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Cerebral palsy research news

Monday 19 October 2020

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Interventions and Management

1. Surgical Technique of Xu's CC7 Procedure "Contralateral C7 to C7 Cross Nerve Transfer Through a Trans Longus Colli, Prespinal Route for Treating Spastic Arm"
Wen-Dong Xu

Oper Neurosurg (Hagerstown). 2020 Oct 12;opaa325. doi: 10.1093/ons/opaa325. Online ahead of print.

Background: The contralateral C7 transfer has been used for the treatment of brachial plexus root avulsion since 1986, and several modifications of this surgery have been described. Previous trial has verified the safety and effectiveness of the contralateral C7 to C7 cross nerve transfer for patients with longstanding spastic paralysis due to cerebral injuries, including stroke, traumatic brain injury, or cerebral palsy. However, the procedures for the surgery were not introduced in detail, with only rough descriptions. Objective: To introduce and promote the Xu's CC7 procedure (contralateral C7 to C7 cross nerve transfer through a trans longus colli, prespinal route). Methods: The renewed procedures were elaborated step by step, and the tips and tricks were clarified by case illustration in detail. Briefly, a modified trans longus colli, prespinal route was created, allowing the displaced C7 nerve to pass through the channel safely at the shortest distance. Results: Tension-free anastomosis of the bilateral C7 nerves was achieved via the Xu's CC7 procedure with less surgical trauma while reducing the surgery time, postoperative recovery time, and nerve regeneration time. Conclusion: The Xu's CC7 procedure is a safer and more efficient technique for contralateral C7 to C7 cross nerve transfer. The detailed description in this article provides meaningful information for surgeons interested in the procedure.

PMID: 33047132

2. Hip Reconstruction in Nonambulatory Children With Cerebral Palsy: Identifying Risk Factors Associated With Postoperative Complications and Prolonged Length of Stay
Jodie Shea, Kianna D Nunally, Patricia E Miller, Rachel Difazio, Travis H Matheney, Brian Snyder, Benjamin J Shore

J Pediatr Orthop. Nov/Dec 2020;40(10):e972-e977. doi: 10.1097/BPO.0000000000001643.

Background: The purpose of this study is to examine the relationship between preoperative comorbidities, surgical complications, and length of stay (LOS) after hip reconstruction in nonambulatory children with cerebral palsy (CP). Methods: This single-center retrospective cohort study included 127 patients undergoing hip surgery between 2007 and 2016 who were diagnosed with CP (GMFCS IV/V). The cohort was 54% Gross Motor Function Classification System (GMFCS) V with an average age at surgery of 9 years (range, 3-19 y). Preoperative comorbidities included: presence of a gastrostomy tube, respiratory difficulty requiring positive-pressure ventilation or tracheostomy, history of seizures, and nonverbal status. Complications were dichotomized into major and minor complications according to severity. Multivariable general linear modeling was used to identify factors associated with complications and prolonged LOS. Results: The median LOS in the hospital was 6 days (interquartile range, 5-9 d). The majority of procedures (72%) involved both the femur and acetabulum and

82% of surgeries were performed bilaterally. Patients who experienced a major complication were mostly GMFCS level V and were more likely to spend time in intensive care unit than postanesthetic care unit (P=0.001). Multivariable analysis for a major complication determined that the addition of each comorbid risk fact increased the odds of developing a major complication by 2.6 times (odds ratio, 2.64; 95% confidence interval, 1.56-4.47; P<0.001) regardless of GMFCS level. Multivariable analysis for prolonged LOS determined that major complications (P<0.001), bilaterality (P=0.01), age (P=0.02), female sex (P=0.01), and GMFCS V (P<0.001) were all factors that increased LOS. Migration percentage, acetabular index odds ratio, and pelvic obliquity were not associated with prolonged LOS or the presence of a major complication. Conclusions: From our analysis, the authors found that a patient's premorbid comorbidities were more predictive of the likelihood of sustaining a major complication than their GMFCS level. Identifying high-risk patients preoperatively may help reduce complications and LOS, which ultimately will improve the quality of care the authors deliver to nonambulatory children with CP undergoing hip reconstruction surgery. Level of evidence: Level III-retrospective cohort study.

PMID: 33045159

3. Soft tissue surgery as an initial treatment for hip displacement in spastic cerebral palsy
Luiz Antônio Angelo da Silva, Patricia Maria de Moraes Barros Fucs

SICOT J. 2020;6:38. doi: 10.1051/sicotj/2020036. Epub 2020 Oct 12.

Objective: To use the measurement of migration percentage (MP) to evaluate the long-term radiographic results of soft tissue surgery as the first treatment for hip displacement in spastic bilateral cerebral palsy. A secondary objective was to identify predictive factors of stability (i.e., less than 30% of MP in the long term), after surgical correction. Methods: In this longitudinal cohort study, we reviewed the electronic medical records and radiographs of all consecutive patients with cerebral palsy operated for the correction of hip displacement between 1984 and 2013 in a referral orthopedic public hospital in Brazil. Patients were included if they had received, as the first surgical procedure, soft-tissue release. All surgeries were bilateral and symmetrical. We used the available radiographs to evaluate the migration percentage (MP), acetabular index (AI), pelvic obliquity (PO) angle, head-shaft angle (HSA), congruence and femoral head sphericity, and function using the GMFCS (Gross Motor Function Classification System). Results: we included 93 patients, all operated before being 12 years old, with follow-up of 10 years in average, 73 (78%) of them with good results (MP < 30%). We found association between preoperative MP ≤ 40%, AI ≤ 25°, and postoperative symmetry with good results, with a cut-off value of 38% of MP and 27° of acetabular index being predictive. Discussion: The role of soft tissue releases remains controversial owing to small sample sizes, heterogeneity, variety range of ages, definitions used for outcome, and lack of statistical quality. Our results were better in combined tenotomies, in diparetic patients aged more than six years, and in patients with lower initial values of MP and AI. Radiographic variables had good correlation with each other and association with results, with cut-off values for MP and AI PRE.

PMID: 33043882

4. Effects of plyometric exercises on muscle-activation strategies and response-capacity to balance threats in children with hemiplegic cerebral palsy
Ragab K Elnaggar

Physiother Theory Pract. 2020 Oct 12;1-9. doi: 10.1080/09593985.2020.1833389. Online ahead of print.

Objective: Children with hemiplegic cerebral palsy (hCP) experience a disorganized muscle activation pattern that adversely affect their ability to respond to balance perturbations. This study examined the effect of plyometric exercises on muscle-activation strategies and response-capacity to balance threats in children with hCP. Methods: In a pre-, posttest control-group study, 34 children with hCP were allocated randomly to either the control group (n = 17; received a traditional physical rehabilitation program, lasted for 45 minutes/session, twice/week for three successive months) or the plyometric group (n = 17; received a progressive plyometric training program in three blocks, twice/week over three months plus the traditional physical rehabilitation). Quadriceps/hamstring co-contraction ratio (Q/H Co-CR) and response-capacity to balance threats were assessed pre- and post-treatment. Results: Post-treatment, the Q/H Co-CR and balance control improved significantly in the control (P = .03, P = .0003 respectively) and plyomteric group (P = .001, P < 0.001 respectively). However, the plyometric group showed better improvements in Q/H Co-CR (P = .0001) and balance control (P = .027) when compared to the control group. Conclusion: Incorporation of plyometric exercises into traditional physical rehabilitation could improve muscle-activation strategies and enhance balance control in children with hCP.

PMID: 33044886

5. MRI changes in calf muscles of two children with cerebral palsy following Botulinum Toxin Type A injections: a preliminary report
Geraldo de Coulon, Federico Canavese, Stéphane Armand, Alice Bonnefoy-Mazure, Laura Merlini

J Pediatr Orthop B. 2020 Oct 8. doi: 10.1097/BPB.0000000000000816. Online ahead of print.

PMID: 33038149

6. The Stability of the Gross Motor Function Classification System in Children with Cerebral Palsy Living in Stockholm and Factors Associated with Change
Emma Nylén, Wilhelmus J A Grooten

Phys Occup Ther Pediatr. 2020 Oct 13;1-12. doi: 10.1080/01942638.2020.1830915. Online ahead of print.

Aim: To determine the degree of stability in the Gross Motor Function Classification System (GMFCS) for children with cerebral pares (CP) and to analyze factors associated with changes of the over time, in Stockholm between the year 2000 and 2019. Method: A register study on 768 children with at least two GMFCS ratings, linear regression analysis was used to study factors associated to a change in GMFCS level. Results: 72% of the children kept the same GMFCS level. A change in GMFCS level was most common for children in GMFCS level II (68%). The first change in GMFCS level happened most commonly between the ages 2 and 4. Initial GMFCS level (Beta 0.127; $p < 0.001$) and one or more intensive training periods with a physiotherapist (Beta 0.097; $p = 0.018$) were associated with a change in GMFCS level. Interpretation: Most children with CP remain stable in their GMFCS level, but for those classified in level II, a change occurs for almost seven out of ten. Classifications made before the child turns four are less certain than those made later. Further studies are needed to clarify if occurrence of intensive training is the cause or result of the change in GMFCS level.

PMID: 33045899

7. A comparative evaluation of telehealth and direct assessment when screening for spasticity in residents of two long-term care facilities
Kelly A Harper, Emily C Butler, Mallory L Hacker, Aaditi Naik, Bryan R Eoff, Fenna T Phibbs, David A Isaacs, Stephen J Gallion, Esmeralda P Thomas, Jim L Scott, Shelby Ploucher, Jacqueline C Meystedt, Megan E McLeod, Philip David Charles

Clin Rehabil. 2020 Oct 11;269215520963845. doi: 10.1177/0269215520963845. Online ahead of print.

Objective: To evaluate the performance of telehealth as a screening tool for spasticity compared to direct patient assessment in the long-term care setting. Design: Cross-sectional, observational study. Setting: Two long-term care facilities: a 140-bed veterans' home and a 44-bed state home for individuals with intellectual and developmental disabilities. Subjects: Sixty-one adult residents of two long-term care facilities (aged 70.1 ± 16.2 years) were included in this analysis. Spasticity was identified in 43% of subjects (Modified Ashworth Scale rating mode = 2). Contributing diagnoses included traumatic brain injury, spinal cord injury, birth trauma, stroke, cerebral palsy, and multiple sclerosis. Main measures: Movement disorders neurologists conducted in-person examinations to determine whether spasticity was present (reference standard) and also evaluated subjects with spasticity using the Modified Ashworth Scale. Telehealth screening examinations, facilitated by a bedside nurse, were conducted remotely by two teleneurologists using a three-question screening tool. Telehealth screening determinations of spasticity were compared to the reference standard determination to calculate sensitivity, specificity, and the area under the curve (AUC) in receiver operating characteristics. Teleneurologist agreement was evaluated using Cohen's kappa. Results: Teleneurologist 1 had a specificity of 89% and sensitivity of 65% to identify the likely presence of spasticity ($n = 61$; AUC = 0.770). Teleneurologist 2 showed 100% specificity and 82% sensitivity ($n = 16$; AUC = 0.909). There was almost perfect agreement between the two examiners at 94% (kappa = 0.875, 95% CI: 0.640-1.000). Conclusion: Telehealth may provide a useful, efficient method of identifying residents of long-term care facilities that likely need referral for spasticity evaluation.

PMID: 33040604

8. Early Parenting Acceptance and Commitment Therapy 'Early PACT' for parents of infants with cerebral palsy: a study protocol of a randomised controlled trial
Koa Whittingham, Jeanie Sheffield, Catherine Mak, Corrine Dickinson, Roslyn N Boyd

BMJ Open. 2020 Oct 10;10(10):e037033. doi: 10.1136/bmjopen-2020-037033.

Introduction: New international clinical practice guidelines exist for identifying infants at high risk of cerebral palsy (CP) earlier: between 12 to 24 weeks corrected age, significantly earlier than previous diagnosis windows in Australia at 19 months. The earlier detection of infants at high risk of CP creates an opportunity for earlier intervention. The quality of the parent-infant relationship impacts various child outcomes, and is leveraged in other forms of intervention. This paper presents the protocol of a randomised controlled trial of an online parent support programme, Early Parenting Acceptance and Commitment Therapy (Early PACT) for families of infants identified as at high risk of CP. We predict that participating in the Early PACT programme will be associated with improvements in the parent-infant relationship, in parent mental health and well-being as well as infant behaviour and quality of life. Methods and analysis: This study aims to recruit 60 parents of infants (0 to 2 years old corrected age) diagnosed with CP or identified as at high risk of having CP. Participants will be randomly allocated to one of two groups: Early PACT or waitlist control (1:1). Early PACT is an online parent support programme grounded in Acceptance and Commitment Therapy (ACT). It is delivered as a course on an open source course management system called edX. Early PACT is designed to support parental adjustment and parent-infant relationship around the time of early diagnosis. Assessments will be conducted at baseline, following completion of Early PACT and at 6-month follow-up (retention). The primary outcome will be the quality of parent-child interactions as measured by the Emotional Availability Scale. Standard analysis methods for randomised controlled trial will be used to make comparisons between the two groups (Early PACT and waitlist control). Retention of effects will be examined at 6-month follow-up. Ethics and dissemination: This study is approved through appropriate Australian and New Zealand ethics committees (see in text) with parents providing written informed consent. Findings from this trial will be disseminated through peer-reviewed journal publications and conference presentations. Trial registration details: This trial has been prospectively registered on 12 June 2018 to present (ongoing) with the Australian New Zealand Clinical Trials Registry (ACTRN12618000986279); https://www.anzctr.org.au/Trial/Registration/TrialReview.aspx?id=3 74 896.

PMID: 33039994

9. Role of child neurologists and neurodevelopmentalists in the diagnosis of cerebral palsy: A survey study
Bhooma R Aravamuthan, Michael Shevell, Young-Min Kim, Jenny L Wilson, Jennifer A O'Malley, Toni S Pearson, Michael C Kruer, Michael Fahey, Jeff L Waugh, Barry Russman, Bruce Shapiro, Ann Tilton

Review Neurology. 2020 Oct 12;10.1212/WNL.0000000000011036. doi: 10.1212/WNL.0000000000011036. Online ahead of print.

Objective: To contextualize the role of child neurologists and neurodevelopmentalists (CN/NDDs) in cerebral palsy (CP) care, we review the changing landscape of CP diagnosis and survey stakeholder CN/NDDs regarding their roles in CP care. Methods: The optimal roles of the multiple specialties involved in CP care are currently unclear, particularly regarding CP diagnosis. We developed recommendations regarding the role of CN/NDDs noting: (1) increasing complexity of CP diagnosis given a growing number of genetic etiologies and treatable motor disorders that can be misdiagnosed as CP, and (2) the views of a group of physician stakeholders (CN/NDDs from the Child Neurology Society Cerebral Palsy Special Interest Group). Results: CN/NDDs felt that they were optimally suited to diagnose CP. Many (76%) felt CN/NDDs should always be involved in CP diagnosis. However, 42% said their CP patients were typically not diagnosed by CN/NDDs and 18% did not receive referrals to establish the diagnosis of CP at all. CN/NDDs identified areas of their expertise critical for CP diagnosis including knowledge of the neurologic exam across development and early identification of features atypical for CP. This contrasts with their views on CP management, where CN/NDDs felt they could contribute to the medical team, but were necessary primarily when neurologic co-existing conditions were present. Discussion: Given its increasing complexity, we recommend early referral for CP diagnosis to a CN/NDD or specialist with comparable expertise. This contrasts with current consensus guidelines which either do not address or do not recommend specific specialist referral for CP diagnosis.

PMID: 33046609

10. Neuroimaging Perspectives of Perinatal Arterial Ischemic Stroke
Asthik Biswas, Kshitij Mankad, Manohar Shroff, Prasad Hanagandi, Pradeep Krishnan

Review Pediatr Neurol. 2020 Aug 22;113:56-65. doi: 10.1016/j.pediatrneurol.2020.08.011. Online ahead of print.

Perinatal stroke ranks second only to that of adult stroke in the overall stroke incidence. It is a major contributor to long-term neurological morbidity, which includes cognitive dysfunction, cerebral palsy and seizures. Risk factors for stroke in the perinatal period differ from those in children and tend to be multifactorial. Differences in territorial predilection, response to injury, and stroke evolution exist when compared with childhood and adult stroke, and also among differing gestation age groups in the perinatal period (i.e., extreme preterm versus preterm versus term). The role of imaging is to diagnose stroke, exclude stroke mimics, establish the nature of stroke (arterial versus venous), and aid in prognostication. Magnetic resonance imaging is the mainstay of neuroimaging in perinatal stroke. Advanced imaging techniques such as diffusion tensor imaging and perfusion-weighted imaging are emerging as useful supplements to conventional imaging sequences. Here we describe the neuroimaging of perinatal arterial ischemic stroke with emphasis on imaging techniques, imaging phenotypes, stroke evolution, role of advanced imaging, and differences between stroke in preterm and term neonates. We also briefly describe the emerging role of fetal magnetic resonance imaging in the diagnosis of in utero stroke.

PMID: 33038575

11. Blood Biomarkers and 6- to 7-Year Childhood Outcomes Following Neonatal Encephalopathy
Athina Pappas, Seetha Shankaran, Scott A McDonald, Waldemar A Carlo, Abbot R Laptook, Jon E Tyson, Abhik Das, Kristin Skogstrand, David M Hougaard, Rosemary D Higgins

Am J Perinatol. 2020 Oct 10. doi: 10.1055/s-0040-1717072. Online ahead of print.

Objective: This study aimed to profile the cytokine/chemokine response from day 0 to 7 in infants (≥36 weeks of gestational age) with neonatal encephalopathy (NE) and to explore the association with long-term outcomes. Study design: This was a secondary study of the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) Neonatal Research Network randomized controlled trial of whole body hypothermia for NE. Eligible infants with moderate-severe NE were randomized to cooling or normothermia. Blood spots were collected on days 0 to 1, 2 to 4, and 6 to 7. Twenty-four cytokines/chemokines were measured using a multiplex platform. Surviving infants underwent neurodevelopmental assessment at 6 to 7 years. Primary outcome was death or moderate-severe impairment defined by any of the following: intelligence quotient <70, moderate-severe cerebral palsy (CP), blindness, hearing impairment, or epilepsy. Results: Cytokine blood spots were collected from 109 participants. In total 99 of 109 (91%) were assessed at 6 to 7 years; 54 of 99 (55%) developed death/impairment. Neonates who died or were impaired had lower early regulated upon activation normal T cell expressed and secreted (RANTES) and higher day 7 monocyte chemotactic protein (MCP)-1 levels than neonates who survived without impairment. Though TNF-α levels had no association with death/impairment, higher day 0 to 1 levels were observed among neonates who died/developed CP. On multiple regression analysis adjusted for center, treatment group, sex, race, and level of hypoxic ischemic encephalopathy, higher RANTES was inversely associated with death/impairment (odds ratio (OR): 0.31, 95% confidence interval [CI]: 0.13-0.74), while day seven MCP-1 level was directly associated with death/impairment (OR: 3.70, 95% CI: 1.42-9.61). Targeted cytokine/chemokine levels demonstrated little variation with hypothermia treatment. Conclusion: RANTES and MCP-1 levels in the first week of life may provide potential targets for future therapies among neonates with encephalopathy. Key points: · Elevation of specific cytokines and chemokines in neonates with encephalopathy has been noted along with increased risk of neurodevelopmental impairment in infancy.. · Cytokine/chemokines at <7 days were assessed among neonates in a trial of hypothermia for HIE.. · Neonates who died or were impaired at 6 to 7 years following hypoxic-ischemic encephalopathy had lower RANTES and higher MCP-1 levels than those who survived without impairment..

PMID: 33038899

Prevention and Cure

12. Erythropoietin Improves Atrophy, Bleeding and Cognition in the Newborn Intraventricular Hemorrhage
Carmen Hierro-Bujalance, Carmen Infante-Garcia, Daniel Sanchez-Sotano, Angel Del Marco, Ana Casado-Revuelta, Carmen

Maria Mengual-Gonzalez, Carmen Lucena-Porras, Marcos Bernal-Martin, Isabel Benavente-Fernandez, Simon Lubian-Lopez, Monica Garcia-Alloza

Front Cell Dev Biol. 2020 Sep 16;8:571258. doi: 10.3389/fcell.2020.571258. eCollection 2020.

The germinal matrix-intraventricular hemorrhage (GM-IVH) is one of the most devastating complications of prematurity. The short- and long-term neurodevelopmental consequences after severe GM-IVH are a major concern for neonatologists. These kids are at high risk of psychomotor alterations and cerebral palsy; however, therapeutic approaches are limited. Erythropoietin (EPO) has been previously used to treat several central nervous system complications due to its role in angiogenesis, neurogenesis and as growth factor. In addition, EPO is regularly used to reduce the number of transfusions in the preterm infant. Moreover, EPO crosses the blood-brain barrier and EPO receptors are expressed in the human brain throughout development. To analyze the role of EPO in the GM-IVH, we have administered intraventricular collagenase (Col) to P7 mice, as a model of GM-IVH of the preterm infant. After EPO treatment, we have characterized our animals in the short (14 days) and the long (70 days) term. In our hands, EPO treatment significantly limited brain atrophy and ventricle enlargement. EPO also restored neuronal density and ameliorated dendritic spine loss. Likewise, inflammation and small vessel bleeding were also reduced, resulting in the preservation of learning and memory abilities. Moreover, plasma gelsolin levels, as a feasible peripheral marker of GM-IVH-induced damage, recovered after EPO treatment. Altogether, our data support the positive effect of EPO treatment in our preclinical model of GM-IVH, both in the short and the long term.

PMID: 33043002

13. Is Stem Cell Therapy the New Savior for Cerebral Palsy Patients? A Review
Varun Vankeshwaram, Ankush Maheshwary, Divya Mohite, Janet A Omole, Safeera Khan

Review Cureus. 2020 Sep 2;12(9):e10214. doi: 10.7759/cureus.10214.

Cerebral Palsy (CP) is one of the foremost causes of childhood motor disability and disrupts the individual's development and ability to function. Several factors contribute to the development of CP such as preterm delivery, low birth weight, infection/inflammation, and additional pregnancy complications, both in preterm and term infants. As there is no specific treatment for CP, rehabilitation is the current option for the management of patients. The serious nature of this condition creates deficits that last a lifetime. We collected studies that were published in the past 10 years, using PubMed as our main database. We chose studies that were relevant to CP and stem cell therapy. We mainly focused on various types of stem cells that can be used in treatment, mechanism of action (MOA) of stem cells, routes, dosage, and adverse effects, their efficacy, and safety in CP patients. Of all the 38 studies we reviewed, we found that five articles discussed the utilization of human umbilical cord blood [hUCB], four articles discussed autologous bone marrow stem cells, and one discussed allogeneic umbilical cord blood usage. One article discussed neural stem-like cells (NSLCs) derived from bone marrow and the remaining 27 articles were about CP and its treatment. We reviewed detailed information about the possible stem cell therapies and their benefits in patients with CP. We found that immune modulation is the major mechanism of action of stem cells, and among all the types of stem cells. Autologous umbilical cord mesenchymal stem cells appear to be safe and most effective in treatment compared to other stem cell treatments. Among all symptoms, motor symptoms are best corrected by stem cell therapy. Still, it did not show any marked improvement in treating other symptoms like speech defects, sensory or cognitive defects, or visual impairment.

PMID: 33042660