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## Interventions and Management

### **1. A new child-friendly 3D bimanual protocol to assess upper limb movement in children with unilateral cerebral palsy: Development and validation**

Marine Cacioppo, Antoine Marin, H el ene Rauscent, Estelle Le Pabic, Florence Gaillard, Sylvain Brochard, Ronan Garlandezec, Armel Cretual, Isabelle Bonan

J Electromyogr Kinesiol. 2020 Oct 10;55:102481. doi: 10.1016/j.jelekin.2020.102481. Online ahead of print.

Unilateral cerebral palsy (uCP) causes upper limb movement disorders that impact on daily activities, especially in bimanual condition. However, a few studies have proposed bimanual tasks for 3D motion analysis. The aim of this study was to validate the new version of a child-friendly, 3D, bimanual protocol for the measurement of joint angles and movement quality variables. Twenty children with uCP and 20 typically developing children (TDC) performed the five-task protocol integrated into a game scenario. Each task specifically targeted one or two upper limb degrees of freedom. Joint angles, smoothness and trajectory straightness were calculated. Elbow extension, supination, wrist extension and adduction amplitudes were reduced; hand trajectories were less smooth and straight in children with uCP compared to TDC. Correlations between the performance-based score and kinematic variables were strong. High within and between-session reliability was found for most joint angle variables and lower reliability was found for smoothness and straightness in most tasks. The results therefore demonstrated the validity and reliability of the new protocol for the objective assessment of bimanual function in children with uCP. The evaluation of both joint angles and movement quality variables should increase understanding of pathological movement patterns and help clinicians to optimize treatment. ClinicalTrials.gov identifier: NCT03888443.

PMID: [33091791](#)

### **2. Effects of Virtual Reality-Based Rehabilitation on Upper Extremity Function among Children with Cerebral Palsy**

Hyun Jung Chang, Kyo Hun Ku, Young Sook Park, Jin Gee Park, Eun Sol Cho, Jae Sam Seo, Chang Woo Kim, Se Hwi O

Healthcare (Basel). 2020 Oct 10;8(4):E391. doi: 10.3390/healthcare8040391.

Background: Deterioration in upper extremity function has been a common problem among children with cerebral palsy (CP). The present study evaluated the effects of virtual reality (VR)-based rehabilitation combined with conventional occupational therapy (COT) on upper extremity function and caregiver assistance among children with CP. Methods: Medical records of 17 children with CP who regularly participated in a rehabilitation program at Samsung Changwon Hospital were retrospectively reviewed. Ten children received VR-based rehabilitation, which utilized RAPAEEL Smart Kids and video games combined with COT. Seven children received COT alone, which was provided by a trained occupational therapist and focused on their upper extremities. Clinical outcomes were determined using the Quality of Upper Extremity Skills Test (QUEST) and Pediatric Evaluation of Disability Inventory (PEDI), which were administered before and 8 weeks after the first intervention session. Results: The smart glove (SG) group showed significant improvements in all QUEST domains and five PEDI

domains ( $p < 0.05$ ), whereas the COT group showed a significant change only in total QUEST scores. A comparison between both groups revealed that the SG group had significantly greater improvements in five QUEST domains and two PEDI domains ( $p < 0.05$ ). Conclusions: Our results suggest that VR-based rehabilitation combined with COT may improve the upper extremity functions and decrease caregiver burden among children with CP.

PMID: [33050396](#)

### 3. Functional near-infrared spectroscopy to assess sensorimotor cortical activity during hand squeezing and ankle dorsiflexion in individuals with and without bilateral and unilateral cerebral palsy

Theresa Sukal-Moulton, Ana C de Campos, Katharine E Alter, Diane L Damiano

Neurophotonics. 2020 Oct;7(4):045001. doi: 10.1117/1.NPh.7.4.045001. Epub 2020 Oct 6.

**Significance:** Our study is the first comparison of brain activation patterns during motor tasks across unilateral cerebral palsy (UCP), bilateral cerebral palsy (BCP), and typical development (TD) to elucidate neural mechanisms and inform rehabilitation strategies. **Aim:** Cortical activation patterns were compared for distal upper and lower extremity tasks in UCP, BCP, and TD using functional near-infrared spectroscopy (fNIRS) and related to functional severity. **Approach:** Individuals with UCP ( $n=10$ ,  $n=10$ ,  $18.8 \pm 6.8$  years,  $18.8 \pm 6.8$  years), BCP ( $n=14$ ,  $n=14$ ,  $17.5 \pm 9.6$  years,  $17.5 \pm 9.6$  years), and TD ( $n=16$ ,  $n=16$ ,  $17.3 \pm 9.1$  years,  $17.3 \pm 9.1$  years) participated in this cross-sectional cohort study. The fNIRS was used to noninvasively monitor the hemodynamic response to task-related cortical activation. The block design involved repetitive nondominant hand squeezing and ankle dorsiflexion. **Results:** Individuals with UCP demonstrated the highest levels of activation for the squeeze task (UCP > BCP, UCP > TD,  $q=0.049$ ,  $q=0.049$ ; BCP > TD, BCP > TD,  $q < 0.001$ ,  $q < 0.001$ ; and UCP > TD, UCP > TD,  $q=0.001$ ,  $q=0.001$ ) and more activity in the ipsilateral versus contralateral hemisphere. Individuals with BCP showed the highest levels of cortical activation in the dorsiflexion task (BCP > UCP, BCP > TD,  $q < 0.001$ ,  $q < 0.001$ ; BCP > TD, BCP > TD). **Conclusions:** Grouping by CP subtype and manual function or mobility level demonstrated significant differences from TD, even for individuals with the mildest forms of CP. Hemispheric activation patterns showed hypothesized but nonsignificant trends.

PMID: [33062800](#)

### 4. A long-term follow-up study of spinal abnormalities and pain in adults with cerebral palsy and spastic diplegia more than 25 years after selective dorsal rhizotomy

Berendina E Veerbeek, Robert P Lamberts, A Graham Fieggen, Ncedile Mankahla, Richard V P de Villiers, Elsabe Botha, Nelleke G Langerak

J Neurosurg Spine. 2020 Oct 16;1-8. doi: 10.3171/2020.6.SPINE20751. Online ahead of print.

**Objective:** The main purpose of selective dorsal rhizotomy (SDR) is to reduce spasticity in the lower extremities of children diagnosed with cerebral palsy (CP) and spastic diplegia. The potential for developing spinal abnormalities and pain is a concern, especially in the aging CP population. Therefore, the aim of this study was to evaluate spinal abnormalities, level of pain, and disability (due to back or leg pain) in adults with CP, and associations with participant characteristics, more than 25 years after SDR. **Methods:** This is a 9-year follow-up study with data collection conducted in 2008 and 2017. Radiographs were assessed for the degree of scoliosis, thoracic kyphosis and lumbar lordosis curvatures, and prevalence of spondylolysis and spondylolisthesis, while level of pain and disability was determined with a self-developed questionnaire and the Oswestry Disability Index (ODI) questionnaire, respectively. **Results:** Twenty-five participants were included (15 males; median age 35.9 years, IQR 34.3-41.5 years), with a follow-up time after SDR ranging from 25 to 35 years. No clinically relevant changes were found for spinal curvatures, spondylolysis and spondylolisthesis, perceived pain frequency, and ODI scores between 2008 and 2017. While the prevalence of spondylolysis was 44%, spondylolisthesis was found in 20% (of whom 15% were grade I and 5% grade II), lumbar hyperlordosis was found in 32%, thoracic hyperkyphosis in 4%, and scoliosis in 20%. The Cobb angle was  $< 25^\circ$ , and no patient required surgery for scoliosis. In addition, the low back was reported as the most common site of pain, with 28% of the adults with CP having daily pain. This resulted in 80% of the cohort indicating none or minimal disability due to pain based on the ODI. The only correlation found was between hyperkyphosis and female gender. **Conclusions:** At follow-up more than 25 years after SDR, no progression in spinal abnormalities, level of pain, and disability was found when compared with findings 15 years after SDR. The prevalence of scoliosis, thoracic hyperkyphosis, and lumbar hyperlordosis was within the range reported for adults with CP, while spondylolysis and spondylolisthesis occurred more often than would be expected. It is difficult, however, to establish the role of SDR in this finding, given the limited data on the natural history of CP. Despite the encouraging outcome of this long-term follow-up study after SDR, it is important to continue

monitoring adults with CP during the aging process.

PMID: [33065536](#)

### 5. Risk Factors for Proximal Junctional Kyphosis Following Surgical Deformity Correction in Pediatric Neuromuscular Scoliosis

Brandon J Toll, Shashank V Gandhi, Amir Amanullah, Amer F Samdani, M Burhan Janjua, Qingwu Kong, Joshua M Pahys, Steven W Hwang

Spine (Phila Pa 1976). 2020 Oct 15. doi: 10.1097/BRS.0000000000003755. Online ahead of print.

Study design: Single-center retrospective cohort analysis OBJECTIVE.: To evaluate risk factors associated with the development of proximal junctional kyphosis (PJK) in pediatric neuromuscular scoliosis. Summary of background data: PJK is a common cause of reoperation in adult deformity but has been less well reported in pediatric neuromuscular scoliosis. Methods: 60 consecutive pediatric patients underwent spinal fusion for neuromuscular scoliosis with a minimum 2-year follow-up. PJK was defined as  $> 10^\circ$  increase between the inferior end plate of the upper instrumented vertebra (UIV) and the superior end plate of the vertebra two segments above. Regression analyses as well as binary correlational models and Student's t-tests were employed for further statistical analysis assessing variables of primary and compensatory curve magnitudes, thoracic kyphosis, proximal kyphosis, lumbar lordosis, pelvic obliquity, shoulder imbalance, Risser classification, and sagittal profile. Results: The present cohort consisted of 29 boys and 31 girls with a mean age at surgery of  $14 \pm 2.7$  years. The most prevalent diagnoses were spinal cord injury (23%) and cerebral palsy (20%). Analysis reflected an overall radiographic PJK rate of 27% ( $n = 16$ ) and a proximal junctional failure rate of 7% ( $n = 4$ ). No significant association was identified with previously suggested risk factors such as extent of rostral fixation ( $p = 0.750$ ), rod metal type ( $p = 0.776$ ), laminar hooks ( $p = 0.654$ ), implant density ( $p = 0.386$ ), non-ambulatory functional status ( $p = 0.254$ ), or pelvic fixation ( $p = 0.746$ ). Significant risk factors for development of PJK included perioperative use of halo gravity traction (38%,  $p = 0.029$ ), greater postoperative C2 sagittal translation ( $p = 0.030$ ), decreased proximal kyphosis preoperatively ( $p = 0.002$ ), and loss of correction of primary curve magnitude at follow-up ( $p = 0.047$ ). Increase in lumbar lordosis from post-op to last follow-up trended towards significance ( $p = 0.055$ ). Conclusion: 27% of patients with NMS developed PJK, and 7% had revision surgery. Those treated with halo gravity traction or with greater postoperative C2 sagittal translation, loss of primary curve correction, and smaller preoperative proximal kyphosis had the greatest risk of developing PJK. Level of evidence: 4.

PMID: [33065694](#)

### 6. The efficacy of appropriate paper-based technology for Kenyan children with cerebral palsy

Catherine Barton, John Buckley, Pauline Samia, Fiona Williams, Suzan R Taylor, Rachel Lindoewood

Disabil Rehabil Assist Technol. 2020 Oct 19;1-11. doi: 10.1080/17483107.2020.1830442. Online ahead of print.

Purpose: Appropriate paper-based technology (APT) is used to provide postural support for children with cerebral palsy (CP) in low-resourced settings. This pilot study aimed to evaluate the impact of APT on the children's and families' lives. Materials and methods: A convenience sample of children with CP and their families participated. Inclusion was based on the Gross Motor Function Classification System levels IV and V. APT seating or standing frames were provided for six months. A mixed methods impact of APT devices on the children and families included the Family Impact Assistive Technology Scale for Adaptive Seating (FIATS-AS); the Child Engagement in Daily Life (CEDL) questionnaire; and a qualitative assessment from diary/log and semi-structured interviews. Results: Ten children (median 3 years, range 9 months to 7 years). Baseline to follow-up median (IQR) FIATS-AS were: 22.7 (9.3) and 30.3 (10.2), respectively ( $p = .002$ ). Similarly mean (SD) CEDL scores for "frequency" changed from 30.5 (13.2) to 42.08 (5.96) ( $p = .021$ ) and children's enjoyment scores from 2.23 (0.93) to 2.91 (0.79) ( $p = .019$ ). CEDL questionnaire for self-care was not discriminatory; seven families scored zero at both baseline and 6 months. Qualitative interviews revealed three key findings; that APT improved functional ability, involvement/interaction in daily-life situations, and a reduced family burden of care. Conclusions: APT devices used in Kenyan children with non-ambulant CP had a meaningful positive effect on both the children's and their families' lives. Implications for rehabilitation Assistive devices are often unobtainable for children with cerebral palsy (CP) in low-income countries. APT is a low cost and sustainable solution to make seating and standing devices for disabled children in Kenya. The regular use of a postural support device enhanced the children's motor skills, ability to function and participate in everyday activities, reduced the burden of care for the families and promoted the children's social interaction. The postural support devices were highly valued and utilised by the children and families in this study.

PMID: [33075236](#)

### **7. Peri-operative Botulinum Neurotoxin injection to improve outcomes of surgeries on spastic limbs: A systematic review**

Sepehr Saeidiborojeni, Patricia Branco Mills, Rajiv Reebye, Heather Finlayson

Toxicon. 2020 Oct 10;188:48-54. doi: 10.1016/j.toxicon.2020.10.005. Online ahead of print.

Our objective was to systematically review literature regarding the rationale and current evidence for peri-operative Botulinum Neurotoxin (BoNT) injection to improve outcomes of surgeries on spastic limbs. We conducted a systematic search of databases MEDLINE, EMBASE, and Cochrane Central Register of Controlled until March 2020, using the PRISMA guidelines. After assessing all titles and abstracts against inclusion criteria, full texts were reviewed for studies of potential interest. The inclusion criteria were studies on humans with any study design, published in all languages. Participants had to have underlying limb spasticity and be scheduled to undergo surgery on one or more spastic limb(s). BoNT had to be administered peri-operatively to improve surgical outcomes and not solely for the purpose of alleviating spasticity. The risk of bias was evaluated using the Physiotherapy Evidence Database (PEDro) scoring system for randomized controlled trials (RCTs) and the Downs and Black tool for RCTs and non-randomized trials. Further, the level of evidence was evaluated using a five-level scale (simplified form of Sackett). Five studies met our inclusion criteria comprising a total of 90 participants, of both pediatric and adult age groups, with underlying limb spasticity, who received BoNT perioperatively to improve outcomes of the surgeries performed on spastic limbs. Interventions were intramuscular BoNT injection prior to, at the time of, or after surgery on a spastic limb for the purpose of improving surgical outcomes, and not solely for alleviating muscle spasticity. Outcome measures were surgical success/failure, post-operative pain and analgesic use, sleep quality, adverse events, spasticity control e.g. Modified Ashworth Scale. Our literature search yielded 5 articles that met the inclusion criteria. Current evidence supports peri-operative injection of BoNT to improve outcomes of surgeries performed on spastic limbs. There is level 1 evidence that BoNT administered pre-operatively is effective for reducing pain, spasticity, and analgesic use in pediatric patients with cerebral palsy (CP). This is supported by level 4 evidence from a retrospective case series. Level 5 evidence from case reports highlights the potential for the use of BONT in the peri-operative period. There is level 1 evidence that BoNT administered intra-operatively is not effective for reducing pain and analgesic use in pediatric patients with CP. This lack of benefit may reflect sub-optimal timing of injections, different methods of injection, different timing of the primary outcome measure, and/or differences in adjunctive therapies, but further research is required.

PMID: [33045238](#)

### **8. Predicting Hip Dysplasia in Teenagers with Cerebral Palsy in order to Optimize Prevention and Rehabilitation. A Longitudinal Descriptive Study**

Carlo Bertoncelli, Paola Altamura, Edgar Ramos Vieira, Domenico Bertoncelli, Federico Solla

Dev Neurorehabil. 2020 Oct 15;1-7. doi: 10.1080/17518423.2020.1819459. Online ahead of print.

Objective: To develop a predictive model of neuromuscular hip dysplasia (NHD) in teenagers with cerebral palsy (CP) to optimize rehabilitation. Design: A longitudinal, multicenter, double-blinded, descriptive study of one hundred and two teenagers with CP (age  $16.5 \pm 1.2$  years, range 12-18 years). Data on etiology, diagnosis, spasticity, epilepsy, clinical history, and functional assessments were collected from 2005 to 2017 and entered in the prediction model "PredictMed." Results: Poor walking abilities [ $p < .001$ ; Odd Ratio (OR) Infinity], scoliosis ( $p 0.01$ ; OR 3.22), trunk muscles' tone disorder ( $p 0.002$ ; OR 4.81), spasticity ( $p 0.006$ ; OR 6.6), poor motor function ( $p 0.02$ ; OR 5.5), and epilepsy ( $p 0.03$ ; OR 2.6) were predictors of NHD development. The accuracy of the model was 77%. Conclusion: Trunk muscles' tone disorder, severe scoliosis, epilepsy, and spasticity were predictors of NHD in teenagers with CP. Based on the results we have developed appropriate preventative rehabilitation interventions.

PMID: [33058745](#)

### **9. Promoting Functional and Independent Sitting in Children with Cerebral Palsy Using the Robotic Trunk Support**

**Trainer**

Victor Santamaria, Moiz Khan, Tatiana Luna, Jiyeon Kang, Joseph Dutkowsky, Andrew Gordon, Sunil Agrawal

IEEE Trans Neural Syst Rehabil Eng. 2020 Oct 20;PP. doi: 10.1109/TNSRE.2020.3031580. Online ahead of print.

Seated postural abilities are critical to functional independence and participation in children with cerebral palsy, Gross Motor Functional Classification System (GMFCS) levels III-IV. In this proof-of-concept study, we investigated the feasibility of a motor learning-based seated postural training with a robotic Trunk-Support-Trainer (TruST) in a longitudinal single-subject-design (13y, GMFCS IV), and its potential effectiveness in a group of 3 children (6-14y, GMFCS III-IV). TruST is a motorized -cable driven belt placed on the child's trunk to exert active-assistive forces when the trunk moves beyond stability limits. TruST-intervention addresses postural-task progression by tailoring the assistive-force fields to the child's sitting balance to train trunk control during independent short-sitting posture. TruST-intervention consisted of 2 training blocks of 6 2-hour-sessions per block (3 sessions per week). Pelvic strapping was required in the 1st block to prevent falls. As primary outcomes, we used the modified functional reach test, gross motor function measure-item set (GMFM-IS), Box & Blocks, and postural kinematics. After TruST-intervention children did not require pelvic strapping to prevent a fall, improved trunk stability during reaching (baseline = 5.49cm, 1 week post-training = 16.38cm, 3mos follow-up = 14.63cm,  $p < 0.001$ ) and increased their sitting workspace (baseline = 127.55cm<sup>2</sup>, 1 week post-training = 409.92cm<sup>2</sup>, 3mos follow-up = 270.03cm<sup>2</sup>,  $p < 0.001$ ). Three children also improved in the GMFM-IS. In summary, our novel robotic TruST-intervention is feasible and can effectively maximize functional independent sitting in children with CP GMFCS III-IV.

PMID: [33079652](#)

**10. Evaluation of a passive pediatric leg exoskeleton during gait**

Jessica Zistatsis, Keshia M Peters, Daniel Ballesteros, Heather A Feldner, Kristie Bjornson, Katherine M Steele

Prosthet Orthot Int. 2020 Oct 23;309364620956868. doi: 10.1177/0309364620956868. Online ahead of print.

Background: Children with hemiparesis are commonly prescribed ankle foot orthoses to help improve gait; however, these orthoses often result in only small and variable changes in gait. Research with adult stroke survivors has suggested that orthoses that extend beyond the ankle using long, passive tendon-like structures (i.e. exotendons) can improve walking. Objectives: The aim of this study was to quantify the impact of an exotendon-based exoskeleton on pediatric gait. Study design: Repeated-measures study. Methods: Two typically-developing children and two children with hemiparesis completed a gait analysis, walking without and with the exoskeleton. The exotendon was tested at three stiffness levels. Results: All children were able to walk comfortably with the exoskeleton, with minimal changes in step width. Walking speed increased and lower limb joint symmetry improved for the children with hemiparesis with the exoskeleton. Each participant had changes in muscle activity while walking with the exoskeleton, although the impact on specific muscles and response to exotendon stiffness varied. Conclusion: Exotendon-based exoskeletons may provide an alternative solution for optimizing gait in therapy and in the community for children with hemiparesis. Determining the optimal stiffness and configuration for each child is an important area of future research.

PMID: [33094685](#)

**11. Effect of Robot-Assisted Gait Training on Selective Voluntary Motor Control in Ambulatory Children with Cerebral Palsy**

Dragana Zarkovic, Monika Sorfova, James J Tufano, Patrik Kutilek, Slavka Viteckova, Katja Groleger-Srsen, David Ravnik

Indian Pediatr. 2020 Oct 15;57(10):964-966.

This pilot study investigated the efficacy of a four week robot-assisted gait training in twelve children with spastic diparesis. Short-term results and a 3-month follow-up showed statistically significantly increased selective motor control, walking farther distances, gross motor score, and decreased joint contractures.

PMID: [33089813](#)

## 12. Analysis of a Group-Based Treadmill Program for Children with Neuromotor Delay Who Are Pre-Ambulatory

Katrin Mattern-Baxter

Phys Occup Ther Pediatr. 2020 Oct 21;1-13. doi: 10.1080/01942638.2020.1834055. Online ahead of print.

**Purpose:** To analyze data from a prospective cohort study, a group-based treadmill program, administered twice weekly for 14 weeks, in regard to gross motor skills related to walking and walking attainment in young children with neuromotor delay who are pre-ambulatory. **Methods:** Seventy children (F = 29), mean age 25.6 (SD 10.1) months participated in the program 2×/week for 14 weeks. The Gross Motor Function Measure-88 Dimensions D and E (GMFM D/E), Functional Mobility Scale for 5, 50, and 500 meters (FMS 5, 50, 500), the timed 10-m walk test (10MWT), and the Pediatric Evaluation of Disability Inventory Caregiver Mobility Scale (PEDI) were administered before and after the program. **Results:** Statistically significant improvements were found in the GMFM D, GMFM E, FMS 5, 50, 500 and PEDI, but not in 10MWT. **Conclusions:** A group-based treadmill program was associated with improvements in motor skills related to walking in young children when administered in adjunct to ongoing physical therapy.

PMID: [33086909](#)

## 13. Effect of Long-Term Repeated Interval Rehabilitation on the Gross Motor Function Measure in Children with Cerebral Palsy

Christina Stark, Ibrahim Duran, Kyriakos Martakis, Karoline Spiess, Oliver Semler, Eckhard Schoenau

Neuropediatrics. 2020 Oct 16. doi: 10.1055/s-0040-1715489. Online ahead of print.

**Background:** The efficacy of interventions for cerebral palsy (CP) has been frequently investigated with inconclusive results and motor function measured by the Gross Motor Function Measure (GMFM-66) is common. **Objective:** In this observational analysis, we quantify the GMFM-66 change scores of the second and third year of a multimodal rehabilitation program (interval rehabilitation including home-based, vibration-assisted training) in children with CP. **Methods:** The study was a retrospective analysis of children with CP (2-13 years) participating for a second (n = 262) and third year (n = 86) in the rehabilitation program with GMFM-66 scores at start (M0), after 4 months (M4) of intensive training, and after 8 months of follow-up (M12). A method was previously developed to differentiate between possible treatment effects and expected development under standard of care for GMFM-66 scores using Cohen's d effect size (ES; size of difference). **Results:** After the treatment phase of 4 months (M4) in the second year, 125 of 262 children were responder (ES ≥ 0.2) and 137 children nonresponder (ES < 0.2); mean ES for nonresponder was -0.212 (trivial) and for responder 0.836 (large). After M4 in the third year, 43 children of 86 were responder (ES = 0.881 [large]) and 43 nonresponder (ES = - 0.124 [trivial]). **Discussion and conclusion:** Repeated rehabilitation shows a large additional treatment effect to standard of care in 50% of children which is likely due to the intervention, because in the follow-up period (standard of care), no additional treatment effect was observed and the children followed their expected development.

PMID: [33065752](#)

## 14. Rectus femoris transfer in children with cerebral palsy: comparing a propensity score-matched observational study to a randomized controlled trial

Michael H Schwartz, Andrew J Ries

Dev Med Child Neurol. 2020 Oct 21. doi: 10.1111/dmcn.14709. Online ahead of print.

**Aim:** To test whether an observational study employing propensity score matching could accurately estimate the causal treatment effects of rectus femoris transfer (RFT) as part of single-event multilevel surgery (SEMLS) in ambulatory children with cerebral palsy. **Method:** We used a large clinical database to derive a propensity score for treatment assignment (SEMLS±RFT) and used this score to generate a matched patient cohort. We compared the causal treatment effects estimated from this matched cohort with a previously published randomized controlled trial (RCT). **Results:** The treated arms of the observational study and RCT were well matched. There were 129 limbs (81 males) with a mean age of 10 years 7 months (4y 7mo) in the treated arm of the observational study, and 129 limbs (68 males) with a mean age of 10 years 2 months (3y 9mo) in

the control arm of the observational study. Differences between the observational study and RCT cohorts were clinically meaningless for knee flexion kinematics (1-4°), timing of knee angle extrema (<3% gait cycle), and speed (<5mm/s). Postoperative changes in the observational study matched those from the RCT. All but one of the observational study confidence intervals were completely contained within the corresponding RCT confidence interval; there were no meaningful differences in magnitude or sign of key outcomes related to stiff knee gait. Interpretation: Propensity score matching is an accurate method for estimating the causal treatment effects of RFT as part of an SEMLS. It seems reasonable to extend this approach to other common components of SEMLS treatment in this population.

PMID: [33084049](#)

### **15. Effect of a Nutritional Support System (Diet and Supplements) for Improving Gross Motor Function in Cerebral Palsy: An Exploratory Randomized Controlled Clinical Trial**

Fernando Leal-Martínez, Denise Franco, Andrea Peña-Ruiz, Fabiola Castro-Silva, Andrea A Escudero-Espinosa, Oscar G Rolón-Lacarrière, Mardía López-Alarcón, Ximena De León, Mariana Linares-Eslava, Antonio Ibarra

Foods. 2020 Oct 13;9(10):E1449. doi: 10.3390/foods9101449.

Background: Most patients with cerebral palsy (CP) do not respond to physical therapy due to deterioration in their nutritional status, secondary to gastrointestinal disorders and the catabolic state of the disease itself. However, basic treatments only contemplate the energy requirements and do not consider supplementation with glutamine, zinc, selenium, colexiferol, spirulina, omega 3 or even vegetal proteins. Objective: In this study, we determined the effect of using a nutritional support system (NSS): diet and supplements, on the gross motor function in children with CP with spastic diparesic and Gross Motor Function Classification System III (GMFCS III). Methods: An exploratory study was performed. Thirty patients (from 4 to 12 years old) were randomly assigned to: (1) dietary surveillance (FG), (2) deworming and WHO diet (CG), or (3) deworming and the NSS (IG). Gross motor function was evaluated using the gross motor function measure (GMFM) scale. Results: The IG-treated group presented a significant improvement in standing and walking parameters analyzed in the GMFM compared with FG and CG groups. Fifty percent of the IG-treated patients managed to walk, while in the other groups, no patients were able to walk. Conclusions: The NSS used in the present work improves gross motor function and promotes walking in patients with CP.

PMID: [33066040](#)

### **16. Multidimensional Measures of Physical Activity and Their Association with Gross Motor Capacity in Children and Adolescents with Cerebral Palsy**

Corinna N Gerber, Lena Carcreff, Anisoara Paraschiv-Ionescu, Stéphane Armand, Christopher J Newman

Sensors (Basel). 2020 Oct 16;20(20):E5861. doi: 10.3390/s20205861.

The current lack of adapted performance metrics leads clinicians to focus on what children with cerebral palsy (CP) do in a clinical setting, despite the ongoing debate on whether capacity (what they do at best) adequately reflects performance (what they do in daily life). Our aim was to measure these children's habitual physical activity (PA) and gross motor capacity and investigate their relationship. Using five synchronized inertial measurement units (IMU) and algorithms adapted to this population, we computed 22 PA states integrating the type (e.g., sitting, walking, etc.), duration, and intensity of PA. Their temporal sequence was visualized with a PA barcode from which information about pattern complexity and the time spent in each of the six simplified PA states (PAS; considering PA type and duration, but not intensity) was extracted and compared to capacity. Results of 25 children with CP showed no strong association between motor capacity and performance, but a certain level of motor capacity seems to be a prerequisite for the achievement of higher PAS. Our multidimensional performance measurement provides a new method of PA assessment in this population, with an easy-to-understand visual output (barcode) and objective data for clinical and scientific use.

PMID: [33081346](#)

**17. The mortality burden of non-trauma fracture for adults with cerebral palsy**

Daniel G Whitney, Sarah Bell, Edward A Hurvitz, Mark D Peterson, Michelle S Caird, Karl J Jepsen

Bone Rep. 2020 Oct 7;13:100725. doi: 10.1016/j.bonr.2020.100725. eCollection 2020 Dec.

**Background:** Individuals with cerebral palsy (CP) manifest skeletal fragility problems early in life, are vulnerable to non-trauma fracture (NTFx), and have a high burden of premature mortality. No studies have examined the contribution of NTFx to mortality among adults with CP. The purpose of this study was to determine if NTFx is a risk factor for mortality among adults with CP and if NTFx exacerbates mortality risk compared to adults without CP. **Methods:** Data from 2011 to 2016 Optum Clinformatics® Data Mart and a random 20% sample Medicare fee-for-service were used for this retrospective cohort study. Diagnosis codes were used to identify adults (18+ years) with and without CP, NTFx, and pre-NTFx comorbidities. Crude mortality rates per 100 person years were estimated. Cox regression estimated hazard ratios (HR and 95% confidence interval [CI]) for mortality, comparing: (1) CP and NTFx (CP + NTFx; n = 1777); (2) CP without NTFx (CP w/o NTFx; n = 12,933); (3) without CP and with NTFx (w/o CP + NTFx; n = 433,560); and (4) without CP and without NTFx (w/o CP w/o NTFx; n = 6.8 M) after adjusting for demographics and pre-NTFx comorbidities. **Results:** The 3-, 6-, and 12-month crude mortality rates were highest among CP + NTFx (12-month mortality rate = 6.80), followed by w/o CP + NTFx (12-month mortality rate = 4.91), CP w/o NTFx (12-month mortality rate = 2.15), and w/o CP w/o NTFx (12-month mortality rate = 0.49). After adjustments, the mortality rate was elevated for CP + NTFx for all time points compared to CP w/o NTFx (e.g., 12-month HR = 1.61; 95%CI = 1.29-2.01), w/o CP + NTFx (e.g., 12-month HR = 1.49; 95%CI = 1.24-1.80), and w/o CP w/o NTFx (e.g., 12-month HR = 5.33; 95%CI = 4.42-6.44). There were site-specific effects (vertebral column, lower extremities) on 12-month mortality. **Conclusions:** NTFx is associated with an increase of 12-month mortality risk among adults with CP and compared to adults without CP. Findings suggest that NTFx may be a robust risk factor for mortality among adults with CP.

PMID: [33088868](#)**18. Advanced CKD Among Adults With Cerebral Palsy: Incidence and Risk Factors**

Daniel G Whitney, Andrea L Oliverio, Neil S Kamdar, Benjamin L Viglianti, Abhijit Naik, Mary Schmidt

Kidney Med. 2020 Aug 6;2(5):569-577.e1. doi: 10.1016/j.xkme.2020.05.012. eCollection Sep-Oct 2020.

**Rationale & objective:** Recent evidence suggests that adults with cerebral palsy have an elevated risk for developing advanced chronic kidney disease (CKD). To develop effective interventions, the objective was to identify whether demographics and preexisting medical conditions are risk factors for advanced CKD among adults with cerebral palsy. **Study design:** Retrospective cohort study. **Setting & participants:** Data were from the Optum Clinformatics Data Mart. Adults 18 years or older with cerebral palsy and without advanced CKD (CKD stage 4 or later) were identified from 2013 and subsequently followed up from January 1, 2014, to the development of advanced CKD, death, loss to follow-up, or end of the study period (December 31, 2017), whichever came first. **Diagnostic, procedure, and diagnosis-related group codes** were used to identify cerebral palsy, incident cases of advanced CKD, comorbid intellectual disability, and 10 preexisting medical conditions. **Exposures:** Demographic variables and 10 preexisting medical conditions: CKD stages 1-3, hypertension, diabetes, heart and cerebrovascular disease, non-CKD urologic conditions, bowel conditions, respiratory disease, skeletal fragility, arthritis, and dysphagia. **Outcome:** Incidence of advanced CKD. **Analytic approach:** Crude incidence rate (IR) of advanced CKD and IR ratios with 95% CIs were estimated. Cox proportional hazards regression models that were adjusted for demographics, intellectual disability, and preexisting medical conditions were used to evaluate the adjusted independent effect of predictor variables. **Results:** 237 of the 8,011 adults with cerebral palsy developed advanced CKD during follow-up (IR, 10.16/1,000 person years; 95% CI, 8.87-11.46). In the crude analysis, all preexisting medical conditions were associated with an elevated IR and IR ratio of advanced CKD. In the fully adjusted Cox proportional hazards regression model, the HR was elevated for older age, CKD stages 1-3 (HR, 3.32; 95% CI, 2.39-4.61), diabetes (HR, 2.69; 95% CI, 2.03-3.57), hypertension (HR, 1.54; 95% CI, .10-2.16), heart and cerebrovascular disease (HR, 1.53; 95% CI, 1.12-2.07), and non-CKD urologic conditions (HR, 1.39; 95% CI, 1.05-1.84). **Limitations:** Private insurance database, short follow-up period, and lack of laboratory values, such as albuminuria/proteinuria. **Conclusions:** Advanced CKD was common among adults with cerebral palsy and its development was associated with both traditional and nontraditional urologic risk factors.

PMID: [33094275](#)

### 19. The effect of different dietary structure on gastrointestinal dysfunction in children with cerebral palsy and epilepsy based on gut microbiota

Congfu Huang, Xiuyun Li, Liping Wu, GenFeng Wu, Peiqin Wang, Yuanping Peng, Shuyuan Huang, Zhenyu Yang, Wenkui Dai, Lan Ge, Yansi Lyu, Linlin Wang, Anquan Zhang

Brain Dev. 2020 Oct 15;S0387-7604(20)30276-X. doi: 10.1016/j.braindev.2020.09.013. Online ahead of print.

**Background:** Gastrointestinal (GI) difficulties are very common among children with cerebral palsy (CP) and comorbid epilepsy. GI function is influenced by dietary structure on gut microbiota. The aim of this study was to compare gut microbiota differences in two dietary groups of this population and examine whether such differences are related to GI dysfunction. **Methods:** Forty children with CP and epilepsy were recruited from a social welfare center, including 23 consuming a fluid diet (liquid diet group) and 17 consuming a normal diet (general diet group). Bacterial DNA was extracted from feces, the V3-V4 region of the 16S rRNA gene was amplified from the DNA, and high-throughput sequencing of the amplified sequences was performed. Microbe prevalence levels were compared on multiple phylogenetic levels. **Results:** Gut microbial populations differed substantially between the liquid diet group and general diet group. The only two phyla that differed significantly between the two groups were Bacteroidetes ( $p = 0.034$ ) and Actinobacteria ( $p = 0.013$ ). Regarding representation of genera, *Prevotella* species were selectively predominant in the general diet group (25.849% vs. 3.612% in the liquid diet group,  $p < 0.001$ ), while *Bifidobacterium* species were selectively predominant in the liquid diet group (24.929% vs. 12.947% in the general diet group,  $p = 0.013$ ). The gut microbiota of children in the general diet group contained more butyric acid-producing microbiota which was also common in healthy people (e.g. *Lachnoclostridium*, *Dorea*, *Ruminococcus*, *Faecalibacterium*, *Roseburia*, and *Coprococcus*). The gut microbiota of children in liquid diet group however, were rich in symbiotic pathogenic bacteria (e.g. *Collinsella*, *Alistipes*, and *Eggerthella*). **Conclusion:** The gut microbiota of children with CP and epilepsy consuming a liquid diet had elevated levels of symbiotic pathogens and diminished intestinal barrier protection bacteria, relative to a general diet group. These differences in bacterial microbiota were associated with GI dysfunction symptoms.

PMID: [33071106](#)

### 20. Effectiveness of osteoporosis medication on site-specific fracture-risk attenuation among adults with epilepsy

Daniel G Whitney

Epilepsia. 2020 Oct 14. doi: 10.1111/epi.16700. Online ahead of print.

**Objective:** The objective of this propensity score-matched, observational cohort study was to determine the effectiveness of osteoporosis medication on reducing the risk of non-trauma fracture (NTFx) among adults with epilepsy. **Methods:** Data from 01/01/2012 to 09/30/2015 was extracted from Optum Clinformatics Data Mart. NTFx risk attenuation from 12 months prior to 12 months after the individual's index date was examined for each group of adults  $\geq 50$  years of age as risk ratios (RRs) with 95% confidence intervals [CIs]. Groups were stratified based on: (1) epilepsy status, as with vs without epilepsy (EP); and (2) if and when osteoporosis medication was first prescribed, as new users (treatment naive), consistent users (osteoporosis medication prescribed in pre-index period), and no users. Comparison groups were matched 1:1 to EP new users ( $n = 828$ /group) for demographics, glucocorticoid and antiseizure medication, and the Elixhauser comorbidity index. Difference-in-difference analysis compared the change in pre- to post-index NTFx risk among groups as the ratio of the RR (RRR). **Results:** The pre- to post-index NTFx risk at any site was reduced for EP new users ( $RR = 0.49$ ; 95% CI = 0.40-0.61) and EP consistent users ( $RR = 0.70$ ; 95% CI = 0.38-0.98), but nonsignificantly elevated for EP no users ( $RR = 1.39$ ; 95% CI = 0.93-2.07)-findings were consistent for most sites (eg, vertebral column). EP new users had a larger NTFx risk attenuation at any site compared to EP no users ( $RRR = 0.35$ ; 95% CI = 0.23-0.54) and EP consistent users ( $RRR = 0.70$ ; 95% CI = 0.51-0.97). EP consistent users had a larger NTFx risk attenuation at any site compared to EP no users ( $RRR = 0.50$ ; 95% CI = 0.32-0.79). The extent of NTFx risk attenuation at any site was similar for new users with vs without epilepsy ( $RRR = 0.99$ ; 95% CI = 0.73-1.34) and consistent users with vs without epilepsy ( $RRR = 0.81$ ; 95% CI = 0.55-1.17). There was evidence of site-specific effects (eg, hip). **Conclusion:** Osteoporosis medication is associated with a clinically meaningful 12-month NTFx risk attenuation for adults with epilepsy, especially for those just starting osteoporosis medication.

PMID: [33090479](#)

### 21. Utility Values for the CP-6D, a Cerebral Palsy-Specific Multi-Attribute Utility Instrument, Using a Discrete Choice Experiment

Mina Bahrapour, Richard Norman, Joshua Byrnes, Martin Downes, Paul A Scuffham

Patient. 2020 Oct 19. doi: 10.1007/s40271-020-00468-x. Online ahead of print.

**Background and objective:** The CP-6D is a new preference-based measure derived from the CPQOL, a cerebral palsy-specific quality-of-life questionnaire. The CP-6D contains six dimensions, each with five levels. A preference-based value set is required to score the CP-6D on a utility scale and render it suitable for cost-utility analysis. This study aims to estimate the utility value set for the CP-6D for interventions for people with cerebral palsy (CP). **Methods:** A discrete choice experiment was designed and administered to an adult Australian online panel. Each respondent answered 12 choice sets. Each choice was presented as a combination of the health state from the CP-6D and duration spent in that health state before death. Conditional logit and mixed logit regression were used to analyse the data. The utility values were estimated as a ratio of the coefficient of each dimension to the coefficient of the duration. **Results:** A total of 2002 participants completed the survey and responded to each choice. Generally, the dimension levels were monotonic, meaning the coefficients reflected the ordered nature of the levels in each dimension. The dimensions relating to manual ability, social well-being and acceptance had the greatest effect on choice. The value of the worst 'pits' health state is - 0.582. **Conclusion:** This study provides the first CP-specific utility value set that can potentially be used in cost-utility analyses of interventions for people with CP where the CPQOL has been applied, both prospectively and retrospectively.

PMID: [33073336](#)

## 22. [Analysis of factors related to caregiver burden in carers of persons with cerebral palsy] [Article in Spanish]

C P Chávez Andrade

Rehabilitacion (Madr). 2020 Oct 19;S0048-7120(20)30050-5. doi: 10.1016/j.rh.2020.04.003. Online ahead of print.

**Objective:** Prevalence study describing the perception of burden among the caregivers of patients with cerebral palsy attending a neurological rehabilitation centre. **Material and methods:** This study was carried out in a neuro-rehabilitation centre in Cali, Colombia, with the participation of 117 caregivers of cerebral palsy patients. Information was gathered on caregiver burden, caregivers' sociodemographic characteristics and the patients' clinics between June and August 2017. Information on caregiver burden was collected with the Zarit Burden Interview. Burden was classified into 2 groups (light to moderate burden and moderate to severe burden) for the bivariate analysis. **Results:** Most caregivers experienced light to moderate burden (74%); an increase in the probability of burden among caregivers with moderate to severe burden was observed in the caregivers of women (OR 1.35;  $P > .05$ ), children aged 6 to 10 years (OR 1.9;  $P > .05$ ), and those with greater gross motor function involvement, classified in level iv and v according to the GMFCS (OR 1.60 and 1.11, respectively;  $P > .05$ ). Burden was also higher in caregivers who were separated, divorced or widowed (OR 2.38;  $P > .05$ ), and those with incomplete basic secondary education (OR 2.86;  $P > .05$ ). **Conclusions:** This study suggests that perceived burden among caregivers varies mainly according to the age, sex, and disability of patients with cerebral palsy, as well as the age, marital status and educational level of the caregiver.

PMID: [33092851](#)

## 23. Athetoid Cerebral Palsy

Xi Li, Kapil Arya

In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2020 Jan. 2020 Sep 25.

Athetoid cerebral palsy, also known as dyskinetic cerebral palsy, is a subtype of cerebral palsy (CP). Cerebral palsy is a group of non-progressive, permanent disorders that causes limitation of activity by affecting the developing motor control circuit. These non-progressive disturbances result from insults during fetal development or in the infant's brain. Cerebral palsy as a group is the most common cause of childhood disability. Dyskinetic cerebral palsy is the second most common subtype of cerebral palsy, comprising of around 12 to 14% of patients who are affected, the most common being the spastic subtype. Athetoid cerebral palsy is defined by abnormal postures and movements. These abnormalities are due to impaired muscle tone, impaired movement control, and impaired coordination. These abnormalities can be described by detailing the typical movements themselves, such as dystonic, extrapyramidal, choreoathetotic, choreoathetoid, or athetoid cerebral palsy.

PMID: [33085307](#)

#### 24. Intraventricular hemorrhage in preterm babies

Eren Özek, Sinem Gülcan Kersin

Review Turk Pediatri Ars. 2020 Sep 23;55(3):215-221. doi: 10.14744/TurkPediatriArs.2020.66742. eCollection 2020.

Germinal matrix-intraventricular hemorrhage (GM-IVH) is a major complication of prematurity and inversely associated with gestational age and birth weight. The hemorrhage originates from the germinal matrix with an immature capillary bed where vascularization is intense and active cell proliferation is high. It occurs in around 20% of very low-birth-weight preterm neonates. Germinal matrix-intraventricular hemorrhage is less common in females, the black race, and with antenatal steroid use, but is more common in the presence of mechanical ventilation, respiratory distress, pulmonary bleeding, pneumothorax, chorioamnionitis, asphyxia, and sepsis. Ultrasonography is the diagnostic tool of choice for intraventricular hemorrhage and its complications. Approximately 25-50% of the germinal matrix-intraventricular hemorrhage cases are asymptomatic and diagnosed during routine screening. These cases are usually patients with low-grade hemorrhage. Neurologic findings are prominent in severe intraventricular hemorrhage cases. The major complications of the germinal matrix-intraventricular hemorrhage in preterm babies are periventricular hemorrhagic infarction, posthemorrhagic ventricular dilatation, periventricular leukomalacia, and cerebellar hemorrhage. It is an important cause of mortality and morbidity. The management of hemodynamics and ventilation of patients, appropriate follow-up, and early diagnosis and treatment can minimize morbidity. Prognosis in intraventricular hemorrhage is related to the severity of bleeding, parenchymal damage, and the presence of seizures and shunt surgery. The main determinant of prognosis is periventricular hemorrhagic infarction and its severity. Moderate-severe intraventricular hemorrhage can cause posthemorrhagic hydrocephalus, cerebral palsy, and mental retardation. Even mild germinal matrix-intraventricular hemorrhage can result in developmental disorders. Long-term problems such as neurodevelopmental disorders and cerebral palsy are as important as short-term problems. Improving the quality of life of these babies should be aimed through appropriate treatment and follow-up. In this review, intraventricular hemorrhage and complications are discussed.

PMID: [33061747](#)

#### 25. Short-term outcomes after a neonatal arterial ischemic stroke

Mauricio A López-Espejo, Marta Hernández Chávez, Isidro Huete

Childs Nerv Syst. 2020 Oct 16. doi: 10.1007/s00381-020-04931-w. Online ahead of print.

**Purpose:** The purpose of this study is to determine the frequency and radiological predictors of recurrent acute symptomatic seizures (RASS) and motor impairment at discharge after a neonatal arterial ischemic stroke (NAIS). **Methods:** In a nonconcurrent cohort study, 33 full-term newborns with NAIS confirmed by MRI are admitted into our hospital between January 2003 and December 2012. Stroke size, calculated as stroke volume divided by whole brain volume (WBV), was categorized as  $>$  or  $<$  3.3% of WBV. A univariate analysis of categorical variables was performed using Fisher's exact test. A multivariate analysis was performed using logistic regression models including all variables with a p value  $<$  0.1 in the univariate analysis. **Results:** The median age at NAIS was 2 days (IQR, 1-5.6), 36.4% were girls. The stroke size was  $>$  3.3 of WBV in 48.5% of the cases, and 54.5% showed multifocal lesions. Involvement of the cerebral cortex (54.5%), thalamus (48.5%), posterior limb of the internal capsule (36.4%), basal ganglia (36.4%), and brainstem (28.2%) were found. At discharge, 45.5% of newborns had a motor deficit, and 27.3% had at least two seizures. Multivariate analyses revealed that stroke size  $>$  3.3% of WBV (OR: 8.1, CI: 1.2-53.9) and basal ganglia involvement (OR: 12.8, CI: 1.7-95.4) predicted motor impairment at discharge. Cortical involvement of temporal and frontal lobes (OR: 14, CI: 2.2-88.1; and OR: 9.1, CI: 1.2-72.6) were predictive of RASS. **Conclusion:** Stroke size and location are independent risk factors for adverse short-term neurological outcomes in full-term newborns following a NAIS.

PMID: [33064213](#)

**26. Serum cytokine profiling in neonates with hypoxic ischemic encephalopathy**

H Go, Y Saito, H Maeda, R Maeda, K Yaginuma, K Ogasawara, N Kashiwabara, Y Kawasaki, M Hosoya

J Neonatal Perinatal Med. 2020 Oct 14. doi: 10.3233/NPM-200431. Online ahead of print.

Background: The fetal brain is vulnerable to severe and sustained hypoxia during and after birth, which can lead to hypoxic-ischemic encephalopathy (HIE). HIE is characterized by clinical and laboratory evidence of acute or subacute brain injury. The role of cytokines in the pathogenesis of brain injury and their relation to neurological outcomes of asphyxiated neonates are not fully understood. In this study, we investigated cytokine profile related to cerebral palsy (CP) with neonatal hypoxic ischemic encephalopathy (HIE) and HIE severity. Methods: Eligible subjects were HIE newborns with a gestational age between 36 and 42 weeks. We included newborns who was born at our NICU and did not admit to NICU as healthy controls. The study comprised 52 newborns, including 13 with mild to severe HIE and 39 healthy control. Serum cytokine profiles were performed using a LUMINEX cytokine kit (R&D Systems). Results: VEGF, MCP-1, IL-15, IL-12p70, IL-12p40, IL-1Ra, IL-2, IL-6, IL-7, IL-8, IL-10, IFN- $\gamma$ , G-CSF and eotaxin in the HIE patients were significantly increased compared with the healthy neonates. In the subgroup analysis, IL-6 and G-CSF were significantly increased in CP infants (n = 5) compared with non-CP infants (n = 8). Five and eight HIE patients were classified into the mild HIE and moderate-severe HIE groups, respectively. IL-6, 10, 1Ra, and G-CSF in the moderate-severe HIE group were significantly higher than those in the mild HIE group. Conclusion: We demonstrated that higher serum IL-6 and G-CSF at birth in HIE patients were associated with CP and moderate-severe HIE.

PMID: [33074195](#)**27. Novel Mutations in ATP13A2 Associated with Mixed Neurological Presentations and Iron Toxicity due to Nonsense-Mediated Decay**

Koray Kırımtay, Benan Temizci, Murat Gültekin, Zuhul Yapıcı, Arzu Karabay

Brain Res. 2020 Oct 19;147167. doi: 10.1016/j.brainres.2020.147167. Online ahead of print.

Background: Kufor-Rakeb Syndrome (KRS) is an autosomal recessive disease characterized by Parkinsonism, pyramidal signs, dementia, and supranuclear gaze palsy. KRS is caused by mutations in ATP13A2 producing a transmembrane protein responsible for the regulation of intracellular inorganic cations. Objective: Two siblings born to a Turkish family of consanguineous marriage had mixed neurological presentations with the presence of hypointense images on T2-weighted MRI and were pre-diagnosed as having autosomal recessive spastic paraparesis or ataxia. We aimed to identify the disease-causing mutation by whole-exome sequencing and elucidate the underlying molecular mechanism of the causative mutation. Methods: Prussian blue staining was conducted for the detection of cellular iron accumulation. Disease-causing mutation in ATP13A2 were detected by whole-exome sequencing. Expression levels of ATP13A2 mRNA and protein were assessed by qRT-PCR and Western Blot. Results: Iron deposits in the patients' fibroblasts were detected by Prussian blue staining. Novel homozygous mutation c.1422\_1423del:p.P474fs was detected in the ATP13A2. As this mutation caused a premature termination codon (PTC), the expression of mutant ATP13A2 mRNA through qRT-PCR analysis was found to be degraded by nonsense-mediated decay and this prevented the expression of ATP13A2 protein in the patients' fibroblasts. Conclusions: Novel frameshift mutation causing a PTC in ATP13A2 lead to degradation of ATP13A2 mRNA by NMD. Iron accumulation due to the absence of ATP13A2 protein in the patient's fibroblasts and hypointense areas on T2-weighted images may expand the spectrum of KRS to consider it as neurodegeneration with brain iron accumulation disorders.

PMID: [33091395](#)**28. Emerging Role of the NLRP3 Inflammasome and Interleukin-1 $\beta$  in Neonates**

Murwan Omer, Ashanty Maggvie Melo, Lynne Kelly, Emma Jane Mac Dermott, Timothy Ronan Leahy, Orla Killeen, Ola Didrik Saugstad, Rashmin C Savani, Eleanor J Molloy

Review Neonatology. 2020 Oct 19;1-10. doi: 10.1159/000507584. Online ahead of print.

Infection and persistent inflammation have a prominent role in the pathogenesis of brain injury and cerebral palsy, as well as other conditions associated with prematurity such as bronchopulmonary dysplasia. The NLRP3 inflammasome-interleukin (IL)-1 $\beta$  pathway has been extensively studied in adults and pre-clinical models, improving our understanding of innate immunity

and offering an attractive therapeutic target that is already contributing to clinical management in many auto-inflammatory disorders. IL-1 blockade has transformed the course and outcome of conditions such as chronic infantile neurological, cutaneous, articular (CINCA/NOMID) syndrome. Inflammasome activation and upregulation has recently been implicated in neonatal brain and lung inflammatory disease and may be a novel therapeutic target.

PMID: [33075792](#)

### **29. The Problem of Microbial Dark Matter in Neonatal Sepsis**

Shamim A Sinnar, Steven J Schiff

Emerg Infect Dis. 2020 Nov;26(11):2543-2548. doi: 10.3201/eid2611.200004.

Neonatal sepsis (NS) kills 750,000 infants every year. Effectively treating NS requires timely diagnosis and antimicrobial therapy matched to the causative pathogens, but most blood cultures for suspected NS do not recover a causative pathogen. We refer to these suspected but unidentified pathogens as microbial dark matter. Given these low culture recovery rates, many non-culture-based technologies are being explored to diagnose NS, including PCR, 16S amplicon sequencing, and whole metagenomic sequencing. However, few of these newer technologies are scalable or sustainable globally. To reduce worldwide deaths from NS, one possibility may be performing population-wide pathogen discovery. Because pathogen transmission patterns can vary across space and time, computational models can be built to predict the pathogens responsible for NS by region and season. This approach could help to optimally treat patients, decreasing deaths from NS and increasing antimicrobial stewardship until effective diagnostics that are scalable become available globally.

PMID: [33080169](#)

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## **Prevention and Cure**

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### **30. Prevention and treatment of cerebral palsy with cord blood stem cells and cord-derived mesenchymal stem cells**

Haruo Shintaku

Neural Regen Res. 2021 Apr;16(4):672-673. doi: 10.4103/1673-5374.293139.

PMID: [33063719](#)