoxia (AH) only group, with noticeable sex difference when compared with normoxia behaviour upon recovery. Since gender difference has been reported in stroke risk factors and disease history, it was pertinent to investigate whether any such sex difference also exists in PH's protective mechanism against acute ischemic stroke. In order to elucidate the neural molecular mechanisms behind sex difference in neuroprotection induced by PH, a high throughput proteomics approach utilizing iTRAQ was performed, followed by protein enrichment analysis using ingenuity pathway analysis (IPA) tool. Out of thousands of significantly altered proteins in zebrafish brain, the ones having critical role either in neuroglial proliferation/differentiation or neurotrophic functions were validated by analyzing their expression levels in preconditioned (PH), acute hypoxia (AH), and normoxia groups. The data indicate that female zebrafish brains are more protected against the severity of AH when exposed to the hypoxic preconditioning. The study also sheds light on the involvement of many signalling pathways underlying sex difference in preconditioning-induced neuroprotective mechanism, which can be further validated for the therapeutic approach.

PMID: 32862360

31. Role of apoptosis-inducing factor in perinatal hypoxic-ischemic brain injury
Juan Rodriguez, Tao Li, Yiran Xu, Yanyan Sun, Changlian Zhu

Review Neural Regen Res. 2021 Feb;16(2):205-213. doi: 10.4103/1673-5374.290875.

Perinatal complications, such as asphyxia, can cause brain injuries that are often associated with subsequent neurological

deficits, such as cerebral palsy or mental retardation. The mechanisms of perinatal brain injury are not fully understood, but mitochondria play a prominent role not only due to their central function in metabolism but also because many proteins with apoptosis-related functions are located in the mitochondrion. Among these proteins, apoptosis-inducing factor has already been shown to be an important factor involved in neuronal cell death upon hypoxia-ischemia, but a better understanding of the mechanisms behind these processes is required for the development of more effective treatments during the early stages of perinatal brain injury. In this review, we focus on the molecular mechanisms of hypoxic-ischemic encephalopathy, specifically on the importance of apoptosis-inducing factor. The relevance of apoptosis-inducing factor is based not only because it participates in the caspase-independent apoptotic pathway but also because it plays a crucial role in mitochondrial energetic functionality, especially with regard to the maintenance of electron transport during oxidative phosphorylation and in oxidative stress, acting as a free radical scavenger. We also discuss all the different apoptosis-inducing factor isoforms discovered, focusing especially on apoptosis-inducing factor 2, which is only expressed in the brain and the functions of which are starting now to be clarified. Finally, we summarized the interaction of apoptosis-inducing factor with several proteins that are crucial for both apoptosis-inducing factor functions (pro-survival and pro-apoptotic) and that are highly important in order to develop promising therapeutic targets for improving outcomes after perinatal brain injury.

PMID: 32859765

32. [Effect of injecting mouse nerve growth factor in different ways on motor development, cerebral hemodynamics and biochemical metabolism in children with cerebral palsy][Article in Chinese]

Yan-Na He, Yi Meng, Na-Na Gao, Bing-Jie Zhang, Huan Li, Sha-Sha Ji

Zhongguo Zhen Jiu. 2020 Aug 12;40(8):839-44. doi: 10.13703/j.0255-2930.20190525-0003.

Objective: To compare the effect of acupoint injection and intramuscular injection with mouse nerve growth factor (mNGF) on gross motor function development of children with cerebral palsy (CP), and explore the treatment mechanism. Methods: A total of 63 children with CP were randomly divided into an observation group (32 cases, 4 cases dropped off) and a control group (31 cases, 3 cases dropped off). Based on the routine rehabilitation therapy, the control group received intramuscular injection of mNGF(18 μg/2 mL), and the observation group received acupoint injection of mNGF at Xinshu (BL 15), Ganshu (BL 18), Pishu (BL 20), Shenshu (BL 23), Sanjiaoshu (BL 22), Shenting (GV 24), Baihui (GV 20), Fengfu (GV 16), Dazhui (GV 14), etc. Of them, 5-6 acupoints alternately were selected each time, and each acupoint was given 0.3-0.5 mL, totally 18 μg/2 mL. Both treatment were carried out once every other day for six months. Before and after treatment, the children's development of brain function was assessed using gross motor function classification system (GMFCS). Before treatment (T0), after 2 (T2), 4 (T4) and 6 (T6) months of treatment, the motor function was evaluated by gross motor function measure (GMFM-88). The systolic peak velocity (Vs), mean velocity (Vm) and vascular resistance index (RI) of anterior cerebral artery (ACA) and middle cerebral artery (MCA) were measured, and the level of N-acetyl aspartate acid (NAA), choline (Cho), lactate (Lac) and creatine (Cr) from the basal ganglia, thalamus and periventricular white mater were detected by magnetic resonance spectroscopy (MRS) technology with MAGNETOM Skyra3.0T magnetic resonance imaging system before and after treatment. Results: Compared with before treatment, the GMFCS classification of the observation group after treatment was significantly improved ($P<0.05$); after treatment, the difference of GMFCS classification between the two groups was not significant ($P>0.05$), however, the observation group had a 3.142 times of feasibility for good gross motor function development by more than level 1 compared to the control group ($P<0.05$). After 2, 4, and 6 months of treatment, the GMFM-88 scores of the two groups showed an upward trend ($P<0.01$), and the increase of the observation group was greater than that of the control group ($P<0.05$). Compared with before treatment, in the ACA and MCA, the Vs and Vm increased, RI decreased in both groups after treatment ($P<0.01$), and in the brain, NAA/Cr increased, Cho/Cr and Lac/Cr decreased ($P<0.01$), and after treatment, the Vs, Vm of ACA and MCA and NAA/Cr of brain in the observation group were higher than those in the control group ($P<0.05$), and the RI of ACA and MCA and Cho/Cr and Lac/Cr of brain in the observation group were lower than those in the control group ($P<0.05$). Conclusion: The mNGF acupoint injection has a better effect on the gross motor function in the children with cerebral palsy compared with the intramuscular injection, and the mechanism may be associated with exhibiting the double effects of acupoint effect and the targeting therapy of drug, which can effectively improve the cerebral hemodynamics and the metabolism of cerebral nervous substances.

PMID: 32869592