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## Interventions and Management

### **1. Comparison of the effects of chair height and anterior seat inclination on sit-to-stand ability in children with spastic diplegic cerebral palsy**

Duangporn Suriyaamarit, Sujitra Boonyong

J Biomech. 2020 Oct 27;113:110098. doi: 10.1016/j.jbiomech.2020.110098. Online ahead of print.

The present study aimed to compare the effects of chair height and anterior seat inclination on sit-to-stand (STS) performance in children with spastic diplegic cerebral palsy (SDCP). Twelve children with SDCP were tested with three conditions of STS task: low chair with horizontal seat (control), low chair with anterior seat inclination (AiC), and high chair with horizontal seat (HiC) conditions. A 3D motion analysis system and two force plates were used to collect and analyze the movement time, mechanical work, kinematics, and kinetics. The results showed that in the AiC and HiC conditions, movement time and mechanical work during STS were significantly reduced when compared with the control condition. In addition, in the AiC condition, trunk alignment at the beginning of the STS task improved and the range of pelvis movement reduced, whereas in the HiC condition, the range of movement of hip, knee, and ankle joint and maximum hip and knee extension moment were reduced in children with SDCP when compared with the control condition. These results suggest that chair height and anterior seat inclination may have a positive effect on STS ability in children with SDCP. Trial register No. TCTR20170619003.

PMID: [33171354](https://pubmed.ncbi.nlm.nih.gov/33171354/)

### **2. Sit-to-stand movement in children with cerebral palsy and relationships with the International classification of functioning, disability and health: A systematic review**

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

Review Res Dev Disabil. 2020 Nov 4;107:103804. doi: 10.1016/j.ridd.2020.103804. Online ahead of print.

Background: Studying sit-to-stand (STS) in children with Cerebral Palsy addressing the domains of ICF allows determining the factors influencing STS in this population. Aims: To systematically review the literature on STS in children with CP, identifying which ICF domains have been assessed and how they relate to sit-to-stand. Methods and procedures: A literature search was conducted in electronic databases by combining the keywords (child OR children OR adolescent) AND ("Cerebral Palsy") AND (sit-to-stand). We included cross-sectional articles published in English, that assessed STS movements in children with CP up to 18 years old. Outcomes and results: 25 articles met the inclusion criteria. All of them assessed Body Functions and Structure. According to them, body alignment, muscle strength and postural sway affect STS movement. Six studies related Activity and Participation with STS, demonstrating that worse scores in scales that evaluate activities and participation are related to the poorer STS execution. Contextual factors were addressed in 15 studies: children's age, bench height, manipulation of sensory information and mechanical restriction impact the way children execute STS. Conclusion and implications: Contextual factors and Body Functions and Structure impact the STS in children with CP. However, few studies

have evaluated the participation of these children. Based on the theoretical framework of the ICF, it is important that future studies evaluate functional tasks in children with CP and the components that can affect them. The adoption of the biopsychosocial model strengthens the understanding of functioning, which can contribute to rehabilitation planning.

PMID: [33160191](#)

### **3. Reply to Letter to the Editor: "Improved trunk and neck control after selective dorsal rhizotomy in children with spastic cerebral palsy" by Tacchino et al. (2020)**

Albert Tu

Childs Nerv Syst. 2020 Nov 12. doi: 10.1007/s00381-020-04967-y. Online ahead of print.

PMID: [33179160](#)

### **4. The effect of side-alternating vibration therapy on mobility and health outcomes in young children with mild to moderate cerebral palsy: design and rationale for the randomized controlled study**

Alena Adaikina, Paul L Hofman, Silmara Gusso

BMC Pediatr. 2020 Nov 5;20(1):508. doi: 10.1186/s12887-020-02377-2.

**Background:** Cerebral palsy (CP) is the most common cause of physical disability in early childhood. Vibration therapy (VT) is a promising rehabilitation approach for children with CP with potential to impact mobility, bone and muscle health as demonstrated by extant research. However, it is still unclear how long therapy must be conducted for and what the optimal vibration frequency is in order to gain health benefits. **Methods/design:** The study is a randomized clinical trial evaluating and comparing the effects of two vibration frequency (20 Hz vs 25 Hz) and duration protocols (12 weeks vs 20 weeks) of side-alternating VT on mobility and other health parameters in children with CP. Children aged 5-12 years old with CP and GMFCS level I-III who are able to understand instruction and safely stand are eligible for the study. Exclusion criteria include bone fracture within 12 weeks of enrolment; acute conditions; the history of significant organic disease; the history of taking anabolic agents, glucocorticoids, growth hormone, and botulinum toxin injection into lower limbs within 3 months of enrolment. All participants will act as their own control with a 12-week lead-in period prior to intervention. The intervention period will consist of 20 weeks of home- or school-based VT 9 min per day, 4 times a week. After the baseline assessment, participants will be randomized to either a 20 Hz or 25 Hz vibration-frequency group. The primary outcome is mobility measured by a 6-min walking test, with analysis performed on the principle of intention to treat. Secondary outcomes include body composition, muscle strength, physical activity level, balance, gross motor function, respiratory function, and quality of life. Participants will undergo four assessment visits over the study period: baseline, at weeks 12, 24, and 32. **Discussion:** The results of the study will provide evidence-based insights into the health benefits of side-alternating VT as a therapeutic tool in young children with cerebral palsy. The investigation of different vibration training protocols will help define the optimal parameters of intervention protocols (duration, frequency) of side-alternating VT to maximize outcomes on the health of 5-12-year-old children with CP. Trial registration: Australian New Zealand Clinical Trials Registry (ANZCTR): 12618002026202 (Registration date 18/12/2018).

PMID: [33153439](#)

### **5. Is shortening of Tibialis Anterior in addition to calf muscle lengthening required to improve the active dorsal extension of the ankle joint in patients with Cerebral Palsy?**

Chakravarthy U Dussa, H Böhm, Leonhard Döderlein, Albert Fujak

Gait Posture. 2020 Oct 23;83:210-216. doi: 10.1016/j.gaitpost.2020.10.019. Online ahead of print.

**Introduction:** Shortening of the tibialis anterior tendon (TATS) has been shown to improve the ankle dorsiflexion in swing following the calf muscle lengthening procedure (CMLP) in patients with cerebral palsy (CP). Others have reported the similar improvements following CMLP but without TATS. However there are no studies comparing both procedures. Therefore the purpose of the study was to compare the ankle dorsiflexion in swing and foot position in the sagittal plane during gait following TATS and CMLP to that of CMLP alone. **Materials and methods:** A retrospective study was carried out in CP patients who

presented with fixed equinus deformity. They were grouped into unilateral CP and bilateral CP. Depending on the procedures, each group was again subdivided into subgroup CMLP only and subgroup CMLP and TATS (CMLPTATS). All patients were subjected to pre and postoperative clinical and gait analysis. Results: 44 feet in 44 patients were included in the study. Of these, 24 feet (24 patients) belonged to unilateral and 20 feet (20 patients) to bilateral CP group. The mean age of the patients at surgery was 11.5 years (6.0 - 29.0) in the unilateral CP group and 10.5 years (5.0-34.0) in the bilateral CP group. In the unilateral CP group, 12 feet belonged to subgroup CMLP and 12 to subgroup CMLPTATS with a mean equinus contracture of 7.5° in both subgroups. In bilateral CP group, 11 feet belonged to subgroup CMLP with a mean equinus contracture of 5° and 9 to subgroup CMLPTATS, with a mean equinus contracture of 10°. The subgroups did not vary significantly in the demographics, anthropometry, kinematics and kinetics of ankle joint preoperatively. The mean follow up time was 19.7 months. The surgery produced significant changes in both groups and subgroups. However, none of the relevant gait parameters were significantly different between groups and subgroups. Significance: Adding TATS to CMLP, compared to CMLP alone did not improve ankle dorsiflexion in swing and the foot position more than CMLP alone.

PMID: [33171374](#)

## 6. Impact of Altered Gastrocnemius Morphometrics and Fascicle Behavior on Walking Patterns in Children With Spastic Cerebral Palsy

Matthias Hösl, Annika Kruse, Markus Tilp, Martin Svehlik, Harald Böhm, Antonia Zehentbauer, Adamantios Arampatzis

Front Physiol. 2020 Oct 7;11:518134. doi: 10.3389/fphys.2020.518134. eCollection 2020.

Spastic cerebral palsy (SCP) affects neural control, deteriorates muscle morphometrics, and may progressively impair functional walking ability. Upon passive testing, gastrocnemius medialis (GM) muscle bellies or fascicles are typically shorter, thinner, and less extensible. Relationships between muscle and gait parameters might help to understand gait pathology and pathogenesis of spastic muscles. The current aim was to link resting and dynamic GM morphometrics and contractile fascicle behavior (both excursion and velocity) during walking to determinants of gait. We explored the associations between gait variables and ultrasonography of the GM muscle belly captured during rest and during gait in children with SCP [n = 15, gross motor function classification system (GMFCS) levels I and II, age: 7-16 years] and age-matched healthy peers (n = 17). The SCP children's plantar flexors were 27% weaker. They walked 12% slower with more knee flexion produced 42% less peak ankle push-off power (all p < 0.05) and 7/15 landed on their forefoot. During the stance phase, fascicles in SCP on average operated on 9% shorter length (normalized to rest length) and displayed less and slower fascicle shortening (37 and 30.6%, respectively) during push-off (all p ≤ 0.024). Correlation analyses in SCP patients revealed that (1) longer-resting fascicles and thicker muscle bellies are positively correlated with walking speed and negatively to knee flexion (r = 0.60-0.69, p < 0.0127) but not to better ankle kinematics; (2) reduced muscle strength was associated with the extent of eccentric fascicle excursion (r = -0.57, p = 0.015); and (3) a shorter operating length of the fascicles was correlated with push-off power (r = -0.58, p = 0.013). Only in controls, a correlation (r = 0.61, p = 0.0054) between slower fascicle shortening velocity and push-off power was found. Our results indicate that a thicker gastrocnemius muscle belly and longer gastrocnemius muscle fascicles may be reasonable morphometric properties that should be targeted in interventions for individuals with SCP, since GM muscle atrophy may be related to decreases in walking speed and undesired knee flexion during gait. Furthermore, children with SCP and weaker gastrocnemius muscle may be more susceptible to chronic eccentric muscle overloading. The relationship between shorter operating length of the fascicles and push-off power may further support the idea of a compensation mechanism for the longer sarcomeres found in children with SCP. Nevertheless, more studies are needed to support our explorative findings.

PMID: [33178029](#)

## 7. Motor beta cortical oscillations are related with the gait kinematics of youth with cerebral palsy

Max J Kurz, Hannah Bergwell, Rachel Spooner, Sarah Baker, Elizabeth Heinrichs-Graham, Tony W Wilson

Ann Clin Transl Neurol. 2020 Nov 11. doi: 10.1002/acn3.51246. Online ahead of print.

Objective: It is widely believed that the perinatal brain injuries seen in youth with cerebral palsy (CP) impact neuronal processing of sensory information and the production of leg motor actions during gait. However, very limited efforts have been made to evaluate the connection between neural activity within sensorimotor networks and the altered spatiotemporal gait biomechanics seen in youth with CP. The objective of this investigation was to use magnetoencephalographic (MEG) brain imaging and biomechanical analysis to probe this connection. Methods: We examined the cortical beta oscillations serving motor control of the legs in a cohort of youth with CP (N = 20; Age = 15.5 ± 3 years; GMFCS levels I-III) and healthy controls

(N = 15; Age = 14.1 ± 3 years) using MEG brain imaging and a goal-directed isometric knee target-matching task. Outside the scanner, a digital mat was used to quantify the spatiotemporal gait biomechanics. Results: Our MEG imaging results revealed that the participants with CP exhibited stronger sensorimotor beta oscillations during the motor planning and execution stages compared to the controls. Interestingly, we also found that those with the strongest sensorimotor beta oscillations during motor execution also tended to walk slower and have a reduced cadence. Interpretation: These results fuel the impression that the beta sensorimotor cortical oscillations that underlie leg musculature control may play a central role in the altered mobility seen in youth with CP.

PMID: [33174692](#)

### **8. Physical performance outcome measures used in exercise interventions for adults with childhood-onset disabilities: A scoping review**

Jessica Z Song, Margot Catizzone, Kelly P Arbour-Nicitopoulos, Dorothy Luong, Laure Perrier, Mark Bayley, Sarah E P Munce

Review NeuroRehabilitation. 2020 Nov 3. doi: 10.3233/NRE-203250. Online ahead of print.

Background: People with childhood-onset disabilities face unique physical and social challenges in adulthood. Exercise interventions may improve physical performance in children, but there is a lack of research on adults. Objective: To describe studies that investigate exercise interventions and to evaluate the quality of physical performance outcome measures for adults with childhood-onset disabilities. Methods: Eligible studies reported on exercise interventions for adults (ages 16+) with cerebral palsy, spina bifida, or acquired brain injuries. Only randomized controlled trials published in English from 2008 to 2019 were included. MEDLINE, CINAHL, PEDro, EMBASE, and Cochrane Central Register of Controlled Trials were searched. Two reviewers independently screened studies and abstracted data. Results: This scoping review included 4 trials reporting on cerebral palsy only. Three strength training programs found significant improvements in gait, and one mixed training program found significant improvements in strength and fitness. Only two outcome measures used are valid/reliable for adults (6 Minute Walk Test and Borg-20 Grades). Conclusion: Certain interventions may improve physical performance, but there is a lack of research on appropriate exercise interventions and physical performance outcome measures for adults with childhood-onset disabilities. Different exercise interventions should be investigated using larger sample sizes and outcome measures should be standardized.

PMID: [33164958](#)

### **9. Six Months Guided Exercise Therapy Improves Motor Abilities and White Matter Connectivity in Children with Cerebral Palsy**

Md Safwan Samsir, Rahimah Zakaria, Salmi Abdul Razak, Mohamed Saat Ismail, Mohd Zulkifli Abdul Rahim, Chia-Shu Lin, Nik Mohammad Faez Nik Osman, Mohammad Afiq Asri, Nor Haslina Mohd, Asma Hayati Ahmad

Malays J Med Sci. 2020 Oct;27(5):90-100. doi: 10.21315/mjms2020.27.5.9. Epub 2020 Oct 27.

Background: Diffusion magnetic resonance imaging (dMRI) provides the state of putative connectivity from lesioned areas to other brain areas and is potentially beneficial to monitor intervention outcomes. This study assessed the effect of a 6 months guided exercise therapy on motor abilities and white matter diffusivity in the brains of cerebral palsy (CP) children. Methods: This is a single arm pre-and post-test research design involving 10 spastic CP children, aged 8-18 years and whose Gross Motor Function Classification System Expanded and Revised (GMFCS-E & R) at least Level 21 with the ability to ambulate independently. They were recruited from Paediatric Neurology Clinic, Hospital Universiti Sains Malaysia (HUSM) from December 2015-December 2016. All participants underwent 6 months of therapist-guided exercise session comprising progressive strength training at a frequency of twice a week, 1 h duration per session. The effect of exercise on motor abilities was assessed using the Gross Motor Function Measures (GMFM)-88. Six out of the 10 children consented for dMRI. Probabilistic tractography of the corticospinal tract (CST) was performed to determine the connectivity index of the tracts pre- and post-intervention. Results: All the participants displayed statistically significant increment in GMFM-88 scores pre-to post-exercise intervention. This improvement was concurrent with increased connectivity index in the CST of upper limbs and lower limbs in the brain of these children. Conclusion: Our findings demonstrated that 6 months guided exercise therapy improves motor abilities of CP children concurrent with strengthening the connectivities of the motor pathways in the brain.

PMID: [33154705](#)

### **10. No pain, no gain? Children with cerebral palsy and their experience with physiotherapy**

L Houx, C Pons, H Saudreau, A Dubois, M Creusat, P Le Moine, O Rémy-Néris, J Ropars, J Y LeReste, S Brochard

Ann Phys Rehabil Med. 2020 Oct 28;S1877-0657(20)30193-7. doi: 10.1016/j.rehab.2020.10.002. Online ahead of print.

**Objectives:** Recent studies have shown that physiotherapy can induce pain in children and young adults with cerebral palsy (CP). There is a lack of knowledge of children's pain experiences during therapy sessions and the specific causes of pain. The main objective of this study was to better understand the experience of children and young adults with CP during physiotherapy sessions and to analyse the coping strategies used by children and therapists. **Methods:** Qualitative study with focus groups. Eighteen children/young adults with CP who experienced pain during physiotherapy were interviewed, using focus groups as a source of data collection in a phenomenological perspective. Data collection and analysis were consecutive to ensure that the data saturation point was reached. The transcripts were coded manually using thematic analysis. First, interesting features of the verbatim were coded, then codes were collated into potential themes and then the themes were checked to ensure they worked in relation to the coded extracts. Multiple coding was performed by 3 different researchers, and results were merged at each step. **Results:** This study confirmed that among the 18 children interviewed (mean [SD] age 13.17 [4.02] years, 10 girls), physiotherapy, particularly stretching, induced pain. Participants reported that the experience of pain led to a dislike of physiotherapy, although some believed that the pain was necessary to show that the treatment was effective. The use of distraction techniques and the relationship with the physiotherapist were key elements associated with the perception and experience of pain. **Conclusions:** This study confirmed that patients with CP experience pain during physiotherapy. Stretching seems to be the main source of pain. Beliefs and practices regarding the concept of pain show that physiotherapists need training in this field.

PMID: [33130039](#)

### **11. Collagen-binding peptide reverses bone loss in a mouse model of cerebral palsy based on clinical databases**

Yoon-Kyum Shin, Jeong Hyun Heo, Jue Yeon Lee, Yoon-Jeong Park, Sung-Rae Cho

Ann Phys Rehabil Med. 2020 Oct 28;S1877-0657(20)30190-1. doi: 10.1016/j.rehab.2020.09.009. Online ahead of print.

**Background:** Individuals with cerebral palsy (CP) experience bone loss due to impaired weight bearing. Despite serious complications, there is no standard medication. **Objective:** To develop a new pharmacological agent, we performed a series of studies. The primary aim was to develop an animal model of CP to use our target medication based on transcriptome analysis of individuals with CP. The secondary aim was to show the therapeutic capability of collagen-binding protein (CBP) in reversing bone loss in the CP mouse model. **Methods:** A total of 119 people with CP and 13 healthy adults participated in the study and 140 7-day-old mice were used for the behavioral analysis and discovery of therapeutic effects in the preclinical study. The mouse model of CP was induced by hypoxic-ischemic brain injury. Inclusion and exclusion criteria were established for CBP medication in the CP mouse model with bone loss. **Results:** On the basis of clinical outcomes showing insufficient mechanical loading from non-ambulatory function and that underweight mainly affects bone loss in adults with CP, we developed a mouse model of CP with bone loss. Injury severity and body weight mainly affected bone loss in the mouse CP model. Transcriptome analysis showed SPP1 expression downregulated in adults with CP who showed lower bone density than healthy controls. Therefore, a synthesized CBP was administered to the mouse model. Trabecular thickness, total collagen and bone turnover activity increased with CBP treatment as compared with the saline control. Immunohistochemistry showed increased immunoreactivity of runt-related transcription factor 2 and osteocalcin, so the CBP participated in osteoblast differentiation. **Conclusions:** This study can provide a scientific basis for a promising translational approach for developing new anabolic CBP medication to treat bone loss in individuals with CP.

PMID: [33130040](#)

### **12. Salivary alpha amylase and cortisol levels as stress biomarkers in children with cerebral palsy and their association with a physical therapy program**

Luz Elena Durán-Carabali, Mabel Lucía Henao-Pacheco, Angélica María González-Clavijo, Zulma Dueñas



Res Dev Disabil. 2020 Nov 6;108:103807. doi: 10.1016/j.ridd.2020.103807. Online ahead of print.

**Introduction:** Cerebral palsy (CP) is one of the main causes of physical disabilities in childhood. There is evidence that CP children display high levels of stress, which could interfere with learning processes and interpretation of relevant sensory information during motor skills acquisition and socialization. **Objective:** This study aims to compare basal levels of stress biomarkers (cortisol and alpha-amylase) of healthy children (HC) and children with CP, and to investigate whether a physical therapy session using the neurodevelopmental technique (NDT) interferes with these levels. **Methods:** A cross-sectional design was used. A total of 86 children (HC: n = 45 and CP: n = 41) with matching age, sex, socioeconomic status, and sampling time. Salivary cortisol and alpha-amylase levels were measured by means of electrochemiluminescence and spectrophotometry methods. A single saliva sample was collected in the HC group to determine basal levels. For CP group three samples were collected: a first sample was taken 20-30 min prior to the intervention, while two post-intervention samples were collected (5 and 20 min) to evaluate individual changes in salivary stress biomarkers. **Results:** Higher basal cortisol concentration was found in CP children when compared to HC group. Moreover, CP children showed a significant reduction in cortisol levels 20 min after NDT intervention. No significant differences were observed in alpha-amylase values. **Conclusion:** Present results show that CP causes alteration in basal cortisol values at childhood and suggest that CP children respond to environmental regulatory factors such as NDT, in attempt to reduce stress.

PMID: [33161308](#)

### **13. Healthcare usage for respiratory illness by paediatric inpatients with cerebral palsy**

R Dayman, A C Wilson, A M Blackmore, K Langdon

Acta Paediatr. 2020 Nov 10. doi: 10.1111/apa.15658. Online ahead of print.

Children with severe cerebral palsy (CP) have many medical co-morbidities, often managed by hospital inpatient admissions. Children with CP are hospitalised 7 times more than their neurotypical peers, and the leading cause of medical hospital admissions is respiratory illness.(1) Lower respiratory tract illness in children with CP has multifactorial aetiology, including community-acquired bacterial and viral infections, acute aspiration pneumonia, and chronic aspiration-related airways disease. It requires coordinated care from multiple medical specialties and allied health clinicians.(2) This paper describes the investigations, interventions, and healthcare services used by this population during their respiratory-related hospital admissions at one paediatric hospital.

PMID: [33171532](#)

### **14. Risk Factors Associated with Probable Sleep Bruxism of Children and Teenagers with Cerebral Palsy**

Tae da Silva, A M Silva, Esl Alvarenga, B R Nogueira, R R Prado, R F Mendes

J Clin Pediatr Dent. 2020 Aug 1;44(4):228-233. doi: 10.17796/1053-4625-44.4.3.

**Aim:** To assess the association between probable sleep bruxism (PSB) and other occlusal characteristics in children and teenagers with Cerebral Palsy (CP). **Study design:** A cross-sectional study was carried out with 148 participants (74 with CP and 74 without special needs) aged between 2 and 14 years old. Participants underwent an oral clinical examination to evaluate the occlusal characteristics. Parents/caregivers filled out a questionnaire with information related to the typical sounds of PSB, sociodemographic factors and the presence of harmful oral habits in the study participants. Data analysis was carried out, using Chi-square or Fisher's exact test and Odds Ratio ( $p < 0.05$ ). **Results:** PSB and malocclusion (68.9% and 95.9%, respectively) were more prevalent in participants with CP than in participants without CP. The association between PSB and the presence of a wear facet was statistically significant ( $p < 0.001$ ) in participants with CP. In this group, 64.8% of participants with PSB presented tooth wear. **Conclusion:** Presence of dental wear facets was significantly associated with PSB in individuals with cerebral palsy.

PMID: [33167014](#)

### 15. [Clinical effectiveness of Subjective Global Nutritional Assessment in hospitalized children with cerebral palsy] [Article in Chinese]

Han-You Liu, Deng-Na Zhu, Gong-Xun Chen, Yu-Mei Wang, Yun-Xia Zhao, Qiao-Xiu Li, Hua-Chun Xiong, Jun-Ying Yuan, Yong-Qiang Gao, Yi-Wen Wang, Rui-Xia Wang

Zhongguo Dang Dai Er Ke Za Zhi. 2020 Nov;22(11):1188-1192. doi: 10.7499/j.issn.1008-8830.2007153.

Objective: To investigate the nutritional status of children with cerebral palsy (CP) and the clinical effectiveness of Subjective Global Nutritional Assessment (SGNA) in nutritional assessment of hospitalized children with CP. Methods: A total of 208 children with CP, aged 1-5 years, who were hospitalized from April to October 2019 were enrolled as subjects. SGNA was used to investigate nutritional status, and the Z-score method recommended by the World Health Organization was used as a reference standard to validate the clinical effectiveness of SGNA. Results: The detection rate of malnutrition in children with CP was 42.3% by SGNA and 39.4% by the Z-score method ( $P>0.05$ ). The application of SGNA showed high consistency between different evaluators ( $\kappa=0.621$ ,  $P<0.001$ ). With the Z-score method as the reference standard, SGNA had a sensitivity of 80.5%, a specificity of 82.5%, a positive predictive value of 75.0%, and a negative predictive value of 86.7%, and high consistency was observed between the two evaluation methods ( $\kappa=0.622$ ,  $P<0.001$ ). SGNA was moderately consistent with weight-for-age Z-score and height-for-age Z-score ( $\kappa=0.495$  and  $0.478$  respectively,  $P<0.001$ ) and was poorly consistent with weight-for-height Z-score ( $\kappa=0.197$ ,  $P<0.05$ ). Conclusions: There is a relatively high incidence rate of malnutrition in children with CP. SGNA can be used as a tool to assess the nutritional status of children with CP.

PMID: [33172553](#)

### 16. The Impact of Malnutrition on Hospitalized Children With Cerebral Palsy

Byron Alexander Foster, Jennifer E Lane, Elizabeth Massey, Michelle Noelck, Sarah Green, Jared P Austin

Review Hosp Pediatr. 2020 Nov 5;hpeds.2020-0177. doi: 10.1542/hpeds.2020-0177. Online ahead of print.

Children with cerebral palsy (CP) and other medical complexity comprise an outsized proportion of health care use. In this review, we describe the current science of assessment of nutritional status for children with CP, outline a systematic approach to assessing their nutritional status, delineate ramifications of malnutrition on hospitalization-associated outcomes, and identify knowledge gaps and means of addressing those gaps using quality improvement and clinical research tools. Methods to accurately assess body composition and adiposity in this population by using skinfolds, age, sex, and activity level are available but are not widely used. There are limitations in our current method of estimating energy needs in children with CP, who are at higher risk of both obesity and micronutrient deficiencies. There is some evidence of an association between malnutrition, defined as either underweight or obesity, and hospitalization-associated outcomes in children generally, although we lack specific data for CP. The gaps in our current understanding of optimal nutritional status and between current science and practice need to be addressed to improve health outcomes for this vulnerable patient population.

PMID: [33154081](#)

### 17. Survey on Children with Cerebral Palsy in Tochigi Prefecture, Japan

Hirokazu Yamagishi, Hitoshi Osaka, Satoshi Toyokawa, Yasuki Kobayashi, Hideo Shimoizumi

Pediatr Int. 2020 Nov 11. doi: 10.1111/ped.14536. Online ahead of print.

Background: The incidence of cerebral palsy (CP) is influenced by perinatal medicine and regional medical systems. We investigated the recent incidence of CP and the current problems of children with CP living at home under an advanced perinatal medical system. Methods: A clinical datasheet survey was performed among 13 hospitals and 6 rehabilitation facilities treating children with CP born in Tochigi Prefecture (Japan) to estimate the incidence of CP among children born between 2009 and 2013. The severity of motor and intellectual impairment, presumed causal factors, complications, and provided medical interventions was investigated and compared between preterm-born and term-born children with CP. Results: The incidence of CP was 1.6 per 1000 live births. Shorter gestation period and lower birth weight were associated with a higher incidence of CP. Fifty-one percent of children with CP were non-ambulatory, and 55% had severe to profound intellectual impairment. Episodes of neonatal asphyxia and periventricular leukomalacia were the most frequent causal factors; both were

significantly more frequent in preterm-born children than in term-born children. Approximately 30% of children with CP had respiratory disorders, dysphagia, or epilepsy; 62% received medical interventions, including medication, mechanical ventilation, oxygen therapy, tube feeding, and intraoral/intranasal suction. Conclusion: The recent incidence of CP was lower in comparison to previous Japanese studies. However, the motor and intellectual impairments were severe, and many children with CP and their families were burdened by daily medical care. Public support systems should be developed along with the perinatal medical system.

PMID: [33176036](#)

### **18. Quality of life in children with cerebral palsy: don't forget to ask the child**

Angela Harris

Dev Med Child Neurol. 2020 Oct 31. doi: 10.1111/dmcn.14727. Online ahead of print.

PMID: [33131050](#)

### **19. Partnering clinician- and parent-led organizations for guidance on puberty and menarche in cerebral palsy and intellectual disability**

Lynne Fogel

Dev Med Child Neurol. 2020 Nov 9. doi: 10.1111/dmcn.14728. Online ahead of print.

PMID: [33169373](#)

### **20. Multidisciplinary clinic for care of children with complex obstructive sleep apnea**

Jacquelyn K DeVries, Javan J Nation, Zachary B Nardone, Samuel H Lance, Jacy A Stauffer, George M Abichaker, Rakesh Bhattacharjee, Daniel J Lesser

Int J Pediatr Otorhinolaryngol. 2020 Nov;138:110384. doi: 10.1016/j.ijporl.2020.110384. Epub 2020 Sep 16.

**Objective:** While adenotonsillectomy (AT) remains first line therapy for pediatric obstructive sleep apnea (OSA), management of children who are not candidates for AT or who have residual OSA post AT varies and spans across multiple specialties. We aim to report our experience in managing this population through a multidisciplinary sleep clinic composed of specialists in pediatric dentistry, otolaryngology, plastic surgery, and pulmonary/sleep medicine. **Study design:** Retrospective chart review. **Method:** The medical records of children attending our complex sleep apnea clinic were reviewed. Data pertaining to demographics, underlying diagnoses, prior evaluation and treatment, recommendations, and initial therapy were collected. **Result:** Two-hundred and thirty patients (mean age  $10.7 \pm 5.1$  years, 62.2% male) were assessed. Underlying conditions included Trisomy 21 ( $n = 65$ , 28.2%), other genetic syndromes ( $n = 37$ , 16.1%), obesity in an otherwise typically developing child ( $n = 36$ , 15.2%), cerebral palsy ( $n = 27$ , 11.7%), and craniofacial syndromes ( $n = 7$ , 3.0%). Mean obstructive apnea hypopnea index (OAHI) was 14.2 events/hour at first clinic visit, and the majority of children had previously undergone at least one upper airway surgery ( $n = 168$ , 73.0%), primarily adenotonsillectomy. Recommended initial treatment plans included positive airway pressure (PAP) therapy ( $n = 108$ , 47.0%), surgery ( $n = 75$ , 32.6%), allergy management ( $n = 52$ , 22.6%), and/or weight loss ( $n = 34$ , 14.8%). Patients prescribed PAP therapy with follow up data were found to be adherent 43.9% of the time. Surgical patients with post-operative polysomnography had pre-operative OAHI  $15.6 \pm SD13.4$  decrease to  $10.7 \pm 14.2$  events/hour ( $p = 0.61$ ). **Conclusion:** Genetic conditions and obesity were the most common underlying diagnoses cared for in the complex sleep apnea clinic. Patients presented with severe OSA, most having already had upper airway surgery. Management plans were frequently adjusted, and we observed improvement in SDB in a sub-segment of patients, suggesting benefit to a coordinated, multi-disciplinary approach.

PMID: [33152975](#)



**21. Transient-evoked otoacoustic emission findings in children (1-12 years) with cerebral palsy in Kano, Nigeria**

Yasir Nuhu Jibril, Auwal Adamu, Rabiu Ibrahim Jalo, Zubaida Ladan Farouk, Abubakar Danjuma Salisu, Onyekwere George B Nwaorgu

Niger Postgrad Med J. Oct-Dec 2020;27(4):371-376. doi: 10.4103/npmj.npmj\_240\_20.

Background: Children with cerebral palsy (CP) suffer from multiple problems and potential disabilities. These range from musculoskeletal problems, mental retardation, epilepsy, ophthalmologic and hearing impairment among others. Consequences of hearing loss include problems with speech and language development. Early detection in this difficult-to-test population may prevent these consequences of hearing loss. An otoacoustic emission assessment is useful in this regard. This study assessed transient-evoked otoacoustic emissions (TEOAEs) in children with CP. Materials and methods: The study population were children with CP who presented at the paediatric neurology clinic during the study period. An equal number of control population matched for age and sex were also recruited using simple random sampling. An interviewer-administered questionnaire was used to obtain relevant clinical information. All participants selected underwent a detailed ear, nose and throat examination and TEOAE testing. Results: There were 330 participants in this study, categorised into CP cases (165) and non-CP controls (165). The age range of the participants was 1-12 years, with a mean age of  $4.44 \pm 2.92$  among CP patients and  $4.47 \pm 2.90$  among the controls. The male-to-female ratio was 2:1. TEOAEs were 'failed' in 83.6% of the CP patients and in 28.5% of the controls. This study found a statistically significant difference in 'failed' TEOAE result between the CP patients and the controls ( $P = 0.0001$ ). Conclusion: This study found a high prevalence of 'failed' TEOAEs in children with CP in Kano.

PMID: [33154292](#)

**22. Neurodevelopmental outcomes of very low birth weight infants in the Neonatal Research Network of Japan: Importance of NICU graduate follow-up**

Yumi Kono

Clin Exp Pediatr. 2020 Nov 9. doi: 10.3345/cep.2020.01312. Online ahead of print.

Here we describe the neurodevelopmental outcomes of very low birth weight (VLBW) infants (birth weight  $\leq 1500$  g) at 3 years of age in the Neonatal Research Network of Japan (NRNJ) database in the past decade and review the methodological issues identified in follow-up studies. The follow-up protocol for children at 3 years of chronological age in the NRNJ consists of physical and comprehensive neurodevelopmental assessments in each participating center. Neurodevelopmental impairment (NDI) - moderate to severe neurological disability - is defined as cerebral palsy (CP) with a Gross Motor Function Classification System score  $\geq 2$ , visual impairment such as uni- or bilateral blindness, hearing impairment requiring hearing amplification, or cognitive impairment with a developmental quotient (DQ) of Kyoto Scale of Psychological Development score  $< 70$  or judgment as delayed by pediatricians. We used death or NDI as an unfavorable outcome in all study subjects and NDI in survivors using number of assessed infants as the denominator. Follow-up data were collected from 49% of survivors in the database. Infants with follow-up data had lower birth weights and were of younger gestational age than those without follow-up data. Mortality rates of 40728 VLBW infants born between 2003 and 2012 were 8.2% before discharge and 0.7% after discharge. The impairment rates in the assessed infants were 7.1% for CP, 1.8% for blindness, 0.9% for hearing impairment, 15.9% for a DQ  $< 70$ , and 19.1% for NDI. The mortality or NDI rate in all study subjects, including infants without follow-up data, was 17.4%, while that in the subjects with outcome data was 32.5%. The NRNJ follow-up study results suggested that children born with a VLBW remained at high risk of NDI in early childhood. It is important to establish a network follow-up protocol and complete assessments with fewer dropouts to enable clarification of the outcomes of registered infants.

PMID: [33171036](#)

**23. Childhood-onset seizures: A long-term cohort study of use of antiepileptic drugs, and drugs for neuropsychiatric conditions**

Eva Åndell, Torbjörn Tomson, Per Åmark, Nicklas Pihlström, Kristina Tedroff, Sofia Carlsson

Epilepsy Res. 2020 Oct 24;168:106489. doi: 10.1016/j.eplepsyres.2020.106489. Online ahead of print.

**Objective:** We conducted a long-term follow-up of a cohort of children with newly diagnosed unprovoked seizures to assess treatment with antiepileptic drugs (AEDs), neuroleptics, antidepressants and medication for attention deficit hyperactivity disorder (ADHD) with special attention to the impact of comorbidities on the use of such medication. **Methods:** Our study cohort comprised 769 children (28 days-18 years), living in Stockholm Sweden, with a first unprovoked seizure identified between 2001 and 2006. Information on neurodevelopmental comorbidities and Cerebral Palsy (CP) at seizure onset was collected from medical records. Information on treatment with AEDs, neuroleptics, antidepressants and ADHD medication was retrieved by linkage to the Swedish National Prescription Registry between 2005 and 2014. The association between comorbidities and drug treatments was assessed by odds ratios (OR) with 95 % confidence intervals (CI), adjusted for age and sex. **Results:** Eight years after the index seizure, 31 % of the children were on AEDs, and this was more common among children with any of the comorbidities studied (OR; 4.0 95 % CI 2.9-5.6) compared to those without such comorbidities, and within this group of comorbidities particularly for those with CP (OR; 5.2 95 % CI: 2.9-9.3). Children with neurodevelopmental comorbidity or CP at baseline were more likely to receive neuroleptics (ORs 8 years after the index seizure; 6.9, 95 % CI: 2.4-19.8), antidepressants (OR; 2.3, 95 % CI: 1.0-5.5) and ADHD medication (OR; 3.6, 95 % CI: 1.8-7.2) than children without the studied comorbidities. **Conclusion:** Children with seizures in combination with neurodevelopmental comorbidities or CP, especially CP, have a more frequent use of AEDs, neuroleptics, antidepressants, and ADHD medication up to 13 years following the initial seizure than children without comorbidity. Our data highlight the treatment burden in children with epilepsy and comorbidities.

PMID: [33166848](#)

#### **24. The fetal inflammatory response syndrome: the origins of a concept, pathophysiology, diagnosis, and obstetrical implications**

Eunjung Jung, Roberto Romero, Lami Yeo, Ramiro Diaz-Primera, Julio Marin-Concha, Robert Para, Ashley M Lopez, Percy Pacora, Nardhy Gomez-Lopez, Bo Hyun Yoon, Chong Jai Kim, Stanley M Berry, Chaur-Dong Hsu

Semin Fetal Neonatal Med. 2020 Aug;25(4):101146. doi: 10.1016/j.siny.2020.101146. Epub 2020 Oct 23.

The fetus can deploy a local or systemic inflammatory response when exposed to microorganisms or, alternatively, to non-infection-related stimuli (e.g., danger signals or alarmins). The term "Fetal Inflammatory Response Syndrome" (FIRS) was coined to describe a condition characterized by evidence of a systemic inflammatory response, frequently a result of the activation of the innate limb of the immune response. FIRS can be diagnosed by an increased concentration of umbilical cord plasma or serum acute phase reactants such as C-reactive protein or cytokines (e.g., interleukin-6). Pathologic evidence of a systemic fetal inflammatory response indicates the presence of funisitis or chorionic vasculitis. FIRS was first described in patients at risk for intraamniotic infection who presented preterm labor with intact membranes or preterm prelabor rupture of the membranes. However, FIRS can also be observed in patients with sterile intra-amniotic inflammation, alloimmunization (e.g., Rh disease), and active autoimmune disorders. Neonates born with FIRS have a higher rate of complications, such as early-onset neonatal sepsis, intraventricular hemorrhage, periventricular leukomalacia, and death, than those born without FIRS. Survivors are at risk for long-term sequelae that may include bronchopulmonary dysplasia, neurodevelopmental disorders, such as cerebral palsy, retinopathy of prematurity, and sensorineuronal hearing loss. Experimental FIRS can be induced by intra-amniotic administration of bacteria, microbial products (such as endotoxin), or inflammatory cytokines (such as interleukin-1), and animal models have provided important insights about the mechanisms responsible for multiple organ involvement and dysfunction. A systemic fetal inflammatory response is thought to be adaptive, but, on occasion, may become dysregulated whereby a fetal cytokine storm ensues and can lead to multiple organ dysfunction and even fetal death if delivery does not occur ("rescued by birth"). Thus, the onset of preterm labor in this context can be considered to have survival value. The evidence so far suggests that FIRS may compound the effects of immaturity and neonatal inflammation, thus increasing the risk of neonatal complications and long-term morbidity. Modulation of a dysregulated fetal inflammatory response by the administration of antimicrobial agents, anti-inflammatory agents, or cell-based therapy holds promise to reduce infant morbidity and mortality.

PMID: [33164775](#)

#### **25. Neurologic Outcomes After Prenatal Treatment of Twin-Twin Transfusion Syndrome**

Desmond Sutton, Russell Miller

Review Clin Perinatol. 2020 Dec;47(4):719-731. doi: 10.1016/j.clp.2020.08.002. Epub 2020 Oct 16.

Monochorionic twin gestations possess disproportionately higher risk for perinatal morbidity and mortality when compared with dichorionic twin pregnancies due to their potential to develop specific complications attributable to a shared placenta and intertwin placental circulation. Since the advent of fetoscopic laser surgery, outcomes of pregnancies affected by twin-twin transfusion syndrome (TTTS) have improved, with reduced rates of mortality and morbidity when compared with amnioreduction or expectant management. The focus of this article is to review the literature regarding neurologic outcomes among pediatric survivors of fetal intervention for TTTS.

PMID: [33153657](#)

## **26. Seizure burden and neurodevelopmental outcome in newborns with hypoxic-ischemic encephalopathy treated with therapeutic hypothermia: A single center observational study**

Claudia Basti, Eugenia Maranella, Nicola Cimini, Alessia Catalucci, Simona Ciccarelli, Marianna Del Torto, Luisa Di Luca, Cecilia Di Natale, Arianna Mareri, Valentina Nardi, Veronica Pannone, Sandra Di Fabio

Seizure. 2020 Oct 29;83:154-159. doi: 10.1016/j.seizure.2020.10.021. Online ahead of print.

**Objective:** To examine the relationship between electrographic seizures and developmental outcome at 18 and 24 months in neonates with moderate and severe hypoxic-ischemic encephalopathy [HIE] treated with therapeutic hypothermia [TH]. **Study design:** 30 term infants with moderate-severe HIE treated with TH were enrolled prospectively from June 2012 to May 2018. All had continuous single channel amplitude integrated EEG (aEEG) monitoring for a minimum of 72 h and brain MR within 4 weeks. The aEEG was classified by severity of background and seizure burden. MR images were graded by the severity of injury. **Outcome** (defined abnormal in case of death, dyskinetic or spastic quadriplegic cerebral palsy, epilepsy, or Bayley III score < 85 in all three subscales or < 70 in any individual subscale) was assessed at 18 and 24 months. **Results:** Seizures were recorded in 24 out of 30 [80 %] neonates and an abnormal outcome was observed in 7 [23 %] of infants. Patients with poor outcome had a statistically significant correlation with: high seizure burden ( $p = 0.0004$ ), need for more than one antiepileptic drugs ( $p = 0.006$ ), a persistent abnormal aEEG trace at 48 h ( $p = 0.0001$ ) and moderate-severe brain injury at MRI ( $p = 0.0001$ ). Moreover, infants with status epilepticus or frequent seizures reported a significantly association with abnormal MR imaging and poor outcome than patients with sporadic seizures ( $p = 0.0009$ ). **Conclusion:** The role of seizures in the pathogenesis of brain injury remains controversial. In our cohort the presence of seizures, per se, was not associated with abnormal outcome; however a high seizure burden as well as a persistent abnormal aEEG background pattern and MR lesions resulted significantly associated with poor prognosis.

PMID: [33160202](#)

## **27. [Survival and Neurodevelopmental Outcomes of Premature Infants with Severe Peri-Intraventricular Hemorrhage at 24 Months of Age][Article in Portuguese]**

Joana Amaral, Sara Peixoto, Dolores Faria, Cristina Resende, Adelaide Taborda

Acta Med Port. 2020 Oct 30. doi: 10.20344/amp.12295. Online ahead of print.

**Introduction:** Severe peri-intraventricular haemorrhage has been associated with higher mortality and neurodevelopmental impairment. The impact of peri-intraventricular haemorrhage alone (without white matter injury) remains controversial. The aim of this study was to evaluate the influence of severe peri-intraventricular haemorrhage, associated or not with cystic peri-ventricular leukomalacia, on mortality and neurodevelopment at 24 months. **Material and methods:** Retrospective cohort study, that included newborns with severe peri-intraventricular haemorrhage admitted to a maternity hospital with differentiated perinatal support between 2006 and 2015, and two controls with the same gestational age, without peri-intraventricular haemorrhage, who were admitted immediately after the case. **Neurodevelopmental assessment,** at 24 months, was performed in 99 children, using the Schedule of Growing Skills II scale in 52 and the Ruth Griffiths mental development scale in 47 children. **Severe neurodevelopmental deficit** was diagnosed in the following conditions: cerebral palsy, delayed psychomotor development, deafness requiring hearing aids and blindness. **Results:** The study included 41 cases and 82 controls. Out of these, 23 died, 16 (39.0%) in the group of severe peri-intraventricular haemorrhage and seven (8.5%) in the control group (OR 7.6, 95% CI 2.6 - 20.4,  $p < 0.001$ ). Severe neurodevelopmental deficit was diagnosed in seven (30.4%) in the severe peri-intraventricular haemorrhage group and one (1.3%) in the control group (OR 32; 95% CI 3.7 - 281,  $p < 0.001$ ). Individualized analysis showed that mortality was higher in peri-intraventricular haemorrhage grade III with associated cystic peri-ventricular leukomalacia (OR 4.4 95% CI 1.3 - 14.2,  $p = 0.015$ ) and in peri-intraventricular haemorrhage IV (OR 12; 95% CI 3.5 - 41.2,  $p < 0.001$ ), when compared to controls. Differences were also noticed regarding severe neurodevelopmental deficit when

compared with controls (1.3%) in grade III peri-intraventricular haemorrhage with associated cystic peri-ventricular leukomalacia, (75.0%,  $p < 0.001$ ) and grade IV peri-intraventricular haemorrhage (50.0%,  $p < 0.001$ ). Discussion: This work showed a higher mortality rate and neurodevelopment impairment in preterm newborns with severe peri-ventricular haemorrhage. Analysis by groups stratified according to gestational age and different grades of peri-ventricular haemorrhage displayed the complications associated with peri-ventricular haemorrhage grade IV or grade III, with or without cystic peri-ventricular leukomalacia. Conclusion: Preterm newborns with peri-intraventricular haemorrhage grade IV or grade III with cystic peri-ventricular leukomalacia, had a higher risk of mortality and severe neurodevelopmental impairment.

PMID: [33159726](#)

## **28. First trimester fasting plasma glucose screen in advanced maternal age women: a cost-effectiveness analysis**

Bethany T Waites, Allison R Walker, Ashley A Skeith, Aaron B Caughey

J Matern Fetal Neonatal Med. 2020 Nov 12;1-7. doi: 10.1080/14767058.2020.1847073. Online ahead of print.

Background: The prevalence of preexisting type 2 diabetes mellitus (T2DM) in the United States is on the rise. Women of advanced maternal age (AMA,  $\geq 35$  years) are more likely to have preexisting T2DM in pregnancy because glucose intolerance increases with age. Diabetes in pregnancy is associated with significant maternal and neonatal morbidity and mortality, and earlier treatment initiation improves pregnancy outcomes. However, maternal age is not currently recognized as an independent risk factor that warrants diabetes screening prior to the traditional screen at 24–28 weeks gestation. Objective: To evaluate the cost-effectiveness of screening all AMA women with a first trimester fasting plasma glucose (FPG) test for earlier diagnosis and management of preexisting T2DM. Study design: A decision-analytic model was created to compare pregnancy outcomes in AMA women who undergo a first trimester FPG test vs third trimester oral glucose tolerance test alone. Probabilities were obtained from the literature. Outcomes examined included preeclampsia, preterm delivery, macrosomia, shoulder dystocia, brachial plexus injury (BPI), intrauterine fetal demise (IUID), cerebral palsy, and neonatal death. The cost, quality-adjusted life-years (QALYs), and incremental cost-effectiveness ratio of the first trimester screening strategy were examined as well. Sensitivity analyses and a Monte Carlo simulation were performed to test the model's robustness. Results: In AMA women, screening for preexisting T2DM in the first trimester with an FPG test resulted in fewer cases of preeclampsia, preterm delivery, BPI, IUID, cerebral palsy, and neonatal death compared to performing a third trimester oral glucose tolerance test alone, and is cost-effective. Monte Carlo analysis incorporating the distribution of all probabilities showed that first trimester FPG screening remained cost-effective as long as the incremental cost of initiating diabetes treatment in the first trimester was less than \$150,000 and the cost of the FPG screen was less than \$2700. Conclusion: Compared to third trimester oral glucose tolerance test alone, performing a first trimester FPG screen in AMA women is cost-saving and more effective.

PMID: [33179564](#)

## **29. Hidden etiology of cerebral palsy: genetic and clinical heterogeneity and efficient diagnosis by next-generation sequencing**

Monica Rosello, Alfonso Caro-Llopis, Carmen Orellana, Silvestre Oltra, Marta Alemany-Albert, Ana V Marco-Hernandez, Sandra Monfort, Laia Pedrola, Francisco Martinez, Miguel Tomás

Review Pediatr Res. 2020 Nov 11. doi: 10.1038/s41390-020-01250-3. Online ahead of print.

Cerebral palsy (CP) is a heterogeneous neurodevelopmental disorder that causes movement and postural disabilities. Recent research studies focused on genetic diagnosis in patients with CP of unknown etiology. The present study was carried out in 20 families with one family member affected with idiopathic CP. Chromosomal microarray and exome sequencing techniques were performed in all patients. Chromosomal microarray analysis did not show any pathological or probable pathological structural variant. However, the next-generation sequencing study showed a high diagnostic yield. We report 11/20 patients (55%) with different pathogenic or potentially pathogenic variants detected by exome sequencing analysis: five patients with mutations in genes related to hereditary spastic paraplegia, two with mutations in genes related to Aicardi-Goutières syndrome, three with mutations in genes related to developmental/epileptic encephalopathies, and one with a mutation in the PGK1 gene. The accurate and precise patients' selection, the use of a high-throughput genetic platform, the selection of adequate target genes, and the application of rigorous criteria for the clinical interpretation are the most important elements for a good diagnostic performance. Based on our findings, next-generation sequencing should be considered in patients with cryptogenic CP as the first line of genetic workup. IMPACT: Sequencing techniques in CP of uncertain etiology provides a diagnostic yield of 55%. The appropriate selection of cases optimizes the diagnostic yield. NGS facilitate better understanding of new

phenotypes of certain genetic diseases.

PMID: [33177673](#)