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Interventions and Management

1. Danish Translation, Adaptation and Validation of the ABILHAND-Kids Questionnaire for Children With Cerebral Palsy

Alice Ørts Hansen, Helle S Poulsen, Hanne Kaae Kristensen, Henrik H Lauridsen

Disabil Rehabil. 2020 Jun 22;1-10. doi: 10.1080/09638288.2020.1780482. Online ahead of print.

Purpose: To translate and cross-culturally adapt the ABILHAND-Kids questionnaire into Danish and assess its psychometric properties in children with cerebral palsy (CP). **Materials and methods:** A Danish version of the parent-reported ABILHAND-Kids questionnaire was created through a standardized translation process. Dimensionality (confirmatory factor analysis), reliability, smallest detectable change, floor and ceiling effects, and Rasch analysis were carried out. **Results:** One-hundred-and-fifty children diagnosed with CP were included. No parent had difficulty completing the ABILHAND-Kids (DK). Psychometric testing demonstrated a unidimensional scale, excellent test-retest reliability (ICC2.1A = 0.97) and internal consistency ($\alpha = 0.96$). A smallest detectable change of 5.15 points was considered acceptable. One item showed Differential Item Functioning, four pairs of items showed signs of local dependence and one item had disordered thresholds. Nevertheless, analyses did not lead to the removal of any items. Item thresholds covered most levels of person abilities. Lastly, 24.7% scored within measurement error at the ceiling of the scale, indicating that it was not possible to measure further improvement. **Conclusion:** ABILHAND-Kids (DK) seems to be a valid, reliable and comprehensive measurement scale to assess manual ability in children with CP. It can be used in goal setting and to inform future interventions and rehabilitation evaluation. **IMPLICATIONS FOR REHABILITATION** Impaired hand function leads to limited participation in activities of everyday life in children with cerebral palsy. Adequate outcome measures of hand function are crucial for the planning and evaluation of interventions. The Danish version of ABILHAND-Kids is a valid and reliable measure of manual ability in children with cerebral palsy, and it can be used in clinical practice and for research purposes.

PMID: [32568564](#)

2. The Use of Wearable Inertial Sensors Effectively Quantify Arm Asymmetry During Gait in Children With Unilateral Spastic Cerebral Palsy

Aviva Wolff, Andrew Sama, Mark Lenhoff, Aaron Daluiski

J Hand Ther. 2020 Jun 19;S0894-1130(20)30074-0. doi: 10.1016/j.jht.2020.03.026. Online ahead of print.

PMID: [32571600](#)

3. Impact of Dual Task on Postural Sway During Sit-To-Stand Movement in Children With Unilateral Cerebral Palsy

Camila Resende Gâmbaro Lima, Sílvia Leticia Pavão, Ana Carolina de Campos, Nelci Adriana Cicuto Ferreira Rocha

Clin Biomech (Bristol, Avon). 2020 Jun 3;78:105072. doi: 10.1016/j.clinbiomech.2020.105072. Online ahead of print.

Background: To verify the effect of dual-task on postural oscillation during sit-to-stand movement in children with Cerebral Palsy. **Methods:** 17 children with spastic unilateral cerebral palsy and 20 typically-developing children, aged 5 to 12 years, performed the following tasks: Simple task: sit-to-stand with arms crossed against the chest; bimanual dual-task: sit-to-stand while carrying a tray; unimanual dual-task: sit-to-stand while holding a plastic cup with one hand. For data analysis, sit-to-stand was divided in three phases: preparation (phase 1), rising (phase 2), and stabilization (phase 3). Postural control was measured using a force plate, and the variables analyzed were: area, anterior-posterior and medial-lateral velocity, and STS duration. Analysis of variance was applied to test the effects of group; task conditions and interactions. **Findings:** Children with cerebral palsy presented higher values of postural oscillation when compared to their typical pairs. Bimanual and Unimanual dual tasks presented greater postural oscillation values in sit-to-stand phase 1 compared to simple task. In bimanual dual-task, children with cerebral palsy presented lower values of velocity in phases 3, and greater postural oscillation and duration of the task when compared to single-task and unimanual dual-tasks. **I. Interpretation:** The insertion of a secondary task seems to interfere differently children with cerebral palsy, depending on the specific demands of each task. Thus, the importance of inserting dual tasks in the interventions is emphasized, considering that they are executed extensively in the day to day, and can act as facilitators or challenge in the execution of functional tasks.

PMID: [32562882](#)

4. Modified Desk Height Helps Children With Cerebral Palsy Perform Sit-To-Stand

Hyun Kyoon Lim, Jooyeon Ko, Donghyun Lee, Dong-Uk Han

Disabil Rehabil Assist Technol. 2020 Jun 23;1-7. doi: 10.1080/17483107.2020.1775315. Online ahead of print.

Aim: Children with cerebral palsy (CP) have difficulties performing activities that require the use of fundamental motor skills such as sit-to-stand (STS). In this study, we used a height adjustable chair and desk to investigate the role of desk support in STS and how it might benefit children with CP. **Methods:** Seventeen typically developing children (TDC), average age = 9.7 years, and 28 children with CP (Gross Motor Function Classification System [GMFCS] I and II), average age = 10.3 years, participated in the test. Elapsed time and body sway were measured using a pressure mat and load cell while each child performed a STS task. Two different desk heights were tested for time consumption and sway under the condition of hands-on-desk and arms-crossed. **Results:** We found that the elapsed time of hands-on-desk with the elbow flexion height was the shortest ($p < 0.05$). Sway amount was also significantly reduced for all children when they used the table for STS ($p < 0.05$). **Conclusion:** Results of this study may be a useful reference in rehabilitation training and designing a desk height beneficial for children with CP. **Implications for Rehabilitation:** Better performance of sit-to-stand for a child with cerebral palsy could be made by a desk support. Elapsed time during preparation period for sit-to-stand could be reduced by desk support for all CP children. Sway amount during sit-to-stand could be reduced by desk support, especially for the CP children with GMFCS level II. Desk height is an important parameter and should be studied in detail.

PMID: [32574122](#)

5. Effect of Action Observation Training on Spasticity, Gross Motor Function, and Balance in Children With Diplegia Cerebral Palsy

Young-A Jeong, Byoung-Hee Lee

Children (Basel). 2020 Jun 18;7(6):E64. doi: 10.3390/children7060064.

This study evaluated the effect of action observation training on spasticity, gross motor function, and balance in children with spastic diplegia cerebral palsy. Eighteen children with cerebral palsy participated in this study. The participants were randomized into the action observation training group ($n = 9$) and a control group ($n = 9$). The action observation training group repeatedly practiced the action with their motor skills, while the control group practiced conventional physical therapy. Both groups received 30 min sessions, 3 days a week, for 6 weeks. To confirm the effects of intervention, the spasticity, gross motor function measurement (GMFM), and pediatric reaching test (PRT) were evaluated. The results showed that in the plantar flexor contracture test of both sides, the Modified Tardieu Scale (MTS) of the right side of knee joints, GMFM-B, C, and D were

significantly increased between pre- and post-intervention within both groups ($p < 0.05$). PRT was significantly increased between pre- and post-intervention within the both groups ($p < 0.05$), and there was a significant difference between the two groups ($p < 0.05$). These results suggest that action observation training is both feasible and beneficial for improving spasticity, gross motor function, and balance in children with spastic diplegia cerebral palsy.

PMID: [32570855](#)

6. Treatment Response to Botulinum Neurotoxin-A in Children With Cerebral Palsy Categorized by the Type of Stretch Reflex Muscle Activation

Lynn Bar-On, Erwin Aertbeliën, Anja Van Campenhout, Guy Molenaers, Kaat Desloovere

Front Neurol. 2020 Jun 2;11:378. doi: 10.3389/fneur.2020.00378. eCollection 2020.

While Botulinum NeuroToxin-A (BoNT-A) injections are frequently used to reduce the effects of hyperactive stretch reflexes in children with cerebral palsy (CP), the effects of this treatment vary strongly. Previous research, combining electromyography (EMG) with motion analysis, defined different patterns of stretch reflex muscle activation in muscles, those that reacted more to a change in velocity (velocity dependent -VD), and those that reacted more to a change in length (length dependent -LD). The aim of this study was to investigate the relation between the types of stretch reflex muscle activation in the semitendinosus with post-BoNT-A outcome as assessed passively and with 3D gait analysis in children with spastic CP. Eighteen children with spastic CP (10 bilaterally involved) between the ages of 12 and 18 years were assessed before and on average, 8 weeks post-treatment. EMG and motion analysis were used to assess the degree and type of muscle activation dependency in the semitendinosus during passive knee extensions performed at different joint angular velocities. Three-dimensional gait analysis was used to assess knee gait kinematics as a measure of functional outcome. Pre-treatment, 9 muscles were classified as VD and 9 as LD, but no differences between the groups were evident in the baseline knee gait kinematics. Post-treatment, stretch reflex muscle activation decreased significantly in both groups but the reduction was more pronounced in those muscles classified pre-treatment as VD (-72% vs. -50%, $p = 0.005$). In the VD group, these changes were accompanied by greater knee extension at initial contact and during the swing phase of gait. In the LD group, there was significantly increased post-treatment knee hyperextension in late stance. Although results vary between patients, the reduction of stretch reflex muscle activation in the semitendinosus generally translated to an improved functional outcome, as assessed with 3D gait analysis. However, results were less positive for those muscles with pre-treatment length-dependent type of stretch reflex muscle activation. The study demonstrates the relevance of categorizing the type of stretch reflex muscle activation as a possible predictor of treatment response.

PMID: [32581991](#)

7. Long Term Outcome of Selective Dorsal Rhizotomy for the Management of Childhood Spasticity-Functional Improvement and Complications

Albert Tu, Paul Steinbok

Childs Nerv Syst. 2020 Jun 23. doi: 10.1007/s00381-020-04747-8. Online ahead of print.

Background: Selective dorsal rhizotomy (SDR) for the management of lower extremity spasticity is a surgical technique that has existed since the 1900s. While much evidence supports its efficaciousness in reducing tone in the short term, limited information exists detailing the long-term outcome and evolution over time of patients undergoing SDR. Methods: All publications with 10 years or more of outcome data on patients undergoing SDR were identified from Medline and Embase databases using the search term "Rhizotomy." Only publications that were in English included patients with cerebral palsy under the age of 21 and discussed SDR for lower extremity spasticity were included. Case reports, reviews without primary data, or publications not accessible online were excluded from the review. Results: A total of 2128 publications were initially identified, of which 19 papers describing 1054 patients fit inclusion and exclusion criteria. GMFCS in most patients improved or remained stable over time after surgery, although durability of improvement and final outcome was dependent on initial functional status. Tone was noted to also substantially improve although a small proportion required additional oral or injectable pharmacologic agents and an even smaller proportion required baclofen pumps. Upper extremity function was also noted to improve substantially after SDR. A significant number of patients were independent for activities of daily living and were engaged in secondary education or gainful employment. A significant proportion of patients still required orthopedic surgery to the lower extremities after SDR, although the incidence of spinal deformity was not observed to be substantially elevated over that of natural history. Conclusion: SDR offers substantial improvements to a number of domains beyond pure

tone reduction. These changes are durable over time, although patient selection is crucial in identifying those patients that will have the most benefit. Long-term follow-up is important in this population given the potential need for further interventions that still exist in many patients.

PMID: [32577879](#)

8. Frequency Distribution in Intraoperative Stimulation-Evoked EMG Responses During Selective Dorsal Rhizotomy in Children With Cerebral Palsy-Part 1: Clinical Setting and Neurophysiological Procedure

Simone Wolter, Claudia Spies, John H Martin, Matthias Schulz, Akosua Sarpong-Bengelsdorf, Joachim Unger, Ulrich-W Thomale, Theodor Michael, James F Murphy, Hannes Haberl

Childs Nerv Syst. 2020 Jun 23. doi: 10.1007/s00381-020-04734-z. Online ahead of print.

Introduction: Selective dorsal rhizotomy (SDR) consists of microsurgical partial deafferentation of sensory nerve roots (L1-S2). It is primarily used today in decreasing spasticity in young cerebral palsy (CP) patients. Intraoperative monitoring (IOM) is an essential part of the surgical decision-making process, aimed at improving functional results. The role played by SDR-IOM is examined, while realizing that connections between complex EMG responses to nerve-root stimulation and a patient's individual motor ability remain to be clarified. **Methods:** We conducted this retrospective study, analyzing EMG responses in 146 patients evoked by dorsal-root and rootlet stimulation, applying an objective response-classification system, and investigating the prevalence and distribution of the assessed grades. Part 1 describes the clinical setting and SDR procedure, reintroduced in Germany by the senior author in 2007. **Results:** Stimulation-evoked EMG response patterns revealed significant differences along the segmental levels. More specifically, a comparison of grade 3+4 prevalence showed that higher-graded rootlets were more noticeable at lower nerve root levels (L5, S1), resulting in a typical rostro-caudal anatomical distribution. **Conclusions:** In view of its prophylactic potential, SDR should be carried out at an early stage in all CP patients suffering from severe spasticity. It is particularly effective when used as an integral part of a coordinated, comprehensive spasticity program in which a team of experts pool their information. The IOM findings pertaining to the anatomical grouping of grades could be of potential importance in adjusting the SDR-IOM intervention to suit the specific individual constellation, pending further validation. Trial registration: ClinicalTrials.gov ID: NCT03079362.

PMID: [32577878](#)

9. Frequency Distribution in Intraoperative Stimulation-Evoked EMG Responses During Selective Dorsal Rhizotomy in Children With Cerebral Palsy-Part 2: Gender Differences and Left-Biased Asymmetry

Simone Wolter, Hannes Haberl, Claudia Spies, T Alp Sargut, John H Martin, Sascha Tafelski, Anne van Riesen, Ingeborg K uchler, Brigitte Wegner, Kathrin Scholtz, Ulrich-W Thomale, Theodor Michael, James F Murphy, Matthias Schulz

Childs Nerv Syst. 2020 Jun 25. doi: 10.1007/s00381-020-04735-y. Online ahead of print.

Introduction: Spinal reflexes reorganize in cerebral palsy (CP), producing hyperreflexia and spasticity. CP is more common among male infants, and gender might also influence brain and spinal-cord reorganization. This retrospective study investigated the frequency of higher-graded EMG responses elicited by electrical nerve-root stimulation during selective dorsal rhizotomy (SDR), prior to partial nerve-root deafferentation, considering not only segmental level and body side, but also gender. **Methods:** Intraoperative neuromonitoring (IOM) was used in SDR to pinpoint the rootlets most responsible for exacerbated stimulation-evoked EMG patterns recorded from lower-limb muscle groups. Responses were graded according to an objective response-classification system, ranging from no abnormalities (grade 0) to highly abnormal (grade 4+), based on ipsilateral spread and contralateral involvement. Non-parametric analysis of data with repeated measures was primarily used in investigating the frequency distribution of these various EMG response grades. Over 7000 rootlets were stimulated, and the results for 65 girls and 81 boys were evaluated, taking changes in the composition of patient groups into account when considering GMFCS levels. **Results:** The distribution of graded EMG responses varied according to gender, laterality, and level. Higher-graded EMG responses were markedly more frequent in the boys and at lower segmental levels (L5, S1). Left-biased asymmetry in higher-graded rootlets was also more noticeable in the boys and in patients with GMFCS level I. A close link was observed between higher-grade assessments and left-biased asymmetry. **Conclusions:** Detailed insight into the patient's initial spinal-neurofunctional state prior to deafferentation suggests that differences in asymmetrical spinal reorganization might be attributable to a hemispheric imbalance.

PMID: [32588175](#)

10. Retroperitoneal Kirschner Wire Migration After Surgical Treatment in a Patient With Cerebral Palsy

Gökhan Bülent Sever

Jt Dis Relat Surg. 2020;31(2):382-385. doi: 10.5606/ehc.2020.74846. Epub 2020 Jun 18.

Although Kirschner (K)-wire is among the most commonly used implants in orthopedic surgeries, the migration of this material is a very rare complication. In this article, we present the case of a K-wire migration four years after the surgery detected during the routine control of a 10-year-old male patient who underwent surgical treatment due to the diagnosis of developmental hip dys-plasia on the cerebral palsy. The aim of this study was to raise the awareness regarding this complication particularly for the pediatric orthopedic surgeons, and to recommend the removal of the K-wire as soon as bone union occurs.

PMID: [32584741](#)

11. Outcome Domains and Measures After Lower Limb Orthopaedic Surgery for Ambulant Children With Cerebral Palsy: An Updated Scoping Review

Hajar Almoajil, Nichola Wilson, Tim Theologis, Sally Hopewell, Francine Toye, Helen Dawes

Review Dev Med Child Neurol. 2020 Jun 22. doi: 10.1111/dmcn.14599. Online ahead of print.

Aim: To determine the reported outcome domains and measures used to assess lower limb orthopaedic surgery of ambulant children and young people with cerebral palsy (CP) and map these outcomes to the International Classification of Functioning, Disability and Health - Children and Youth (ICF-CY) framework. **Method:** This updated scoping review included studies published between January 2016 and July 2019 in five databases: MEDLINE, PubMed, EMBASE, CINAHL, and the Cochrane Central Register of Controlled Trials. Studies were included if participants were ambulant individuals with CP aged between 0 and 20 years who had undergone lower limb orthopaedic surgery. Health outcome domains and measures were identified and classified using the ICF-CY framework. **Results:** Forty-four eligible studies were identified with a total of 40 different outcome domains recorded. Among eligible studies, 44 (100%) measured body function and structural impairment and seven (16%) measured activity limitation and participation restriction. The most frequently reported outcome was gait pattern (n=37, 84%). Few studies reported adverse effects of surgery (n=13, 30%). Twenty-nine different outcome measures were identified. Patient-reported outcomes measures were used in 10 studies (23%). **Interpretation:** The review highlights a heterogeneity in the reported outcome domains and measures used in CP studies. The majority of the reported outcomes focus on the ICF-CY domain of body function and structure. The review also highlights a notable shift towards patient-reported outcomes in recent years. Development of a core outcome set for lower limb orthopaedic surgery would guide researchers to use more consistent and complete measurement sets.

PMID: [32567044](#)

12. Reference Centiles to Monitor the 6-minute-walk Test in Ambulant Children With Cerebral Palsy and Identification of Effects After Rehabilitation Utilizing Whole-body Vibration

Kyriakos Martakis, Christina Stark, Mirko Rehberg, Oliver Semler, Ibrahim Duran, Eckhard Schoenau

Dev Neurorehabil. 2020 Jun 21;1-11. doi: 10.1080/17518423.2020.1770891. Online ahead of print.

Background: Children with cerebral palsy present age-driven development in gross motor skills and walking capacity. **Aims:** To precisely monitor the 6-minute walk test (6MWT) in children with CP, GMFCS levels 1 and 2 over 6 months and to assess the effect of a 6-month rehabilitation program including whole-body vibration. **Methods:** Retrospective analysis of data of 157 children with CP who received standardized rehabilitation (DRKS00011331). 6MWT was assessed at the start (M0) and end of the training (M6), as well as at a 6-month follow-up (M12). Centiles were created using the lambda-mu-sigma (LMS) method. **Results:** We created 6MWT percentiles using data of all 157 children (M0 data). A medium treatment effect size (Cohen's d =

0.69) was found (M6 and M12 data). Conclusions: The generated centiles may help monitor 6MWT changes over 6 months. Combining WBV and conventional physiotherapy can significantly improve 6MWT in children with CP. Abbreviations: 6MWT: 6-Minute Walk Test; CP: Cerebral palsy; ES: effect size; GMFCS: Gross Motor Function Classification System; GMFM-66: Gross Motor Function Measure 66; LOESS: locally weighted scatterplot smoothing; LMS: lambda-mu-sigma; MCID: minimal clinical important difference; SD: standard deviation; SRM: standardized response mean; WBV: whole-body vibration.

PMID: [32564635](#)

13. Progressive Resistance Training for Adolescents With Cerebral Palsy: The STAR Randomized Controlled Trial

Jennifer M Ryan, Grace Lavelle, Nicola Theis, Marika Noorkoiv, Cherry Kilbride, Thomas Korff, Vasilios Baltzopoulos, Adam Shortland, Wendy Levin, Star Trial Team

Dev Med Child Neurol. 2020 Jun 26. doi: 10.1111/dmcn.14601. Online ahead of print.

Aim: To evaluate the effect of progressive resistance training of the ankle plantarflexors on gait efficiency, activity, and participation in adolescents with cerebral palsy (CP). **Method:** Sixty-four adolescents (10-19y; 27 females, 37 males; Gross Motor Function Classification System [GMFCS] levels I-III) were randomized to 30 sessions of resistance training (10 supervised and 20 unsupervised home sessions) over 10 weeks or usual care. The primary outcome was gait efficiency indicated by net nondimensional oxygen cost (NNcost). Secondary outcomes included physical activity, gross motor function, participation, muscle strength, muscle and tendon size, and muscle and tendon stiffness. Analysis was intention-to-treat. **Results:** Median attendance at the 10 supervised sessions was 80% (range 40-100%). There was no between-group difference in NNcost at 10 (mean difference: 0.02, 95% confidence interval [CI] -0.07 to 0.11, $p=0.696$) or 22 weeks (mean difference: -0.08, 95% CI -0.18 to 0.03, $p=0.158$). There was also no evidence of between-group differences in secondary outcomes at 10 or 22 weeks. There were 123 adverse events reported by 27 participants in the resistance training group. **Interpretation:** We found that 10 supervised sessions and 20 home sessions of progressive resistance training of the ankle plantarflexors did not improve gait efficiency, muscle strength, activity, participation, or any biomechanical outcome among adolescents with CP.

PMID: [32588919](#)

14. A Biofeedback-Enhanced Therapeutic Exercise Video Game Intervention for Young People With Cerebral Palsy: A Randomized Single-Case Experimental Design Feasibility Study

Alexander MacIntosh, Eric Desailly, Nicolas Vignais, Vincent Vigneron, Elaine Biddiss

PLoS One. 2020 Jun 22;15(6):e0234767. doi: 10.1371/journal.pone.0234767. eCollection 2020.

Importance/background: Movement-controlled video games have potential to promote home-based practice of therapy activities. The success of therapy gaming interventions depends on the quality of the technology used and the presence of effective support structures. **Aim:** This study assesses the feasibility of a novel intervention that combines a co-created gaming technology integrating evidence-based biofeedback and solution-focused coaching (SFC) strategies to support therapy engagement and efficacy at home. **Methods:** Following feasibility and single-case reporting standards (CONSORT and SCRIBE), this was a non-blind, randomized, multiple-baseline, AB, design. Nineteen (19) young people with cerebral palsy (8-18 years old) completed the 4-week home-based intervention in France and Canada. Participant motivations, personalized practice goals, and relevance of the intervention to daily activities were discussed in a Solution Focused Coaching-style conversation pre-, post-intervention and during weekly check-ins. Participants controlled a video game by completing therapeutic gestures (wrist extension, pinching) detected via electromyography and inertial sensors on the forearm (Myo Armband and custom software). Process feasibility success criteria for recruitment response, completion and adherence rates, and frequency of technical issues were established a priori. Scientific feasibility, effect size estimates and variance were determined for Body Function outcome measures: active wrist extension, grip strength and Box and Blocks Test; and for Activities and Participation measures: Assisting Hand Assessment (AHA), Canadian Occupational Performance Measure (COPM) and Self-Reported Experiences of Activity Settings (SEAS). **Results:** Recruitment response (31%) and assessment completion (84%) rates were good and 74% of participants reached self-identified practice goals. As 17% of technical issues required external support to resolve, the intervention was graded as feasible with modifications. No adverse events were reported. Moderate effects were observed in Body Function measures (active wrist extension: SMD = 1.82, 95%CI = 0.85-2.78; Grip Strength: SMD = 0.63, 95%CI = 0.65-1.91; Box and Blocks: Hedge's $g = 0.58$, 95%CI = -0.11-1.27) and small-moderate effects in Activities and Participation measures (AHA: Hedge's $g = 0.29$, 95%CI = -0.39-0.97, COPM: $r = 0.60$, 95%CI = 0.13-

0.82, SEAS: $r = 0.24$, 95%CI = -0.25-0.61). Conclusion: A definitive RCT to investigate the effectiveness of this novel intervention is warranted. Combining SFC-style coaching with high-quality biofeedback may positively engage youth in home rehabilitation to complement traditional therapy. Trial registration: ClinicalTrials.gov, U.S. National Library of Medicine: NCT03677193.

PMID: [32569284](#)

15. Speech in Children With Cerebral Palsy

Cristina Mei, Sheena Reilly, Molly Bickerton, Fiona Mensah, Samantha Turner, Dhanooshini Kumaranayagam, Lindsay Pennington, Dinah Reddihough, Angela T Morgan

Dev Med Child Neurol. 2020 Jun 26. doi: 10.1111/dmcn.14592. Online ahead of print.

Aim: To examine the frequency, characteristics, and factors associated with speech delay and disorder in a community sample of children with cerebral palsy (CP). **Method:** Participants were 84 children (37 females, 47 males; aged between 4y 11mo-6y 6mo) with CP identified through a population-based registry. Speech and oromotor function were systematically evaluated to provide a differential diagnosis of articulation, phonological, and motor speech disorders. **Results:** In total, 82% (69/84) of participants had delayed or disordered speech production, including minimally verbal presentations ($n=20$). Verbal participants ($n=64$) presented with dysarthria (78%), articulation delay or disorder (54%), phonological delay or disorder (43%), features of childhood apraxia of speech (CAS) (17%), or mixed presentations across these conditions. Speech intelligibility was poorest in those with dysarthria and features of CAS. Speech delay or disorder in verbal participants was associated with language impairment ($p=0.002$) and reduced health-related quality of life ($p=0.04$) (Fisher's exact test). Poorer speech accuracy (i.e. lower percentage consonants correct) correlated with greater impairments in both language ($p<0.001$) and oromotor function ($p<0.001$) (Spearman's test). **Interpretation:** The speech profile of children with CP is characterized by impairment at multiple levels of speech production (phonetic, cognitive-linguistic, neuromuscular execution, and high-level planning/programming), highlighting the importance of a personalized differential diagnosis informing targeted treatment.

PMID: [32588921](#)

16. Measuring Speech Production Development in Children With Cerebral Palsy Between 6 and 8 Years of Age: Relationships Among Measures

Phoebe Natzke, Ashley Sakash, Tristan Mahr, Katherine C Hustad

Lang Speech Hear Serv Sch. 2020 Jun 23;1-15. doi: 10.1044/2020_LSHSS-19-00102. Online ahead of print.

Purpose: Accurate measurement of speech intelligibility is essential for children with speech production deficits, but wide variability exists in the measures and protocols used. The current study sought to examine relationships among measures of speech intelligibility and the capacity of different measures to capture change over time. **Method:** Forty-five children with cerebral palsy (CP) with and without speech motor impairment were observed at ages 6, 7, and 8 years. The speech performance of each child was rated using four measures at each time point: standardized articulation test scores, multiword intelligibility scores obtained from naïve listeners, parent ratings of intelligibility, and percent intelligible utterances obtained from language transcripts. We analyzed the correlations of measures within each age and within three different severity groups, and we analyzed how these measures changed year over year in each severity group. **Results:** For children with CP who have mild and moderate speech deficits, different measures of speech production were weakly associated, and for children with CP with severe speech impairment, these measures showed stronger associations. The four measures also differed in their ability to capture change over time. Finally, results from standardized assessments of articulation were not found to inform overall speech intelligibility for children with mild and moderate speech deficits. **Conclusions:** Results suggest that speech production is not fully described by any single clinical measure. In order to adequately describe functional speaking abilities and to capture change over time, multiple levels of measurement are required.

PMID: [32574125](#)

17. [Clinical Effect of Functional Chewing Training in Treatment of Oral Motor Dysfunction in Children With

Cerebral Palsy: A Prospective Randomized Controlled Clinical Trial] [Article in Chinese]

Qiong-Li Fan, Zhi-Feng Wu, Xiu-Mei Yu, Xiao-Yun Zeng, Li-Shuang Peng, Li-Sha Su, Yu-Ping Zhang

Randomized Controlled Trial Zhongguo Dang Dai Er Ke Za Zhi. 2020 Jun;22(6):567-572.

Objective: To study the effect of functional chewing training (FuCT) on masticatory function, the severity of tongue thrust, and the severity and frequency of drooling in children with cerebral palsy. **Methods:** A prospective study was performed for 48 children who were diagnosed with oral motor dysfunction from January 2019 to January 2020, and they were randomly divided into an FuCT group and an oral motor training group, with 24 children in each group. Both groups received FuCT or oral motor training for 12 weeks, and then they were evaluated in terms of the changes in the masticatory function, the severity of tongue thrust, and the severity and frequency of drooling. **Results:** There were no significant differences between the two groups in the masticatory function, the severity of tongue thrust, and the severity and frequency of drooling before treatment ($P>0.05$). After the 12-week training, the FuCT group showed significant improvements in the masticatory function and the severity of tongue thrust and drooling ($P<0.05$), but with no improvement in the frequency of drooling ($P>0.05$), while the oral motor training group had no improvements in the masticatory function, the severity of tongue thrust, and the severity and frequency of drooling ($P>0.05$). After the 12-week training, the FuCT group had more significantly improvements in the severity of tongue thrust and the severity and frequency of drooling than the oral motor training group ($P<0.05$). **Conclusions:** FuCT can effectively improve the masticatory function, the severity of tongue thrust, and the severity and frequency of drooling in children with cerebral palsy.

PMID: [32571453](#)**18. Factors Affecting the Relationship Between Adaptive Behavior and Challenging Behaviors in Individuals With Intellectual Disability and Co-Occurring Disorders**

Giulia Balboni, Gessica Rebecchini, Sandro Elisei, Marc J Tassé

Res Dev Disabil. 2020 Jun 22;104:103718. doi: 10.1016/j.ridd.2020.103718. Online ahead of print.

Previous studies have reported an inverse relationship between adaptive behavior and challenging behaviors in individuals with ID. However, it is unclear which characteristics might influence this relationship in individuals with ID and co-occurring conditions. We found a positive correlation between adaptive behavior (Vineland-II) and challenging behaviors (Nisonger Child Behavior Rating Form) in a study of 105 individuals who presented with mostly severe to profound ID and comorbid physical and mental health conditions. These results might be the consequence of the individual participant characteristics. Therefore, participants were separated out into two groups representing the top ($n = 24$) and bottom quartiles ($n = 28$) for presence of challenging behaviors. The participants with the highest levels of challenging behaviors had higher levels of adaptive behavior, higher frequency of intermittent explosive/conduct disorder, but lower frequency of epilepsy and cerebral palsy. All participants with the highest levels of challenging behaviors lived in an institutional setting; whereas, those with the lowest level of challenging behaviors lived in either an institutional setting or with their family. In participants with severe/profound ID and multiple co-occurring disorders, a minimum level of adaptive behavior seems to be necessary for the expression of challenging behaviors.

PMID: [32585440](#)**19. Six-month Follow-Up of a Mindfulness Yoga Program, MiYoga, on Attention, Executive Function, Behaviour and Physical Outcomes in Cerebral Palsy**

Catherine Mak, Koa Whittingham, Ross Cunnington, Mark Chatfield, Roslyn N Boyd

Disabil Rehabil. 2020 Jun 26;1-7. doi: 10.1080/09638288.2020.1783582. Online ahead of print.

Purpose: A randomised controlled trial (RCT) of a mindfulness-based yoga program, MiYoga, for cerebral palsy (CP) demonstrated improved attention in children and decreased mindfulness in parents post-intervention. This paper evaluates the retention of treatment effects at 6-months follow-up. **Methods:** 42 children with CP and their parents participated in a RCT with two groups MiYoga ($n = 21$) and Waitlist control group ($n = 21$). Waitlist control participants were offered MiYoga following the post-intervention assessment. 23 out of 42 child-parent dyads from both groups completed follow-up assessment 6-months

after completing MiYoga. This paper evaluates and reports data from both groups collapsed ($n = 23$; MiYoga $n = 11$; and waitlist control $n = 12$; 47.8% male; mean age = $9:10 \pm 2.4$ years) to assess retention from post-MiYoga to follow-up and pre-MiYoga to follow-up. The primary outcome was attention, measured by Conner's Continuous Performance Test II (CCPT). Secondary outcomes included child executive function, physical function, behaviour, quality of life, child and parent mindfulness, personal wellbeing, psychological wellbeing and parent-child relationship. Results: Paired t-tests showed no significant changes between post-MiYoga to follow-up and pre-MiYoga to follow-up for variables that showed an intervention effect immediately after MiYoga, namely, children's attention variables and parent's mindfulness. Paired t-tests showed that children's executive function and physical function and parent's wellbeing improved significantly from pre-MiYoga to 6-months follow-up which may potentially reflect sleeper or delayed effects of MiYoga. Conclusion: This study identified possible delayed or sleeper effects in children's executive function and physical function and parent's well-being. Implications for rehabilitation 6-month follow-up evidence for retention of effects of MiYoga on children's attention was inconsistent; therefore, booster sessions or continued practice of MiYoga as a lifestyle option are needed to maintain an effect on attention. Because MiYoga can be practised during daily activities, it may provide additional support for children with CP, complementing standard rehabilitation options. By embedding mindfulness in children and parents' daily activities, MiYoga, could provide families with accessible and time-efficient means of learning and practicing mindfulness.

PMID: [32589851](#)

20. Spatial Analysis of Cerebral Palsy in Children and Adolescents and Its Association With Health Vulnerability

Marcus Valerius Peixoto, Andreza Marques Duque, Allan Dantas Santos, Shirley Verônica Almeida Melo Lima, Társilla Pereira Gonçalves, Ana Paula de Souza Novais, Susana De Carvalho, Silvia Maria Voci, Karina Conceicao Gomes Machado De Araujo, Marco Antônio Prado Nunes

Geospat Health. 2020 Jun 17;15(1). doi: 10.4081/gh.2020.817.

Cerebral Palsy (CP) is commonly associated with low socioeconomic status. Use of spatial statistics and a Geographic Information Systems (GIS) are scarce and may contribute to the understanding of CP in a social context. To that end a spatial analysis of CP in children and adolescents was performed to analyze the association of CP with levels of vulnerability in a city (Aracaju, Sergipe) in north-eastern Brazil. In addition, an ecological study was conducted with data obtained from a populationbased survey and secondary data. Exploratory spatial data analysis and linear regression were used. A total of 288 CP cases were identified, with a prevalence of 1.65/1,000 and differences among city neighbourhoods ranging from 0-4/1,000. The mean age of cases studied was 9 years 1 month, with a standard deviation of 5 years 2 months. Most study subjects with cerebral palsy (163) were male (56.4%). The distribution of CP in the study population was not homogeneous throughout the territory. Some areas had clusters, with more cases associated with areas of high vulnerability. Spatial data analysis using GIS was useful to gain an epidemiological understanding of CP distribution that can guide decisionmaking with respect to production, distribution, and regulation of health goods as well as services at the local level.

PMID: [32575966](#)

21. Efficacy of Interventions to Improve Psychological Adjustment for Parents of Infants With or at Risk of Neurodevelopmental Disability: A Systematic Review

Corrine Dickinson, Koa Whittingham, Jeanie Sheffield, Jane Wotherspoon, Roslyn N Boyd

Infant Ment Health J. 2020 Jun 25. doi: 10.1002/imhj.21871. Online ahead of print.

Background: Supportive and targeted interventions for families are required to optimize parental adjustment and the parent-infant relationship in line with earlier diagnosis of neurodevelopmental risk for infants. Aims: The purpose of this systematic review was to determine the efficacy of interventions in improving psychological adjustment and well-being for parents who have an infant diagnosed with or at risk of neurodevelopmental disability. Methods: The Cochrane Review Group search strategy was followed with search of The Cochrane Central Register of Controlled Trials, PubMed, CINAHL, PsycINFO, and Embase between July and December 2017. Methodological quality of included articles was assessed using the Physiotherapy Evidence Database (PEDro) Scale by two independent reviewers. Results: Twelve studies met the inclusion criteria. A small number of high-quality trials demonstrated moderate to large effectiveness of reducing adverse parent psychological symptoms of trauma and stress. Significant improvements in depression and anxiety symptoms emerged at longer-term (6 months to 8 years) follow-up postinterventions. Conclusions: There is promising support for the effectiveness of some interventions to reduce maladaptive psychological symptoms in parents with infants diagnosed at risk of neurodevelopmental disability. Further

quality RCTs of psychological interventions addressing broader neurodevelopmental risk conditions for infants are required.

PMID: [32583882](#)

22. Engagement in Household Chores in Youth With Chronic Conditions: Health Care Transition Implications

Jordan Richards, Meaghan Nazareth, Miranda A L van Tilburg, Nina Jain, Laura Hart, Richard A Faldowski, Chad Coltrane, Stephen R Hooper, Maria Ferris, Eniko Rak

OTJR (Thorofare N J). 2020 Jun 24;1539449220928142. doi: 10.1177/1539449220928142. Online ahead of print.

This study examined associations between chores engagement, self-management, and transition readiness in youth with chronic conditions. Youths with various chronic conditions attending a therapeutic camp, and their parents participated. Responses of 165 campers and their parents were analyzed (mean camper age 12.3 ± 2.6 years, 47.9% males, 79.4% White). The most common diagnoses were diabetes, spina bifida, cerebral palsy, and sickle cell anemia. Youth who completed chores manifested higher overall health care transition readiness ($\beta = 5.17$, $p = .026$) and better communication with providers ($\beta = 2.98$, $p = .006$) than youth who completed no chores. Higher chores frequency was not more predictive of higher health care transition readiness scores above and beyond the effects of having chores at all. These results suggest that responsible health care behaviors are related to similar actions in other areas of life. Assignment of chores may promote self-management and health care transition readiness in youth with chronic conditions.

PMID: [32578506](#)

23. A Pragmatic Approach to Botulinum Toxin Safety

Joshua A Vova, Enoch Leung

J Pediatr Rehabil Med. 2020 Jun 12. doi: 10.3233/PRM-200716. Online ahead of print.

PMID: [32568125](#)

24. Facts and De Facto Treatment of Spasticity

Heakyung Kim, Ray Stanford

J Pediatr Rehabil Med. 2020 Jun 12. doi: 10.3233/PRM-200737. Online ahead of print.

Recent studies have generally shown favorable outcomes for the use of botulinum toxin (BoNT) injections for the treatment of lower extremity spasticity in children with cerebral palsy. The randomized controlled trials and placebo trials are well described although even those and other studies show high variability in methodology for use of BoNT. This raises questions about which strategies are the most effective. In order to hone the technique, the aim of this review is to discuss these specific parameters: toxin type, dosing, series of injections, localization method, age, number of muscles, and troubleshooting poor outcomes.

PMID: [32568127](#)

25. Trends in Publications About Cerebral Palsy 1990 to 2020

Meghan A Klawonn, Karl Klamar, Margaret A Turk

J Pediatr Rehabil Med. 2020 Jun 12. doi: 10.3233/PRM-200697. Online ahead of print.

Cerebral palsy (CP) is associated with complex health care needs and, although improved, a continued shortened life expectancy. In order to quantify and understand advances in the diagnosis and management of CP, systematic literature searches of key word groupings in the PubMed database were completed and revealed a recent increased incidence of publications focusing on quality of life, physical activity, exercise, and treatment options. Our bibliometric exploration revealed growing emphasis on function, performance, aging, and health compared to earlier studies when diagnostic features and brain pathology dominated research. Our findings highlight the transition from diagnosis and identification to management of specific conditions and providing guidance for the continuum of needs our patients experience over the course of a lifetime. The field must be prepared to advance our understanding of best practices and implement evidence-based interventions and management options.

PMID: [32568124](#)

26. Utilizing Registry Data to Identify Children With Cerebral Palsy Previously Enrolled in the Magnesium Sulfate Randomized Clinical Trial

Ira Adams-Chapman

Dev Med Child Neurol. 2020 Jun 20. doi: 10.1111/dmcn.14600. Online ahead of print.

PMID: [32562498](#)

27. Congenital Anomalies in Children With Pre- Or Perinatally Acquired Cerebral Palsy: An International Data Linkage Study

Shona Goldsmith, Sarah Mcintyre, Guro L Andersen, Catherine Gibson, Kate Himmelmann, Eve Blair, Nadia Badawi, Hayley Smithers-Sheedy, Ester Garne, Comprehensive CA-CP

Dev Med Child Neurol. 2020 Jun 24. doi: 10.1111/dmcn.14602. Online ahead of print.

Aim: To describe the frequency and types of major congenital anomalies present in children with pre- or perinatally acquired cerebral palsy (CP), and compare clinical outcomes for children with and without anomalies. **Method:** This multi-centre total population collaborative study between Surveillance of Cerebral Palsy in Europe, Australian Cerebral Palsy Register, and European Surveillance of Congenital Anomalies (EUROCAT) involved six European and three Australian regions. Data were linked between each region's CP and congenital anomaly register for children born between 1991 and 2009, and then pooled. Children were classified into mutually exclusive categories based on type of anomaly. Proportions of children with congenital anomalies were calculated, and clinical outcomes compared between children with and without anomalies. **Results:** Of 8201 children with CP, 22.8% (95% confidence interval [CI] 21.9, 23.8) had a major congenital anomaly. Isolated cerebral anomalies were most common (45.2%), with a further 8.6% having both cerebral and non-cerebral anomalies. Cardiac anomalies only were described in 10.5% of children and anomalies associated with syndromes were also reported: genetic (8.0%), chromosomal (5.7%), and teratogenic (3.0%). Clinical outcomes were more severe for children with CP and congenital anomalies, particularly cerebral anomalies. **Interpretation:** This large, international study reports major congenital anomalies in nearly one-quarter of children with pre- or perinatally acquired CP. Future research must focus on aetiological pathways to CP that include specific patterns of congenital anomalies.

PMID: [32578204](#)

28. Efficacy of Cannabinoids for Treating Paediatric Spasticity in Cerebral Palsy or Traumatic Brain Injury: What Is the Evidence?

Suzanne Nielsen, Wayne Hall

Dev Med Child Neurol. 2020 Jun 20. doi: 10.1111/dmcn.14606. Online ahead of print.

PMID: [32562496](#)

29. Expanding the Phenotype of COL4A1-related disorders-Four Novel Variants

Naoto Nishimura, Tatsuro Kumaki, Hiroaki Murakami, Yumi Enomoto, Yoshinori Tsurusaki, Megumi Tsuji, Yu Tsuyusaki, Tomohide Goto, Noriko Aida, Kenji Kurosawa

Brain Dev. 2020 Jun 18;S0387-7604(20)30150-9. doi: 10.1016/j.braindev.2020.05.009. Online ahead of print.

Objective: COL4A1 variant causes severe central nervous system (CNS) anomalies, including hydranencephaly. However, the pathogenic mechanism underlying the COL4A1 phenotype remains unclear. Here, we report de novo COL4A1 variants in four Japanese patients with typical or rare CNS involvement and exhibiting diverse phenotypes. **Methods:** We identified and enrolled four patients with white matter abnormalities and cerebral structural defects suggestive of cerebrovascular disease. Genetic analysis was performed using panel sequencing. **Results:** All the patients were perinatally asymptomatic during the infantile period but exhibited developmental delay and growth retardation later. All the patients exhibited CNS symptoms, including psychomotor disability, spastic paralysis, and epilepsy. Brain magnetic resonance imaging revealed hydranencephaly (n = 1), ventriculomegaly (n = 4) associated with cerebral hemorrhage, and atretic encephalocele (n = 1). Three patients had developed congenital cataract, while two had hematuria. We identified two COL4A1 missense variants [exon32:c.2555G > A p.(Gly852Asp), exon40:c.3407G > A p.(Gly1136Asp)] and two in frame variants [exon32:c.2603_2609delinsATCCTGA p.(Ala868_Gly870delinsAspProGlu), exon36:c.3054delinsTGTAGAT p.(Leu1018delinsPheValAsp)]. The in frame variants were associated with severe CNS anomalies, hydranencephaly, and severe ventriculomegaly. Atretic encephalocele has never been reported in individuals with COL4A1 variants. **Conclusions:** Our findings suggest that COL4A1 variants cause variable CNS symptoms. Association between clinical phenotypes and each COL4A1 variant would clarify their underlying etiologies.

PMID: [32565002](#)

30. Femoral Anteversion: Significance and Measurement

Matteo Scorcelletti, Neil D Reeves, Jörn Rittweger, Alex Ireland

Review J Anat. 2020 Jun 24. doi: 10.1111/joa.13249. Online ahead of print.

Femoral neck anteversion (FNA) is the angle between the femoral neck and femoral shaft, indicating the degree of torsion of the femur. Differences in FNA affect the biomechanics of the hip, through alterations in factors such as moment arm lengths and joint loading. Altered gait associated with differences in FNA may also contribute to the development of a wide range of skeletal disorders including osteoarthritis. FNA varies by up to 30° within apparently healthy adults. FNA increases substantially during gestation and thereafter decreases steadily until maturity. There is some evidence of a further decrease at a much lower rate during adulthood into old age, but the mechanisms behind it have never been studied. Development of FNA appears to be strongly influenced by mechanical forces experienced during everyday movements. This is evidenced by large differences in FNA in groups where movement is impaired, such as children born breech or individuals with neuromuscular conditions such as cerebral palsy. Several methods can be used to assess FNA, which may yield different values by up to 20° in the same participant. While MRI and CT are used clinically, limitations such as their cost, scanning time and exposure to ionising radiation limit their applicability in longitudinal and population studies, particularly in children. More broadly, applicable measures such as ultrasound and functional tests exist, but they are limited by poor reliability and validity. These issues highlight the need for a valid and reliable universally accepted method. Treatment for clinically problematic FNA is usually de-rotational osteotomy; passive, non-operative methods do not have any effect. Despite observational evidence for the effects of physical activity on FNA development, the efficacy of targeted physical activity remains unexplored. The aim of this review is to describe the biomechanical and clinical consequences of FNA, factors influencing FNA and the strengths and weaknesses of different methods used to assess FNA.

PMID: [32579722](#)

31. Classics in Neuroimaging: Development of Positron Emission Tomography Tracers for Imaging the GABAergic Pathway

Emily Murrell, Jonathan M Pham, Alexandra R Sowa, Allen F Brooks, Michael R Kilbourn, Peter J H Scott, Neil Vasdev

ACS Chem Neurosci. 2020 Jun 24. doi: 10.1021/acchemneuro.0c00343. Online ahead of print.

Advances in drug discovery and diverse radiochemical methodologies have led to the discovery of novel positron emission tomography (PET) radiotracers used to image the GABAergic system, shaping our fundamental understanding of a variety of brain health illnesses, including epilepsy, stroke, cerebral palsy, schizophrenia, autism, Alzheimer's disease, and addictions. In this Viewpoint, we review the state-of-the-art of PET imaging with radiotracers that target the GABAA-benzodiazepine receptor complex, challenges and opportunities for imaging GABAB receptors and GABA transporters, and highlight an ongoing need to develop more sensitive radiotracers for imaging GABA release in the central nervous system.

PMID: [32578977](#)

32. Association of Chorioamnionitis With Cerebral Palsy at Two Years After Spontaneous Very Preterm Birth: The EPIPAGE-2 Cohort Study

Emeline Maisonneuve, Elsa Lorthe, Héloïse Torchin, Pierre Delorme, Louise Devisme, Laurence Foix L'Hélias, Stéphane Marret, Damien Subtil, Florence Bodeau-Livinec, Véronique Pierrat, Loïc Sentilhes, François Goffinet, Pierre-Yves Ancel, Gilles Kayem, EPIPAGE-2 Obstetric writing group

J Pediatr. 2020 Jul;222:71-78.e6. doi: 10.1016/j.jpeds.2020.03.021.

Objective: To assess whether chorioamnionitis is associated with cerebral palsy (CP) or death at 2 years' corrected age in infants born before 32 weeks of gestation after spontaneous birth. **Study design:** EPIPAGE-2 is a national, prospective, population-based cohort study of children born preterm in France in 2011; recruitment periods varied by gestational age. This analysis includes infants born alive after preterm labor or preterm premature rupture of membranes from 240/7 to 316/7 weeks of gestation. We compared the outcomes of CP, death at 2 years' corrected age, and "CP or death at age 2" according to the presence of either clinical chorioamnionitis or histologic chorioamnionitis. All percentages were weighted by the duration of the recruitment period. **Results:** Among 2252 infants born alive spontaneously before 32 weeks of gestation, 116 (5.2%) were exposed to clinical chorioamnionitis. Among 1470 with placental examination data available, 639 (43.5%) had histologic chorioamnionitis. In total, 346 infants died before 2 years and 1586 (83.2% of the survivors) were evaluated for CP at age 2 years. CP rates were 11.1% with and 5.0% without clinical chorioamnionitis ($P = .03$) and 6.1% with and 5.3% without histologic chorioamnionitis ($P = .49$). After adjustment for confounding factors, CP risk rose with clinical chorioamnionitis (aOR 2.13, 95% CI 1.12-4.05) but not histologic chorioamnionitis (aOR 1.21, 95% 0.75-1.93). Neither form was associated with the composite outcome "CP or death at age 2." **Conclusions:** Among infants very preterm born spontaneously, the risk of CP at a corrected age of 2 years was associated with exposure to clinical chorioamnionitis but not histologic chorioamnionitis.

PMID: [32586536](#)

33. Novel Dominant KCNQ2 Exon 7 Partial In-Frame Duplication in a Complex Epileptic and Neurodevelopmental Delay Syndrome

Pedro A Lazo, Juan L García, Paulino Gómez-Puertas, Íñigo Marcos-Alcalde, Cesar Arjona, Alvaro Villarroel, Rogelio González-Sarmiento, Carmen Fons

Case Reports Int J Mol Sci. 2020 Jun 23;21(12):E4447. doi: 10.3390/ijms21124447.

Complex neurodevelopmental syndromes frequently have an unknown etiology, in which genetic factors play a pathogenic role. This study utilizes whole-exome sequencing (WES) to examine four members of a family with a son presenting, since birth, with epileptic-like crises, combined with cerebral palsy, severe neuromotor and developmental delay, dystonic tetraparesis, axonal motor affectation, and hyper-excitability of unknown origin. The WES study detected within the patient a de novo heterozygous in-frame duplication of thirty-six nucleotides within exon 7 of the human KCNQ2 gene. This insertion duplicates the first twelve amino acids of the calmodulin binding site I. Molecular dynamics simulations of this KCNQ2 peptide duplication, modelled on the 3D structure of the KCNQ2 protein, suggest that the duplication may lead to the dysregulation of calcium inhibition of this protein function.

PMID: [32585800](#)

34. Epigenetic Marks at the Ribosomal DNA Promoter in Skeletal Muscle Are Negatively Associated With Degree of Impairment in Cerebral Palsy

Ferdinand von Walden, Rodrigo Fernandez-Gonzalo, Jessica Pingel, John McCarthy, Per Stål, Eva Pontén

Front Pediatr. 2020 Jun 3;8:236. doi: 10.3389/fped.2020.00236. eCollection 2020.

Introduction: Cerebral palsy (CP) is the most common motor impairment in children. Skeletal muscles in individuals with CP are typically weak, thin, and stiff. Whether epigenetic changes at the ribosomal DNA (rDNA) promoter are involved in this dysregulation remains unknown. **Methods:** Skeletal muscle samples were collected from 19 children with CP and 10 typically developed (TD) control children. Methylation of the rDNA promoter was analyzed using the Agena EpiTyper Mass array and gene expression by qRT-PCR. **Results:** Biceps brachii muscle ribosome biogenesis was suppressed in CP as compared to TD. Average methylation of the rDNA promoter was not different between CP and TD but negatively correlated to elbow flexor contracture in the CP group. **Discussions:** We observed a negative correlation between rDNA promoter methylation and degree of muscle contracture in the CP group. Children with CP with more severe motor impairment had less methylation of the rDNA promoter compared to less affected children. This finding suggests the importance of neural input and voluntary muscle movements for promoter methylation to occur in the biceps muscle.

PMID: [32582584](#)

35. MRI Features in a Rat Model of H-ABC Tubulinopathy

Angeles Garduno-Robles, Milvia Alata, Valeria Piazza, Carmen Cortes, Jose R Eguibar, Sergio Pantano, Victor H Hernandez

Front Neurosci. 2020 Jun 3;14:555. doi: 10.3389/fnins.2020.00555. eCollection 2020.

Tubulinopathies are a group of recently described diseases characterized by mutations in the tubulin genes. Mutations in TUBB4A produce diseases such as dystonia type 4 (DYT4) and hypomyelination with atrophy of the basal ganglia and cerebellum (H-ABC), which are clinically diagnosed by magnetic resonance imaging (MRI). We propose the taiep rat as the first animal model for tubulinopathies. The spontaneous mutant suffers from a syndrome related to a central leukodystrophy and characterized by tremor, ataxia, immobility, epilepsy, and paralysis. The pathological signs presented by these rats and the morphological changes we found by our longitudinal MRI study are similar to those of patients with mutations in TUBB4A. The diffuse atrophy we found in brain, cerebellum and spinal cord is related to the changes detectable in many human tubulinopathies and in particular in H-ABC patients, where myelin degeneration at the level of putamen and cerebellum is a clinical trademark of the disease. We performed Tubb4a exon analysis to corroborate the genetic defect and formulated hypotheses about the effect of amino acid 302 change on protein physiology. Optical microscopy of taiep rat cerebella and spinal cord confirmed the optical density loss in white matter associated with myelin loss, despite the persistence of neural fibers.

PMID: [32581692](#)

Prevention and Cure

36. Multiple Doses of Umbilical Cord Blood Cells Improve Long-Term Brain Injury in the Neonatal Rat

Tayla R Penny, Yen Pham, Amy E Sutherland, Jamie G Mihelakis, Joohyung Lee, Graham Jenkin, Michael C Fahey, Suzanne L Miller, Courtney A McDonald

Brain Res. 2020 Jun 22;147001. doi: 10.1016/j.brainres.2020.147001. Online ahead of print.

Background: Hypoxic ischemic (HI) insults during pregnancy and birth can result in neurodevelopmental disorders, such as cerebral palsy. We have previously shown that a single dose of umbilical cord blood (UCB) cells is effective at reducing short-term neuroinflammation and improves short and long-term behavioural outcomes in rat pups. A single dose of UCB was not able to modulate long-term neuroinflammation or brain tissue loss. In this study we examined whether multiple doses of UCB can modulate neuroinflammation, decrease cerebral tissue damage and improve behavioural outcomes when followed up long-term. **Methods:** HI injury was induced in postnatal day 10 (PND10) rat pups using the Rice-Vannucci method of carotid artery

ligation. Pups received either 1 dose (PND11), or 3 doses (PND11, 13, 20) of UCB cells. Rats were followed with behavioural testing, to assess both motor and cognitive outcomes. On PND50, brains were collected for analysis. Results: HI brain injury in rat pups caused significant behavioural deficits. These deficits were significantly improved by multiple doses of UCB. HI injury resulted in a significant decrease in brain weight and left hemisphere tissue, which was improved by multiple doses of UCB. HI resulted in increased cerebral apoptosis, loss of neurons and upregulation of activated microglia. Multiple doses of UCB modulated these neuropathologies. A single dose of UCB at PND11 did not improve behavioural or neuropathological outcomes. Conclusions: Treatment with repeated doses of UCB is more effective than a single dose for reducing tissue damage, improving brain pathology and restoring behavioural deficits following perinatal brain injury.

PMID: [32585139](#)