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Interventions and Management

1. Clinical Characteristics Associated with Reduced Selective Voluntary Motor Control in the Upper Extremity of Individuals with Spastic Cerebral Palsy

Theresa Sukal-Moulton, Deborah Gaebler-Spira, Kristin J Krosschell

Dev Neurorehabil. 2020 Oct 30;1-7. doi: 10.1080/17518423.2020.1839980. Online ahead of print.

Background: Selective voluntary motor control (SVMC) in the upper extremity is often impaired in individuals with cerebral palsy (CP) and can be assessed quantitatively and qualitatively using the Test of Arm Selective Control (TASC). Methods: Fifty-six individuals with spastic CP (5-18 years old) were included. Descriptors associated with administration of the TASC were analyzed according to the type of CP and arm joint using Chi-square and Kruskal-Wallis tests. ABILHAND-Kids scores were compared between participants with and without mirror movements using a t-test. Results: All groups of children with spastic CP had incidence of TASC movement descriptors. There was a main effect of topography of CP on extra movements, decreased active range of motion, tightness, spasticity, and mirroring, and an additional main effect of joint on mirroring. Participants with mirroring had lower ABILHAND-Kids scores than those without mirroring. Conclusions: Systematically observing arm movements using the TASC revealed differences across participants.

PMID: [33124931](#)

2. Comparing short-term outcomes between conus medullaris and cauda equina surgical techniques of selective dorsal rhizotomy

Elizabeth A Duffy, Alexander L Hornung, Brian Po-Jung Chen, Meghan E Munger, Nanette Aldahondo, Linda E Krach, Tom F Novacheck, Michael H Schwartz

Dev Med Child Neurol. 2020 Oct 25. doi: 10.1111/dmcn.14716. Online ahead of print.

Aim: To compare short-term outcomes between conus medullaris (conus) and cauda equina (cauda) selective dorsal rhizotomy (SDR) techniques in children with spastic cerebral palsy. Method: This was a retrospective review of SDR at a single center from 2013 to 2017. Gait and functional outcome measures were assessed at no more than 18 months pre-SDR (baseline) and 8 to 36 months post-SDR (follow-up). Transient complications during inpatient stay were quantified. Results: In total, 21 and 59 children underwent conus and cauda SDR respectively. Ashworth Scale scores were nearly normalized at follow-up. Most physical examination and functional measures exhibited similar baseline to follow-up responses for both groups. From baseline to follow-up, sagittal plane knee kinematics for both groups significantly improved ($p < 0.01$) by 11° at initial contact, 9° to 10° in stance phase, and 4° in swing phase. Sagittal plane ankle kinematics improved more for the cauda group than the conus group in both stance phase (10° vs 2° , $p < 0.01$) and swing phase (13° vs 3° , $p < 0.01$). Post-surgical complications were similar between groups. Interpretation: Conus and cauda SDR techniques resulted in similar short-term outcomes except in ankle kinematics at follow-up. The cauda group exhibited a large improvement towards dorsiflexion,

while there was residual equinus in the conus group despite Ashworth Scale scores normalizing equally in both groups.

PMID: [33103255](#)

3. Measuring skeletal muscle morphology and architecture with imaging modalities in children with cerebral palsy: a scoping review

Sian A Williams, N Susan Stott, Jane Valentine, Catherine Elliott, Siobhán L Reid

Review Dev Med Child Neurol. 2020 Oct 27. doi: 10.1111/dmcn.14714. Online ahead of print.

Aim: To investigate the use of ultrasound and magnetic resonance imaging (MRI) methodologies to assess muscle morphology and architecture in children with cerebral palsy (CP). **Method:** A scoping review was conducted with systematic searches of Medline, Embase, Scopus, Web of Science, PubMed, and PsycInfo for all original articles published up to January 2019 utilizing ultrasound and/or MRI to determine morphological and architectural properties of lower limb skeletal muscle in children with CP. **Results:** Eighty papers used ultrasound (n=44), three-dimensional ultrasound (n=16), or MRI (n=20) to measure at least one muscle parameter in children and adolescents with CP. Most research investigated single muscles, predominantly the medial gastrocnemius muscle, included children classified in Gross Motor Function Classification System levels I (n=62) and II (n=65), and assessed fascicle length (n=35) and/or muscle volume (n=35). Only 21 papers reported reliability of imaging techniques. Forty-six papers assessed measures of Impairment (n=39), Activity (n=24), and Participation (n=3). **Interpretation:** Current research study design, variation in methodology, and preferences towards investigation of isolated muscles may oversimplify the complexities of CP muscle but provide a foundation for the understanding of the changes in muscle parameters in children with CP.

PMID: [33107594](#)

4. Barriers and facilitators to treating insomnia in children with autism spectrum disorder and other neurodevelopmental disorders: Parent and health care professional perspectives

Kim M Tan-MacNeill, Isabel M Smith, Anastasija Jemcov, Laura Keeler, Jill Chorney, Shannon Johnson, Shelly K Weiss, Esmot Ara Begum, Cary A Brown, Evelyn Constantin, Roger Godbout, Ana Hanlon-Dearman, Osman Ipsiroglu, Graham J Reid, Sarah Shea, Penny V Corkum

Res Dev Disabil. 2020 Oct 24;107:103792. doi: 10.1016/j.ridd.2020.103792. Online ahead of print.

Background/aims: Insomnia is highly prevalent in children with neurodevelopmental disorders (NDDs), yet little research exists on sleep treatment access, utilization, and provision in this population. This study explores barriers and facilitators to access, use, and provision of treatment for sleep problems as experienced by parents of children with NDDs, including Autism Spectrum Disorder (ASD), Attention-Deficit/Hyperactivity Disorder (ADHD), Cerebral Palsy (CP) and Fetal Alcohol Spectrum Disorder (FASD), and health care professionals who work with children with these conditions. **Method:** Transcripts from online focus groups and interviews, conducted separately with parents of children with NDDs (n = 43) and health care professionals (n = 44), were qualitatively analyzed using content analysis for key themes. **Results:** Barriers included limited access to/availability of treatment, lack of knowledge/training, NDD-specific factors (e.g., symptoms, medications, and comorbidities), parent factors (e.g., capacity to implement treatment, exhaustion), and the challenging, intensive nature of sleep treatment. Facilitators included positive beliefs and attitudes, education, support, and ability to modify treatments for NDD symptoms. Barriers and facilitators were similar across all four NDDs. **Conclusions:** Results highlight a need for more education about sleep in NDDs and to develop accessible interventions, as well as the potential of a transdiagnostic approach to sleep treatment in this population.

PMID: [33126148](#)

5. High Frequency Deep Brain Stimulation of Superior Cerebellar Peduncles in a Patient with Cerebral Palsy

Suzhen Lin, Chencheng Zhang, Hongxia Li, Yuhan Wang, Yunhao Wu, Tao Wang, Yixin Pan, Bomin Sun, Yiwen Wu, Dianyou Li

Case Reports Tremor Other Hyperkinet Mov (N Y). 2020 Oct 7;10:38. doi: 10.5334/tohm.551.

Background: Globus pallidus internus (GPi) deep brain stimulation (DBS) is widely used in patients with isolated dystonia; however, its use remains controversial in patients with acquired dystonia and cerebral palsy. Case presentation: We report the first case of a cerebral palsy patient, who failed to recover 2 years after GPi DBS; DBS was administered on both superior cerebellar peduncles (SCPs) and dentate nuclei (DNs). The monopolar stimulation results suggested that DBS was better administered via the SCPs than via the DNs. At six months follow-up, the patient exhibited a significant improvement of dystonia and spasticity, as well as in her quality of life. Discussion: SCP DBS may be a potential treatment for cerebral palsy patients with dystonia and spasticity who do not respond well to GPi DBS.

PMID: [33101764](#)

6. Motor neuroprosthesis implanted with neurointerventional surgery improves capacity for activities of daily living tasks in severe paralysis: first in-human experience

Thomas J Oxley, Peter E Yoo, Gil S Rind, Stephen M Ronayne, C M Sarah Lee, Christin Bird, Victoria Hampshire, Rahul P Sharma, Andrew Morokoff, Daryl L Williams, Christopher MacIsaac, Mark E Howard, Lou Irving, Ivan Vrljic, Cameron Williams, Sam E John, Frank Weissenborn, Madeleine Dazenko, Anna H Balabanski, David Friedenber, Anthony N Burkitt, Yan T Wong, Katharine J Drummond, Patricia Desmond, Douglas Weber, Timothy Denison, Leigh R Hochberg, Susan Mathers, Terence J O'Brien, Clive N May, J Mocco, David B Grayden, Bruce C V Campbell, Peter Mitchell, Nicholas L Opie

J Neurointerv Surg. 2020 Oct 28;neurintsurg-2020-016862. doi: 10.1136/neurintsurg-2020-016862. Online ahead of print.

Background: Implantable brain-computer interfaces (BCIs), functioning as motor neuroprostheses, have the potential to restore voluntary motor impulses to control digital devices and improve functional independence in patients with severe paralysis due to brain, spinal cord, peripheral nerve or muscle dysfunction. However, reports to date have had limited clinical translation. Methods: Two participants with amyotrophic lateral sclerosis (ALS) underwent implant in a single-arm, open-label, prospective, early feasibility study. Using a minimally invasive neurointervention procedure, a novel endovascular Stentrode BCI was implanted in the superior sagittal sinus adjacent to primary motor cortex. The participants undertook machine-learning-assisted training to use wirelessly transmitted electrocorticography signal associated with attempted movements to control multiple mouse-click actions, including zoom and left-click. Used in combination with an eye-tracker for cursor navigation, participants achieved Windows 10 operating system control to conduct instrumental activities of daily living (IADL) tasks. Results: Unsupervised home use commenced from day 86 onwards for participant 1, and day 71 for participant 2. Participant 1 achieved a typing task average click selection accuracy of 92.63% (100.00%, 87.50%-100.00%) (trial mean (median, Q1-Q3)) at a rate of 13.81 (13.44, 10.96-16.09) correct characters per minute (CCPM) with predictive text disabled. Participant 2 achieved an average click selection accuracy of 93.18% (100.00%, 88.19%-100.00%) at 20.10 (17.73, 12.27-26.50) CCPM. Completion of IADL tasks including text messaging, online shopping and managing finances independently was demonstrated in both participants. Conclusion: We describe the first-in-human experience of a minimally invasive, fully implanted, wireless, ambulatory motor neuroprosthesis using an endovascular stent-electrode array to transmit electrocorticography signals from the motor cortex for multiple command control of digital devices in two participants with flaccid upper limb paralysis.

PMID: [33115813](#)

7. Immersive Virtual Environments and Wearable Haptic Devices in rehabilitation of children with neuromotor impairments: a single-blind randomized controlled crossover pilot study

Iliaria Bortone, Michele Barsotti, Daniele Leonardis, Alessandra Crecchi, Alessandra Tozzini, Luca Bonfiglio, Antonio Frisoli

J Neuroeng Rehabil. 2020 Oct 28;17(1):144. doi: 10.1186/s12984-020-00771-6.

Background: The past decade has seen the emergence of rehabilitation treatments using virtual reality. One of the advantages in using this technology is the potential to create positive motivation, by means of engaging environments and tasks shaped in the form of serious games. The aim of this study is to determine the efficacy of immersive Virtual Environments and wearable haptic devices (VERA) for rehabilitation of upper limb in children with Cerebral Palsy (CP) and Developmental Dyspraxia (DD). Methods: A two period cross-over design was adopted for determining the differences between the proposed therapy and a conventional treatment. Eight children were randomized into two groups: one group received the VERA treatment in the first period and the manual therapy in the second period, and viceversa for the other group. Children were assessed at the beginning and the end of each period through both the Nine Hole Peg Test (9-HPT, primary outcome) and Kinesiographical Measurements

obtained during the performing of similar tasks in a real setting scenario (secondary outcomes). Results: All subjects, not depending from which group they come from, significantly improved in both the performance of the 9-HPT and in the parameters of the kinesiological measurements (movement error and smoothness). No statistically significant differences have been found between the two groups. Conclusions: These findings suggest that immersive VE and wearable haptic devices is a viable alternative to conventional therapy for improving upper extremity function in children with neuromotor impairments. Trial registration ClinicalTrials, NCT03353623. Registered 27 November 2017-Retrospectively registered, <https://clinicaltrials.gov/ct2/show/NCT03353623>.

PMID: [33115487](https://pubmed.ncbi.nlm.nih.gov/33115487/)

8. Gross Motor Function in Children with Congenital Zika Syndrome

Eliana Harumi Morioka Takahasi, Maria Teresa Seabra Soares de Britto Alves, Marizélia Rodrigues Costa Ribeiro, Valéria Ferreira Pereira Souza, Vanda Maria Ferreira Simões, Marcella Costa Ribeiro Borges, Gláucio Andrade Amaral, Lillian Nunes Gomes, Ricardo Khouri, Patricia da Silva Sousa, Antônio Augusto Moura da Silva

Neuropediatrics. 2020 Oct 27. doi: 10.1055/s-0040-1718919. Online ahead of print.

Background: Little information on gross motor function of congenital Zika syndrome (CZS) children is available. Objectives: To evaluate gross motor function in CZS children aged up to 3 years, and its associated factors and changes in a minimum interval of 6 months. Methods: One hundred children with CZS and cerebral palsy (36 with confirmed and 64 with presumed CZS) were evaluated with the Gross Motor Function Classification System (GMFCS) and Gross Motor Function Measure (GMFM-88/GMFM-66). Forty-six were reevaluated. Wilcoxon tests, Wilcoxon tests for paired samples, percentile scores, and score changes were performed. Results: Clinical and socioeconomic characteristics (except maternal age), GMFM scores and GMFCS classification of confirmed and probable cases, which were analyzed together, were similar. The mean age was 25.6 months (± 5.5); the median GMFM-88 score was 8.0 (5.4-10.8); and the median GMFM-66 score was 20.5 (14.8-23.1); 89% were classified as GMFCS level V. Low economic class, microcephaly at birth, epilepsy, and brain parenchymal volume loss were associated with low GMFM-66 scores. The median GMFM-66 percentile score was 40 (20-55). On the second assessment, the GMFM-66 scores in two GMFCS level I children and one GMFCS level IV child improved significantly. In one GMFCS level III child, one GMFCS level IV child, and the group of GMFCS level V children, no significant changes were observed. Conclusions: Almost all CZS children had severe cerebral palsy; in the third year of life, most presented no improvement in gross motor function and were likely approaching their maximal gross motor function potential.

PMID: [33111304](https://pubmed.ncbi.nlm.nih.gov/33111304/)

9. Functional connectivity and quality of life in young adults with cerebral palsy: a feasibility study

Diana Tajik-Parvinchi, Andrew Davis, Sophia Roth, Peter Rosenbaum, Sarah N Hopmans, Aya Dudin, Geoffrey Hall, Jan Willem Gorter, MyStory Study Group

BMC Neurol. 2020 Oct 23;20(1):388. doi: 10.1186/s12883-020-01950-7.

Background: Cerebral Palsy (CP) is a group of disorders that affect the development of movement and posture. CP results from injuries to the immature brain during the prenatal, perinatal, or postnatal stage of development. Neuroimaging research in CP has focused on the structural changes of the brain during early development, but little is known about brain's structural and functional changes during late adolescence and early adulthood, a period in time when individuals experience major changes as they transition into adulthood. The work reported here served as a feasibility study within a larger program of research (MyStory Study). We aimed to determine whether it would be feasible to scan and obtain good quality data without the use of sedation during a resting state condition for functional connectivity (FC) analyses in young adults with CP. Second, we aimed to identify the FC pattern(s) that are associated with depressive mood ratings, indices of pain and fatigue, and quality of life in this group. Methods: Resting state functional images were collected from 9 young people with CP (18-29 years). We applied a stringent head motion correction and quality control methods following preprocessing. Results: We were able to scan and obtain good quality data without the use of sedation from this group of young individuals with CP who demonstrated a range of gross motor ability. The functional connectivity networks of interest were identified in the data using standard seed regions. Our analyses further revealed that higher well-being scores were associated with higher levels of FC between the Medial Pre-Frontal Cortex and the right Lateral Parietal regions, which are implicated in prosocial and emotion regulations skills. The implications of this association are discussed. Conclusion: The findings of the present study demonstrate that it is feasible to conduct resting state functional connectivity in young adults with CP with different gross motor abilities without the use of

sedation. Our results also highlight a neural circuitry that is associated with the self-report of quality of life and emotion regulation. These findings identify these regions/circuitries as important seeds for further investigations into mental health and wellbeing in CP.

PMID: [33096988](#)

10. Validity of Parent Ratings of Speech Intelligibility for Children with Cerebral Palsy

Ashley Sakash, Tristan Mahr, Katherine C Hustad

Dev Neurorehabil. 2020 Oct 25;1-9. doi: 10.1080/17518423.2020.1830447. Online ahead of print.

Aim: To examine the relationship between subjective parent ratings of intelligibility and objectively measured intelligibility scores for children with cerebral palsy (CP) with differing levels of speech severity. **Method:** Fifty children (84-96 months) with CP were classified into groups based on intelligibility scores during a speech elicitation task - high intelligibility (90% or higher), mild-moderate intelligibility reduction (61-89%), and severe intelligibility reduction (60% or lower). Parent ratings of understandability (on a 7-point scale) were compared to intelligibility scores gathered from 100 naïve listeners. **Results:** For children with mild-moderate and severe intelligibility reduction, there was a large range of variability in parent ratings. For children with high intelligibility, ratings were consistent with intelligibility scores. There was a range of intelligibility scores within each rating, especially in the middle of the scale. **Conclusions:** For children with mild-moderate intelligibility deficits, parent ratings may best be used in conjunction with objective measurement of intelligibility.

PMID: [33100123](#)

11. Impact of a family-centred early intervention programme in South India on caregivers of children with developmental delays

Sankar Sahayaraj Muthukaruppan, Cathy Cameron, Zoé Campbell, Dinesh Krishna, Rahim Moineddin, Aravind Bharathwaj, Bala Murugan Poomariappan, Sathiya Mariappan, Natalie Boychuk, Ramasubramanian Ponnusamy, Janna MacLachlan, Marie Brien, Stephanie Nixon, Sankara Raman Srinivasan

Disabil Rehabil. 2020 Oct 25;1-10. doi: 10.1080/09638288.2020.1836046. Online ahead of print.

Background: This study evaluated the impact on caregiver strain and family empowerment among caregivers of children with disabilities who received training and education as part of a family-centred community-based early intervention programme in South India. **Methods:** This prospective open cohort longitudinal study compared change from baseline to two years post-intervention among caregivers of the first cohort of children who were enrolled in the programme. Paired t-tests determined effect on the Modified Caregiver Strain Index (MCSI) and Family Empowerment Scale (FES), and p-values were adjusted for multiple comparisons using the False Discovery Rate approach. **Results:** Of the 308 caregivers (91% women), 44% provided care to children with cerebral palsy and 56% to children with other developmental delays. The mean age of the children at baseline was 3.3 (± 1.5 years). The overall mean change from baseline in the FES was 4.1 (95% CI: 3.3, 4.9; $p < 0.001$) representing improved empowerment. The mean change for the MCSI score was -3.7 (95% CI: -4.5, -2.9; $p < 0.001$) representing reduced caregiver strain. **Conclusions:** A family-centred early intervention programme that provides training and education to caregivers of children with developmental delays demonstrated positive change in caregiver strain and family empowerment. Implications for Rehabilitation The well-being of a child is influenced by the well-being of their caregiver. Improving caregiver well-being can help improve care and support for children with developmental delays. A family-centred early intervention therapy programme that includes training and education to caregivers can reduce strain and improve family empowerment.

PMID: [33103498](#)

12. Comment in Dystonia: genetics, phenomenology, and pathophysiology.

Vidailhet M, Méneret A, Roze E.

Lancet Neurol. 2020 Nov;19(11):881-882. doi: 10.1016/S1474-4422(20)30366-5.

PMID: [33098786](#)

13. Monogenic variants in dystonia: an exome-wide sequencing study

Michael Zech, Robert Jech, Sylvia Boesch, Matej Škorvánek, Sandrina Weber, Matias Wagner, Chen Zhao, Angela Jochim, Ján Necpál, Yasemin Dincer, Katharina Vill, Felix Distelmaier, Malgorzata Stoklosa, Martin Krenn, Stephan Grunwald, Tobias Bock-Bierbaum, Anna Fečíková, Petra Havránková, Jan Roth, Iva Příhodová, Miriam Adamovičová, Olga Ulmanová, Karel Bechyně, Pavlína Danhofer, Branislav Veselý, Vladimír Haň, Petra Pavelekova, Zuzana Gdovinová, Tobias Mantel, Tobias Meindl, Alexandra Sitzberger, Sebastian Schröder, Astrid Blaschek, Timo Roser, Michaela V Bonfert, Edda Haberlandt, Barbara Plecko, Birgit Leineweber, Steffen Berweck, Thomas Herberhold, Berthold Langguth, Jana Švantnerová, Michal Minár, Gonzalo Alonso Ramos-Rivera, Monica H Wojcik, Sander Pajusalu, Katrin Öunap, Ulrich A Schatz, Laura Pölsler, Ivan Milenkovic, Franco Laccone, Veronika Pilshofer, Roberto Colombo, Steffi Patzer, Arcangela Iuso, Julia Vera, Monica Troncoso, Fang Fang, Holger Prokisch, Friederike Wilbert, Matthias Eckenweiler, Elisabeth Graf, Dominik S Westphal, Korbinian M Riedhammer, Theresa Brunet, Bader Alhaddad, Riccardo Berutti, Tim M Strom, Martin Hecht, Matthias Baumann, Marc Wolf, Aida Telegrafi, Richard E Person, Francisca Millan Zamora, Lindsay B Henderson, David Weise, Thomas Musacchio, Jens Volkmann, Anna Szuto, Jessica Becker, Kirsten Cremer, Thomas Sycha, Fritz Zimprich, Verena Kraus, Christine Makowski, Pedro Gonzalez-Alegre, Tanya M Bardakjian, Laurie J Ozelius, Annalisa Vetro, Renzo Guerrini, Esther Maier, Ingo Borggraefe, Alice Kuster, Saskia B Wortmann, Annette Hackenberg, Robert Steinfeld, Birgit Assmann, Christian Staufner, Thomas Opladen, Evžen Růžička, Ronald D Cohn, David Dymont, Wendy K Chung, Hartmut Engels, Andres Ceballos-Baumann, Rafal Ploski, Oliver Daumke, Bernhard Haslinger, Volker Mall, Konrad Oexle, Juliane Winkelmann

Multicenter Study Lancet Neurol. 2020 Nov;19(11):908-918. doi: 10.1016/S1474-4422(20)30312-4.

Background: Dystonia is a clinically and genetically heterogeneous condition that occurs in isolation (isolated dystonia), in combination with other movement disorders (combined dystonia), or in the context of multisymptomatic phenotypes (isolated or combined dystonia with other neurological involvement). However, our understanding of its aetiology is still incomplete. We aimed to elucidate the monogenic causes for the major clinical categories of dystonia. **Methods:** For this exome-wide sequencing study, study participants were identified at 33 movement-disorder and neuropaediatric specialty centres in Austria, Czech Republic, France, Germany, Poland, Slovakia, and Switzerland. Each individual with dystonia was diagnosed in accordance with the dystonia consensus definition. Index cases were eligible for this study if they had no previous genetic diagnosis and no indication of an acquired cause of their illness. The second criterion was not applied to a subset of participants with a working clinical diagnosis of dystonic cerebral palsy. Genomic DNA was extracted from blood of participants and whole-exome sequenced. To find causative variants in known disorder-associated genes, all variants were filtered, and unreported variants were classified according to American College of Medical Genetics and Genomics guidelines. All considered variants were reviewed in expert round-table sessions to validate their clinical significance. Variants that survived filtering and interpretation procedures were defined as diagnostic variants. In the cases that went undiagnosed, candidate dystonia-causing genes were prioritised in a stepwise workflow. **Findings:** We sequenced the exomes of 764 individuals with dystonia and 346 healthy parents who were recruited between June 1, 2015, and July 31, 2019. We identified causative or probable causative variants in 135 (19%) of 728 families, involving 78 distinct monogenic disorders. We observed a larger proportion of individuals with diagnostic variants in those with dystonia (either isolated or combined) with coexisting non-movement disorder-related neurological symptoms (100 [45%] of 222; excepting cases with evidence of perinatal brain injury) than in those with combined (19 [19%] of 98) or isolated (16 [4%] of 388) dystonia. Across all categories of dystonia, 104 (65%) of the 160 detected variants affected genes which are associated with neurodevelopmental disorders. We found diagnostic variants in 11 genes not previously linked to dystonia, and propose a predictive clinical score that could guide the implementation of exome sequencing in routine diagnostics. In cases without perinatal sentinel events, genomic alterations contributed substantively to the diagnosis of dystonic cerebral palsy. In 15 families, we delineated 12 candidate genes. These include IMPDH2, encoding a key purine biosynthetic enzyme, for which robust evidence existed for its involvement in a neurodevelopmental disorder with dystonia. We identified six variants in IMPDH2, collected from four independent cohorts, that were predicted to be deleterious de-novo variants and expected to result in deregulation of purine metabolism. **Interpretation:** In this study, we have determined the role of monogenic variants across the range of dystonic disorders, providing guidance for the introduction of personalised care strategies and fostering follow-up pathophysiological explorations. **Funding:** Else Kröner-Fresenius-Stiftung, Technische Universität München, Helmholtz Zentrum München, Medizinische Universität Innsbruck, Charles University in Prague, Czech Ministry of Education, the Slovak Grant and Development Agency, the Slovak Research and Grant Agency.

PMID: [33098801](#)

14. Updates on congenital lacrimal drainage anomalies and their association with syndromes and systemic disorders: A major review

Mohammad Javed Ali

Ann Anat. 2020 Oct 21;151613. doi: 10.1016/j.aanat.2020.151613. Online ahead of print.

Background: To review and update the syndromic and non-syndromic systemic associations of congenital lacrimal drainage anomalies. **Methods:** The authors performed a PubMed search of all articles published in English on congenital lacrimal drainage anomalies (CLDA). The current review provides an update from January 2017 to August 2020 on all CLDA associated with clinical syndromes or non-syndromic systemic disorders. The update intends to appraise the readers on all papers that were published in the interim 3-year period since the publication of the previous major review by authors (1933-2016). Patients with specific syndromes or systemic disorders were then reviewed. Pertinent cross-references from each of the short-listed articles were also included. Data reviewed include syndromic descriptions, systemic details, demographics, lacrimal presentations, management, and outcomes. **Results:** There have been significant new updates. Eleven new syndromes have been added to the list of syndromic associations, of which three were suspects. Among the new syndromic associations, three (PHACE, Williams-Beuren, and Peter's plus syndromes) described CLDA details in depth. Several new non-syndromic systemic conditions with associated CLDA also came to light, the foremost amongst them being proboscis lateralis, diprosopus dirrhinus, cerebral palsy, and NGLY-1 related disorders. Although familial presentations have been reported, the inheritance patterns are unclear for most anomalies. Surgical challenges in these patients are distinct, and a thorough pre-operative assessment, including detailed imaging when indicated, may facilitate good outcomes. Two updated tables reflecting the summary of syndromic and non-syndromic systemic associations are provided to capture the details at a glance. **Conclusion:** It is not very uncommon to find CLDA in syndromic or non-syndromic systemic disorders. Diagnosis of a craniofacial syndrome should prompt the physician to look out for CLDA. Similarly, a diagnosis of multiple CLDA should alert the examiner for the possible presence of associated systemic anomalies.

PMID: [33098980](#)

15. General anesthesia for cesarean delivery and childhood neurodevelopmental and perinatal outcomes: a secondary analysis of a randomized controlled trial

L S Robbins, C T Blanchard, F J Biasini, M F Powell, B M Casey, A T Tita, L M Harper

Int J Obstet Anesth. 2020 Aug 25;S0959-289X(20)30112-6. doi: 10.1016/j.ijoa.2020.08.007. Online ahead of print.

Background: In 2016, the U.S. Food and Drug Administration expressed concern that neurodevelopment may be negatively affected by anesthesia or sedation exposure in pregnancy or before three years of age. We examined the association between general anesthesia at the time of cesarean delivery and early childhood neurodevelopment. **Methods:** A secondary analysis of a multicenter randomized controlled trial assessing magnesium for prevention of cerebral palsy in infants at risk for preterm delivery. Exposure was general compared to neuraxial anesthesia. The primary outcome was motor or mental delay at two years of age, assessed by Bayley Scales of Infant Development II (BSIDII). Secondary outcomes included BSIDII subdomains and perinatal outcomes. Multivariable logistic regression models were performed to control for confounders. **Results:** Of 557 women undergoing cesarean delivery, 119 (21%) received general anesthesia. There were no differences in the primary composite outcome of developmental delay (aOR 0.93, 95% CI 0.61 to 1.43) or the BSIDII subdomains of mild, moderate, or severe mental delay, or mild or moderate motor delay. Severe motor delay was more common among infants exposed to general anesthesia (aOR 1.98, 95% CI 1.06 to 3.69). Infants exposed to general anesthesia had longer neonatal intensive care stays (51 vs 37 days, P=0.010). **Conclusions:** General anesthesia for cesarean delivery was not associated with overall neurodevelopmental delay at two years of age, except for greater odds of severe motor delay. Future studies should evaluate this finding, as well as the impact of longer or multiple anesthetic exposures across all gestational ages on neurodevelopment.

PMID: [33121885](#)

16. Neonatal and Childhood Outcomes Following Preterm Premature Rupture of Membranes

Lillian B Boettcher, Erin A S Clark

Review Obstet Gynecol Clin North Am. 2020 Dec;47(4):671-680. doi: 10.1016/j.ogc.2020.09.001. Epub 2020 Oct 7.

Preterm premature rupture of membranes (PPROM) is almost uniformly associated with preterm birth and thus sequelae of prematurity explain many of the complications associated with this condition. However, the unique inflammatory environment and oligohydramnios associated with PPRM may impart unique neonatal and childhood morbidity compared with other preterm birth pathways.

PMID: [33121652](#)

17. Oral Myiasis of Maxilla (Palatal Gingiva)

Vanmathi Vasanthakumar, Parasuraman R Varalakshmi, Ramya Vanmathi

Case Reports Contemp Clin Dent. Apr-Jun 2020;11(2):162-164. doi: 10.4103/ccd.ccd_49_20. Epub 2020 Aug 7.

Myiasis is an invasion of tissues and organs of humans or animals by fly larvae. Oral myiasis is a rare pathology associated with a medical condition, poor oral hygiene, mouth breathing, and incompetent lip. We present a case of oral myiasis of the maxillary anterior region of the palate, in a 12-year-old male with cerebral palsy and poor oral hygiene. The diagnosis was made on the presence of larvae. The mechanical removal of larvae with hemostat was carried out with ivermectin oral therapy.

PMID: [33110330](#)

18. The Challenge of Diagnosing Rare Life Threatening Skin Lesions [Article in Hebrew]

Ayelet Gavri Beker, Naama Elisha, Leah Leibovitch, Irit Schushan Eisen, Ram Palti, Zipora Strauss

Skin lesions seen after delivery are frequent and mostly shallow, without the need for special care or diagnosis challenge. In the following case, an infant was born at 35 weeks gestation, presented after the delivery with a well-demarcated, necrotic plaque over the right forearm with neurologic deficit. The differential diagnosis includes life-threatening reasons, therefore, emergent laboratory and imaging tests were held. Treatment was given after consulting a multidisciplinary team of experts, including antibiotic treatment, blood products and anticoagulation and physiotherapy treatment was started. Under this treatment, improvement was noticed but there was still a motor restriction. He was discharged home on his 24th day of life, with the working diagnosis of Congenital Volkmann Ischemic Contracture (CVIC). On his seventh week of life, he arrived to the emergency room with focal seizure resulting from an infarct seen on an MRI. He was diagnosed with cerebral palsy at the age of five months. In conclusion, Congenital Volkmann Ischemic Contracture is a rare diagnosis, however, awareness is of importance since fast treatment is crucial for future prognosis.

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19. Test-Retest Reliability and Correlates of Vertebral Bone Marrow Lipid Composition by Lipidomics Among Children With Varying Degrees of Bone Fragility

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The reliability of lipidomics, an approach to identify the presence and interactions of lipids, to analyze the bone marrow lipid composition among pediatric populations with bone fragility is unknown. The objective of this study was to assess the test-retest reliability, standard error of measurement (SEM), and the minimal detectable change (MDC) of vertebral bone marrow lipid composition determined by targeted lipidomics among children with varying degrees of bone fragility undergoing routine orthopedic surgery. Children aged 10 to 19 years, with a confirmed diagnosis of adolescent idiopathic scoliosis (n = 13) or neuromuscular scoliosis and cerebral palsy (n = 3), undergoing posterior spinal fusion surgery at our institution were included in this study. Transpedicular vertebral body bone marrow samples were taken from thoracic vertebrae (T11, 12) or lumbar vertebrae (L1 to L4). Lipid composition was assessed via targeted lipidomics and all samples were analyzed in the same batch. Lipid composition measures were examined as the saturated, monounsaturated, and polyunsaturated index and as individual fatty acids. Relative and absolute test-retest reliability was assessed using the intraclass correlation coefficient (ICC), SEM, and MDC. Associations between demographics and index measures were explored. The ICC, SEM, and MDC were 0.81 (95% CI,

0.55-0.93), 1.6%, and 4.3%, respectively, for the saturated index, 0.66 (95% CI, 0.25-0.87), 3.5%, and 9.7%, respectively, for the monounsaturated index, and 0.60 (95% CI, 0.17-0.84), 3.6%, and 9.9%, respectively, for the polyunsaturated index. For the individual fatty acids, the ICC showed a considerable range from 0.04 (22:2n-6) to 0.97 (18:3n-3). Age was positively correlated with the saturated index ($r^2 = 0.36$; $p = 0.014$) and negatively correlated with the polyunsaturated index ($r^2 = 0.26$; $p = 0.043$); there was no difference in index measures by sex ($p > 0.58$). The test-retest reliability was moderate-to-good for index measures and poor to excellent for individual fatty acids; this information can be used to power research studies and identify measures for clinical or research monitoring. © 2020 The Authors. JBMR Plus published by Wiley Periodicals LLC on behalf of American Society for Bone and Mineral Research.

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20. Systemic dendrimer-drug nanomedicines for long-term treatment of mild-moderate cerebral palsy in a rabbit model

Zhi Zhang, Yi-An Lin, Soo-Young Kim, Lilly Su, Jinhuan Liu, Rangaramanujam M Kannan, Sujatha Kannan

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Background: Neuroinflammation mediated by microglia plays a central role in the pathogenesis of perinatal/neonatal brain injury, including cerebral palsy (CP). Therapeutics mitigating neuroinflammation potentially provide an effective strategy to slow the disease progression and rescue normal brain development. Building on our prior results which showed that a generation-4 hydroxyl poly(amidoamine) (PAMAM) dendrimer could deliver drugs specifically to activated glia from systemic circulation, we evaluated the sustained efficacy of a generation-6 (G6) hydroxyl-terminated PAMAM dendrimer that showed a longer blood circulation time and increased brain accumulation. N-acetyl-L-cysteine (NAC), an antioxidant and anti-inflammatory agent that has high plasma protein binding properties and poor brain penetration, was conjugated to G6-PAMAM dendrimer-NAC (G6D-NAC). The efficacy of microglia-targeted G6D-NAC conjugate was evaluated in a clinically relevant rabbit model of CP, with a mild/moderate CP phenotype to provide a longer survival of untreated CP kits, enabling the assessment of sustained efficacy over 15 days of life. **Methods:** G6D-NAC was conjugated and characterized. Cytotoxicity and anti-inflammatory assays were performed in BV-2 microglial cells. The efficacy of G6D-NAC was evaluated in a rabbit model of CP. CP kits were randomly divided into 5 groups on postnatal day 1 (PND1) and received an intravenous injection of a single dose of PBS, or G6D-NAC (2 or 5 mg/kg), or NAC (2 or 5 mg/kg). Neurobehavioral tests, microglia morphology, and neuroinflammation were evaluated at postnatal day 5 (PND5) and day 15 (PND15). **Results:** A single dose of systemic 'long circulating' G6D-NAC showed a significant penetration across the impaired blood-brain-barrier (BBB), delivered NAC specifically to activated microglia, and significantly reduced microglia-mediated neuroinflammation in both the cortex and cerebellum white matter areas. Moreover, G6D-NAC treatment significantly improved neonatal rabbit survival rate and rescued motor function to nearly healthy control levels at least up to 15 days after birth (PND15), while CP kits treated with free NAC died before PND9. **Conclusions:** Targeted delivery of therapeutics to activated microglia in neonatal brain injury can ameliorate pro-inflammatory microglial responses to injury, promote survival rate, and improve neurological outcomes that can be sustained for a long period. Appropriate manipulation of activated microglia enabled by G6D-NAC can impact the injury significantly beyond inflammation.

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