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Cerebral palsy research news

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Interventions and Management

1. IncobotulinumtoxinA Efficacy/Safety in Upper-Limb Spasticity in Pediatric Cerebral Palsy: Randomized Controlled Trial

Edward Dabrowski, Henry G Chambers, Deborah Gaebler-Spira, Marta Banach, Petr Kaňovský, Hanna Dersch, Michael Althaus, Thorin L Geister, Florian Heinen

Pediatr Neurol. 2021 May 21;123:10-20. doi: 10.1016/j.pediatrneurol.2021.05.014. Online ahead of print.

Background: This randomized phase 3 study with double-blind main period (MP) and open-label extension (OLEX; NCT02002884) assessed incobotulinumtoxinA safety and efficacy for pediatric upper-limb spasticity treatment in ambulant/nonambulant (Gross Motor Function Classification System [GMFCS] I-V) patients, with the option of combined upper- and lower-limb treatment. Methods: Patients were aged two to 17 years with unilateral or bilateral spastic cerebral palsy (CP) and Ashworth Scale (AS) score ≥2 in treatment-selected clinical patterns. In the MP, patients were randomized (2:1:1) to incobotulinumtoxinA 8, 6, or 2 U/kg body weight (maximum 200, 150, 50 U/upper limb), with optional lower-limb injections in one of five topographical distributions (total body dose ≤16 to 20 U/kg, maximum 400 to 500 U, depending on body weight and GMFCS level). In the OLEX, patients received three further treatment cycles, at the highest MP doses (8 U/kg/upper limb group). Outcomes included AS, Global Impression of Change Scale (GICS), and adverse events (AEs). Results: AS scores improved from baseline to week 4 in all MP dose groups (n = 350); patients in the incobotulinumtoxinA 8 U/kg group had significantly greater spasticity improvements versus the 2 U/kg group (least-squares mean [standard error] for upper-limb main clinical target pattern -1.15 [0.06] versus -0.93 [0.08]; P = 0.017). Investigator's, child/adolescent's, and parent/caregiver's GICS scores showed improvements in all groups. Treatment benefits were sustained over further treatment cycles. AE incidence did not increase with dose or repeated treatment across GMFCS levels. Conclusions: Data provide evidence for sustained efficacy and safety of multipattern incobotulinumtoxinA treatment in children and adolescents with upper-limb spasticity.

PMID: 34339951

2. Upper Limb Motor Planning in Individuals with Cerebral Palsy Aged between 3 and 21 Years Old: A Systematic Review

Ophélie Martinie, Catherine Mercier, Andrew M Gordon, Maxime T Robert

Review Brain Sci. 2021 Jul 12;11(7):920. doi: 10.3390/brainsci11070920.

Individuals with cerebral palsy have difficulties performing activities of daily living. Beyond motor execution impairments, they exhibit motor planning deficits contributing to their difficulties. The objective of this review is to synthesize the behavioral evidence of motor planning deficits during an upper limb motor task in children, adolescents and young adults with

cerebral palsy aged between 3 and 21 years. Methods: The inclusion criteria were: (1) including individuals with cerebral palsy from 3 to 21 years old; (2) assessing upper limb motor planning. Six databases were screened. The quality assessment of the studies was performed. Results: Forty-six studies and 686 participants were included. Five articles have been identified as very high quality, 12 as high, 20 as moderate, six as low, three as very low. Force planning studies reported a deficit for the more affected hand but adequate performances for the less affected hand. Object-manipulation studies reported hand posture planning deficits irrespectively of the hand assessed. Conclusions: Motor planning deficits has been shown in the more affected hand for force scaling, while the results for other variables showed overall deficits. Hence, variables affected by motor planning deficits in both hands should be considered in children with cerebral palsy to optimize intervention.

PMID: 34356154

3. Constraint Induced Movement Therapy in Infants and Toddlers with Hemiplegic Cerebral Palsy: A Scoping Review
Casey Walker, Angela Shierk, Heather Roberts

Occup Ther Health Care. 2021 Aug 2;1-17. doi: 10.1080/07380577.2021.1953206. Online ahead of print.

Cerebral Palsy (CP) is the leading cause of motor disability in childhood. Recent studies have investigated the effectiveness of constraint induced movement therapy (CIMT) as an early intervention for infants and toddlers with hemiplegic CP. This scoping review aims to identify current evidence for CIMT protocols for children 3 months to 5 years 11 months as well as clinical applications for practice and gaps in research. Selected databases and additional studies were searched and reviewed with 10 studies were selected for review. Results show CIMT for infants and toddlers is a feasible and effective treatment consisting of caregiver coaching, treatment in the child's typical environment, and just right activities. Future research is needed to determine the effects of different dosages in early CIMT, and the long term developmental effects throughout childhood.

PMID: 34339315

4. Assessment of hip displacement in children with cerebral palsy using machine learning approach
Thanh-Tu Pham, Minh-Binh Le, Lawrence H Le, John Andersen, Edmond Lou

Med Biol Eng Comput. 2021 Aug 6. doi: 10.1007/s11517-021-02416-9. Online ahead of print.

Manual measurements of migration percentage (MP) on pelvis radiographs for assessing hip displacement are subjective and time consuming. A deep learning approach using convolution neural networks (CNNs) to automatically measure the MP was proposed. The pre-trained Inception ResNet v2 was fine tuned to detect locations of the eight reference landmarks used for MP measurements. A second network, fine-tuned MobileNetV2, was trained on the regions of interest to obtain more precise landmarks' coordinates. The MP was calculated from the final estimated landmarks' locations. A total of 122 radiographs were divided into 57 for training, 10 for validation, and 55 for testing. The mean absolute difference (MAD) and intra-class correlation coefficient (ICC [2,1]) of the comparison for the MP on 110 measurements (left and right hips) were 4.5 [Formula: see text] 4.3% (95% CI, 3.7-5.3%) and 0.91, respectively. Sensitivity and specificity were 87.8% and 93.4% for the classification of hip displacement (MP-threshold of 30%), and 63.2% and 94.5% for the classification of surgery-needed hips (MP-threshold of 40%). The prediction results were returned within 5 s. The developed fine-tuned CNNs detected the landmarks and provided automatic MP measurements with high accuracy and excellent reliability, which can assist clinicians to diagnose hip displacement in children with CP.

PMID: 34357510

5. Correlation between the Korean Version of the Trunk Control Measurement Scale and the Selective Control Assessment of the Lower Extremity Scores in Children with Cerebral Palsy
Misoo Lim, Haneul Lee, Hyoungwon Lim

Medicina (Kaunas). 2021 Jul 6;57(7):687. doi: 10.3390/medicina57070687.

Background and Objectives: The purpose of this study was to investigate the correlation between the Korean version of the trunk control measurement scale (K-TCMS) and the selective control assessment of the lower extremity (SCALE). Through this, we tried to find out the effect of proximal stabilization on distal motor development. Materials and Methods: Fifty-one children with gross motor function classification system level I-III, diagnosed with cerebral palsy (CP), were studied. The K-TCMS was used to evaluate the body control ability of the children. SCALE was used to quantify selective voluntary motor control (SVMC). Results: Analysis of SCALE and K-TCMS showed a significant positive correlation in all items. Multiple regression analysis showed that the SCALE score decreased as age increased, and that it increased as the static sitting balance ability score and the dynamic sitting balance ability score of the K-TCMS increased significantly ($p < 0.05$). Conclusions: In children with cerebral palsy, there was a close correlation between trunk control and selective voluntary motor control of the lower extremities. Therefore, when trying to improve the lower extremity function of a child with cerebral palsy, a trunk control intervention should be considered.

PMID: 34356967

6. Instrumented gait analysis for management of gait disorders in children with cerebral palsy: A scoping review
Rebecca A States, Joseph J Krzak, Yasser Salem, Ellen M Godwin, Amy Winter Bodkin, Mark L McMulkin

Review Gait Posture. 2021 Aug 3;90:1-8. doi: 10.1016/j.gaitpost.2021.07.009. Online ahead of print.

Background: The use of Instrumented Gait Analysis (IGA) for the clinical management of individuals with cerebral palsy (CP) has increased in recent years. Previous systematic reviews have been completed to evaluate and summarize the evidence related to the efficacy of IGA in general. However, a focused summary of research studies on IGA for children with CP related gait disorders is needed. Research question: The purpose of the current work was to perform a scoping review to describe and categorize the range of existing literature about IGA as applied to the clinical management of children with CP related gait disorders. Method: A health sciences librarian developed a search strategy to include four key inclusion criteria of original research study, population included children with CP, study employed IGA, available in English. The available literature was organized into six study categories: reliability and validity, documentation of subgroups or model development, IGA for clinical decision making, effectiveness of treatments that depend on IGA, cost effectiveness, IGA used to evaluate the outcome of surgical, medical or rehabilitation treatment. Results: 909 studies met the inclusion criteria and were placed into the six study categories. 14 % of studies were in reliability and validity, 33 % in subgroups or modeling, 2% in IGA for clinical decision making, 2% in treatments that depend on IGA, 1% in cost effectiveness, and 49 % of studies had IGA used as an outcome measure for treatment. Significance: This scoping review has documented the wide range, diversity and extent of original research studies investigating the use of IGA for the clinical management of children with CP related gait disorders. The large volume of studies provides a basis for future work to develop a CPG about the use of IGA for the clinical management of children with CP related gait disorders.

PMID: 34358847

7. The Ability to Run in Young People with Cerebral Palsy before and after Single Event Multi-Level Surgery
Roman Rethwilm, Harald Böhm, Leonhard Döderlein, Peter A Federolf, Chakravarthy U Dussa

J Pers Med. 2021 Jul 14;11(7):660. doi: 10.3390/jpm11070660.

The objective of the study is to identify and evaluate possible factors that influence the ability to run before and after single event multi-level surgery (SEMLS). Young patients (6-25 years) with spastic cerebral palsy (GMFCSI-II) were retrospectively included. Type and number of surgical procedures, time for recovery and 3D gait analysis variables were analyzed with respect to the ability to run. In total, 98 patients (38 females; 60 males) who received SEMLS (12 years, SD 3.4) were included and compared to a control group of 71 conservatively treated patients. Of 60 runners pre-surgery, 17 (28%) lost the ability, while gained in 8 of 38 (21%) non-runners. The number of surgical procedures was a significant predictor and those who lost their ability to run had significantly more (mean = 5.9, SD = 1.7), compared to the patients who gained the ability (mean = 3.5, SD = 0.9). Further, pre-surgical function (e.g., gait speed) was significantly different ($p < 0.001$). Pre-surgical function and the number of surgical procedures seem to play an important role for the gain or loss of the ability to run after surgery. Caution is warranted in patients with lower pre-surgical function and the ability to run, as they seem at a higher risk to lose the ability.

PMID: 34357127

8. Evaluation of Multilevel Surgeries in Children With Spastic Cerebral Palsy Based on Surface Electromyography
Sujiao Li, Xueqin Luo, Song Zhang, Yuanmin Tang, Jiming Sun, Qingyun Meng, Hongliu Yu, Chengyan Sun

Front Neurosci. 2021 Jul 15;15:680645. doi: 10.3389/fnins.2021.680645. eCollection 2021.

The root mean square (RMS) of the surface electromyography (sEMG) signal can respond to neuromuscular function, which displays a positive correlation with muscle force and muscle tension under positive and passive conditions, respectively. The purpose of this study was to investigate the changes in muscle force and tension after multilevel surgical treatments, functional selective posterior rhizotomy (FSPR) and tibial anterior muscle transfer surgery, and evaluate their clinical effect in children with spastic cerebral palsy (SCP) during walking. Children with diplegia (n = 13) and hemiplegia (n = 3) with ages from 4 to 18 years participated in this study. They were requested to walk barefoot at a self-selected speed on a 15-m-long lane. The patient's joints' range of motion (ROM) and sEMG signal of six major muscles were assessed before and after the multilevel surgeries. The gait cycle was divided into seven phases, and muscle activation state can be divided into positive and passive conditions during gait cycle. For each phase, the RMS of the sEMG signal amplitude was calculated and also normalized by a linear envelope (10-ms running RMS window). The muscle tension of the gastrocnemius decreased significantly during the loading response, initial swing, and terminal swing ($p < 0.05$), which helped the knee joint to get the maximum extension when the heel is on the ground and made the heel land smoothly. The muscle force of the gastrocnemius increased significantly ($p < 0.05$) during the mid-stance, terminal stance, and pre-swing, which could generate the driving force for the human body to move forward. The muscle tension of the biceps femoris and semitendinosus decreased significantly ($p < 0.05$) during the terminal stance, pre-swing, and initial swing. The decreased muscle tension could relieve the burden of the knee flexion when the knee joint was passively flexed. At the terminal swing, the muscle force of the tibial anterior increased significantly ($p < 0.05$), which could improve the ankle dorsiflexion ability and prevent foot drop and push forward. Thus, the neuromuscular function of cerebral palsy during walking can be evaluated by the muscle activation state and the RMS of the sEMG signal, which showed that multilevel surgical treatments are feasible and effective to treat SCP.

PMID: 34335161

9. Effects of Ankle Continuous Passive Motion on Soleus Hypertonia in Individuals with Cerebral Palsy: A Case Series
Li-Ling Chuang, Yu-Fen Chuang, Ya-Jhu Jhu, An-Lun Hsu, Chia-Ling Chen, Alice M K Wong, Ya-Ju Chang

Biomed J. 2021 Jul 28;S2319-4170(21)00097-4. doi: 10.1016/j.bj.2021.07.010. Online ahead of print.

Background: Continuous passive motion device (CPM) provides repetitive movement over extended periods of time for those who have low functional ability. The purpose of this research was to evaluate the effects of a four-week program of continuous passive motion of the ankle joint on the changes in soleus hypertonia in individuals with cerebral palsy who suffered from life-long hypertonia. Material and methods: A single group, repeated-measures study was conducted. Eight individuals (7 males and 1 female with a mean age of 21.8 ± 8.5 years) with spastic cerebral palsy underwent bilateral ankle CPM for 1 hour a day, 5 days a week, for 4 weeks. The outcome measures included the Modified Ashworth Scale (MAS) score, passive range of motion (PROM) of the ankle, the ratio of maximum H reflex to maximum soleus M-response (H/M ratio), and post-activation depression (PAD). All outcomes were measured before and after the intervention. A paired t-test was used to examine treatment effects pre-versus post-intervention. Results: Paired t-tests showed that the CPM program significantly decreased the Modified Ashworth Scale score (P=0.006), decreased the maximum H/M ratio (P=0.001), improved PAD (P=0.003, P=0.040, and P=0.032 at 0.2 Hz, 1 Hz, and 2 Hz, respectively), and increased the passive ankle range of motion (P=0.049). Conclusions: Ankle CPM not only reduced soleus hypertonia but also improved the passive range of motion in individuals with cerebral palsy. The results of this study show ankle CPM to be an effective intervention for individuals with cerebral palsy.

PMID: 34332162

10. Pilot evaluation of changes in motor control after wearable robotic resistance training in children with cerebral palsy
Benjamin C Conner, Michael H Schwartz, Zachary F Lerner

J Biomech. 2021 Jul 8;126:110601. doi: 10.1016/j.jbiomech.2021.110601. Online ahead of print.

Cerebral palsy (CP) is characterized by deficits in motor function due to reduced neuromuscular control. We leveraged the guiding principles of motor learning theory to design a wearable robotic intervention intended to improve neuromuscular control of the ankle. The goal of this study was to determine the neuromuscular and biomechanical response to four weeks of exoskeleton ankle resistance therapy (exo-therapy) in children with CP. Five children with CP (12 - 17 years, GMFCS I - II, two diplegic and three hemiplegic, four males and one female) were recruited for ten 20-minute sessions of exo-therapy. Surface electromyography, three-dimensional kinematics, and metabolic data were collected at baseline and after training was complete. After completion of training and with no device on, participants walked with decreased co-contraction between the plantar flexors and dorsiflexors (-29 ± 11%, $p = 0.02$), a more typical plantar flexor activation profile (33 ± 13% stronger correlation to a typical soleus activation profile, $p = 0.01$), and increased neural control complexity (7 ± 3%, $p < 0.01$ measured via muscle synergy analysis). These improvements in neuromuscular control led to a more mechanically efficient gait pattern (58 ± 34%, $p < 0.05$) with a reduced metabolic cost of transport (-29 ± 15%, $p = 0.02$). The findings from this study suggest that ankle exoskeleton resistance therapy shows promise for rapidly improving neuromuscular control for children with CP, and may serve as a meaningful rehabilitative complement to common surgical procedures.

PMID: 34332214

11. Brain-Computer Interfaces for Children With Complex Communication Needs and Limited Mobility: A Systematic Review
Silvia Orlandi, Sarah C House, Petra Karlsson, Rami Saab, Tom Chau

Front Hum Neurosci. 2021 Jul 14;15:643294. doi: 10.3389/fnhum.2021.643294. eCollection 2021.

Brain-computer interfaces (BCIs) represent a new frontier in the effort to maximize the ability of individuals with profound motor impairments to interact and communicate. While much literature points to BCIs' promise as an alternative access pathway, there have historically been few applications involving children and young adults with severe physical disabilities. As research is emerging in this sphere, this article aims to evaluate the current state of translating BCIs to the pediatric population. A systematic review was conducted using the Scopus, PubMed, and Ovid Medline databases. Studies of children and adolescents that reported BCI performance published in English in peer-reviewed journals between 2008 and May 2020 were included. Twelve publications were identified, providing strong evidence for continued research in pediatric BCIs. Research evidence was generally at multiple case study or exploratory study level, with modest sample sizes. Seven studies focused on BCIs for communication and five on mobility. Articles were categorized and grouped based on type of measurement (i.e., non-invasive and invasive), and the type of brain signal (i.e., sensory evoked potentials or movement-related potentials). Strengths and limitations of studies were identified and used to provide requirements for clinical translation of pediatric BCIs. This systematic review presents the state-of-the-art of pediatric BCIs focused on developing advanced technology to support children and youth with communication disabilities or limited manual ability. Despite a few research studies addressing the application of BCIs for communication and mobility in children, results are encouraging and future works should focus on customizable pediatric access technologies based on brain activity.

PMID: 34335203

12. Value of Rehabilitation Training for Children with Cerebral Palsy Diagnosed and Analyzed by Computed Tomography Imaging Information Features under Deep Learning
Xi Zhang, Zhenfang Wang, Jun Liu, Lulin Bi, Weilan Yan, Yueyue Yan

J Healthc Eng. 2021 Jul 20;2021:6472440. doi: 10.1155/2021/6472440. eCollection 2021.

To analyze the brain CT imaging data of children with cerebral palsy (CP), deep learning-based electronic computed tomography (CT) imaging information characteristics were used, thereby providing help for the rehabilitation analysis of children with CP and comorbid epilepsy. The brain CT imaging data of 73 children with CP were collected, who were outpatients or inpatients in our hospital. The images were randomly divided into two groups. One group was the artificial intelligence image group, and hybrid segmentation network (HSN) model was employed to analyze brain images to help the treatment. The other group was the control group, and original images were used to help diagnosis and treatment. The deep learning-based HSN was used to segment the CT image of the head of patients and was compared with other CNN methods. It was found that HSN had the highest Dice score (DSC) among all models. After treatment, six cases in the artificial intelligence image group returned to normal (20.7%), and the artificial intelligence image group was significantly higher than the control group ($X 2 = 335191$, $P < 0.001$). The cerebral hemodynamic changes were obviously different in the two groups of children

before and after treatment. The VP of the cerebral artery in the child was (139.68 ± 15.66) cm/s after treatment, which was significantly faster than (131.84 ± 15.93) cm/s before treatment, $P < 0.05$. To sum up, the deep learning model can effectively segment the CP area, which can measure and assist the diagnosis of future clinical cases of children with CP. It can also improve medical efficiency and accurately identify the patient's focus area, which had great application potential in helping to identify the rehabilitation training results of children with CP.

PMID: 34336162

13. Jejunal Volvulus Around Gastrostomy Tube: An Exceptional Complication in Cerebral Palsy
Hind S Alsaif, Ali Hassan, Hassan Alsaleem, Osamah J Refai, Khaled Awary, Faten Alaqeel, Raed Alsulaiman

Case Reports Am J Case Rep. 2021 Aug 4;22:e932075. doi: 10.12659/AJCR.932075.

BACKGROUND Cerebral palsy may be accompanied by gastrointestinal disorders. Percutaneous endoscopic gastrostomy (PEG) tube placement is an increasingly performed procedure in these patients. While PEG tube feeding can result in weight gain and a decrease in aspiration episodes, this insertion of a PEG tube is not without complications. Specifically, intestinal volvulus following PEG tube insertion is an exceedingly rare complication. CASE REPORT A 34-year-old man with cerebral palsy was brought to the emergency department with a history of recurrent vomiting. He had a history of PEG tube insertion 2 months prior to his presentation. The physical examination was non-contributory. Abdominal computed tomography was suggestive of an intestinal volvulus around the PEG tube. Subsequently, the patient underwent an exploratory laparotomy, which confirmed the diagnosis and enabled successful management. Unexpectedly, the patient suffered cardiac arrest 5 days following the operation. Cardiopulmonary resuscitation was performed with pharmacological intervention and defibrillation in accordance with the advanced cardiac life support guidelines. He recovered successfully and was discharged after a 4-day observation. CONCLUSIONS Clinicians should have a high index of suspicion for small bowel volvulus in patients who had a PEG tube inserted, along with intestinal obstruction. Furthermore, caregivers should be educated to recognize the early signs of intestinal obstruction and seek medical attention, since a delay can result in fatal outcomes.

PMID: 34347761

14. Placebo-Controlled Clinical Trial of IncobotulinumtoxinA for Sialorrhea in Children: SIPEXI
Steffen Berweck, Marcin Bonikowski, Heakyung Kim, Michael Althaus, Birgit Flatau-Baqué, Daniela Mueller, Marta Dagmara Banach

Neurology. 2021 Aug 2;10.1212/WNL.0000000000012573. doi: 10.1212/WNL.0000000000012573. Online ahead of print.

Background and objectives: This prospective phase III study (SIPEXI) investigated efficacy and safety of repeated injections of incobotulinumtoxinA (incoBoNT/A) for treatment of chronic sialorrhea (drooling) associated with neurological disorders (e.g., cerebral palsy, traumatic brain injury) and/or intellectual disability in children/adolescents. Methods: The study enrolled 2-17-year-olds with sialorrhea due to neurological disorders and/or intellectual disability. Patients received body weight-dependent doses of incoBoNT/A (20 U to 75 U). A main period with 1 injection cycle (placebo-controlled, double-blind, 6-17-year-olds) was followed by an open-label extension with up to 3 further cycles. An additional cohort of 2-5-year-olds received active treatment throughout the study. Co-primary endpoints were the change in unstimulated salivary flow rate (uSFR) from baseline to week 4, and the carers' global impression of change scale (GICS) rating at week 4. Adverse events were recorded. Results: In the main period, 220 patients aged 6-17 years were randomized and treated (148 patients in incoBoNT/A group, 72 patients in placebo group). 35 patients aged 2-5 years received incoBoNT/A (no placebo). 214 patients aged 6-17 years and 33 patients aged 2-5 years continued treatment in the open-label extension period. For the 6-17-year-olds, a significant difference between incoBoNT/A and placebo was seen in the mean uSFR decrease (difference: -0.06 g/min; $p = 0.0012$) and the carers' GICS rating (difference: 0.28 points; $p = 0.032$) at week 4, in favor of active treatment. The secondary endpoints consistently supported these results. A sustained benefit was observed during the extension. Incidences of adverse events were comparable between incoBoNT/A and placebo and did not increase notably with repeated injections. The most common adverse events were respiratory infections. Efficacy and safety were also favorable in the uncontrolled cohort of 2-5-year-olds. Discussion: Both co-primary efficacy endpoints were reached and superiority of incoBoNT/A over placebo was confirmed. IncoBoNT/A (up to 75 U, up to 4 cycles) is an effective and well-tolerated treatment for sialorrhea associated with neurological disorders in children. Study registrations: Clinicaltrials.gov: NCT02270736 (www.clinicaltrials.gov/ct2/show/results/NCT02270736); EU Clinical Trials Register: 2013-004532-30 (www.clinicaltrialsregister.eu/ctr-search/search?query=2013-004532-30). Classification of evidence: This study provides Class I evidence that injection of incobotulinumtoxinA decreases drooling in

children aged 6-17 years with neurological disorders.

PMID: 34341153

15. Oral health status and microbial load of Streptococcus mutans in children with Cerebral palsy in a tertiary care hospital in Delhi
Drishti Kaushal, Namita Kalra, Amit Khatri, Rishi Tyagi, N P Singh, Anju Aggarwal, Rumpa Saha

J Indian Soc Pedod Prev Dent. Apr-Jun 2021;39(2):214-220. doi: 10.4103/JISPPD.JISPPD_194_20.

Background: Cerebral palsy (CP) is a childhood debilitating condition which impairs the physical and mental ability of an individual to maintain oral health. Aim: The objective of the present study was assessment of dental neglect and burden of treatment needs of children affected with CP as compared to normal children in a tertiary care hospital in Delhi. Settings and design: A sample size of 104 children of age group of 6-14 years was selected, in which 52 children of CP (case group) and 52 normal school children (control group) were recruited. Materials and methods: Children from both groups were examined, and calculation of drug master files (DMFS), defs, oral hygiene index (OHI), and gingival index was done. The presence of trauma and malocclusion was assessed. Present caries activity was assessed by the level of Streptococcus mutans present in saliva in both groups. Treatment needs were then assessed based on intraoral findings. Statistical analysis: Data were analyzed by SPSS 20.0 software. Student's t-test and nonparametric statistical tests such as Chi-square test and Mann-Whitney test were used as per the nature of variables studied for statistical analysis with the level of significance denoted at $P < 0.05$. Results: The mean DMFS, gingival index, OHI, and treatment needs were observed to be higher in the CP group. Increased S. mutans levels were observed in saliva of CP patients. Defs score, trauma, and malocclusion were not statistically significantly higher in CP group as compared to the control group. Conclusion: Cerebral palsy group had a poor oral and gingival health, a higher DMFT and burden of treatment needs and an increased risk of further caries progression due to high caries activity indicated by increased level of salivary Streptococcus mutans than the control group.

PMID: 34341244

16. Social-Emotional Development and Associated Risk Factors in Chinese Toddlers with Cerebral Palsy
You Wu, Jianyong Tang, Yanni Chen, Yanxia Huang

Neuropsychiatr Dis Treat. 2021 Jul 24;17:2451-2463. doi: 10.2147/NDT.S308138. eCollection 2021.

Objective: This study aimed to analyze the social-emotional behaviors of Chinese toddlers with cerebral palsy and to identify the risk factors associated with these behaviors. Methods: A total of 300 Chinese toddlers and their parents were recruited in this study. A Chinese version of the Infant-Toddler Social-Emotional Assessment was used to assess the children and basic information and clinical data were collected using an author-designed questionnaire. The patients were also assessed using a coping style questionnaire and the hospital anxiety and depression scale. Multiple logistic regression analysis was performed to identify risk factors. Results: The scores of the externalizing and competence domains for Chinese toddlers with cerebral palsy at different ages were lower compared to healthy children of the same age and gender ($p<0.05$). For the boys with cerebral palsy aged between 12-17 and 18-23 months, the scores of the internalizing and dysregulation domains were significantly lower compared to the national normal ($p<0.01$). The effect of perinatal factors on the externalizing and competence domains was more significant compared to other domains, whilst the coping style of the parents significantly affected the dysregulation domain ($p=0.001$). Multivariate analysis showed that the parental emotional state, education level, coping style and perinatal factors were closely associated with the social-emotional problems of children with cerebral palsy. Conclusion: Children with cerebral palsy are more likely to have behavioral, emotional, and psychiatric issues that are mostly ignored. These children may benefit from early screening and intervention for risk factors to improve rehabilitation and long-term prognosis.

PMID: 34335026

17. Exploring participation in family activities among Serbian children with cerebral palsy and children with typical development: diversity, frequency, children's presence, and engagement
Milena Milićević

Disabil Rehabil. 2021 Aug 3;1-12. doi: 10.1080/09638288.2021.1958931. Online ahead of print.

Purpose: This study aimed to characterize the participation in family activities in two groups of children: children with cerebral palsy (CP group) and children with typical development (TD group), with regard to diversity, frequency, children's presence, and engagement. Method: The convenience sample of this descriptive and comparative cross-sectional study conducted in Serbia included 48 children with CP and 74 children with TD, aged 7-12 years. Parents completed the Child Participation in Family Activities (Child-PFA) questionnaire. Mann-Whitney U test was used for data analysing. Results: Children with CP experienced less diverse and less frequent family activities compared to children with TD, with more pronounced differences in the diversity of family activities than in their frequency. In the occurring family activities, children with CP were present in a comparable proportion as children with TD. Once in an activity, children with CP were less engaged. Conclusions: Our results confirmed that children with CP do not have the same opportunities to participate and be engaged in everyday family life activities as children with TD. Greater efforts are needed to address these differences and facilitate access to and engagement of children with CP in a variety of family activities. IMPLICATIONS FOR REHABILITATION: In comparison to children with typical development, family activities are less diverse and less frequent in families of children with cerebral palsy, and children are less engaged, specifically when activities include family's or children's social network. In line with current practice, this study confirms the importance of addressing opportunities for children with cerebral palsy to be often and more engaged in everyday family life activities. Professionals should support a family context that optimizes the engagement of children with cerebral palsy in activities with other family members, thus providing them everyday natural learning opportunities.

PMID: 34342549

18. Functional development in children with cerebral palsy in Uganda: population-based longitudinal cohort study
Carin Andrews, Lukia Namaganda, Ann-Christin Eliasson, Angelina Kakooza-Mwesige, Hans Forssberg

Dev Med Child Neurol. 2021 Aug 4. doi: 10.1111/dmcn.14996. Online ahead of print.

Aim: To follow the functional development of a population-based cohort of children with cerebral palsy (CP) in rural Uganda and compare their development with the developmental trajectories of children from high-income countries (HIC). Method: Eighty-one children (33 females, 48 males) aged 2 to 17 years (mean 8y 6mo, SD 4y 6mo) with CP were initially assessed in 2015 and then 4 years later using the 66-item Gross Motor Function Measure (GMFM-66), Pediatric Evaluation of Disability Inventory, Ugandan version (PEDI-UG), and functional classification systems. We calculated actual and reference scores (level of deviation from the developmental trajectories in HIC). A Wilcoxon signed-rank test was used for statistical analyses. Results: Children and young people with CP in Uganda exhibited no differences in scores between the first and second assessments for the GMFM-66 and PEDI-UG mobility skills, whereas they exhibited increased PEDI-UG social function ($p<0.001$) and self-care skills scores ($p<0.001$). Reference scores were more negative at the second assessment than at the first for the GMFM-66 ($p=0.002$) and PEDI-UG mobility ($p=0.036$) but not for PEDI-UG self-care. The increased difference in reference scores over the 4 years was primarily driven by younger children (2-5y) and children with milder impairments. Interpretation: The increased difference in reference scores between assessments suggests that children with CP in Uganda develop motor skills at a slower rate than peers in HIC. Limited access to health care and rehabilitation likely contributed to the lower scores and slower rate of development.

PMID: 34346507

19. Evaluation of immunization status in patients with cerebral palsy: a multicenter CP-VACC study
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Eur J Pediatr. 2021 Aug 5. doi: 10.1007/s00431-021-04219-4. Online ahead of print.

Children with chronic neurological diseases, including cerebral palsy (CP), are especially susceptible to vaccine-preventable infections and face an increased risk of severe respiratory infections and decompensation of their disease. This study aims to examine age-appropriate immunization status and related factors in the CP population of our country. This cross-sectional

prospective multicentered survey study included 18 pediatric neurology clinics around Turkey, wherein outpatient children with CP were included in the study. Data on patient and CP characteristics, concomitant disorders, vaccination status included in the National Immunization Program (NIP), administration, and influenza vaccine recommendation were collected at a single visit. A total of 1194 patients were enrolled. Regarding immunization records, the most frequently administrated and schedule completed vaccines were BCG (90.8%), hepatitis B (88.9%), and oral poliovirus vaccine (88.5%). MMR was administered to 77.3%, and DTaP-IPV-HiB was administered to 60.5% of patients. For the pneumococcal vaccines, 54.1% of children received PCV in the scope of the NIP, and 15.2% of children were not fully vaccinated for their age. The influenza vaccine was administered only to 3.4% of the patients at any time and was never recommended to 1122 parents (93.9%). In the patients with severe (grades 4 and 5) motor dysfunction, the frequency of incomplete/none vaccination of hepatitis B, BCG, DTaP-IPV-HiB, OPV, and MMR was statistically more common than mild to moderate (grades 1-3) motor dysfunction ($p = 0.003$, $p < 0.001$, $p < 0.001$, $p < 0.00$, and $p < 0.001$, respectively). Physicians' influenza vaccine recommendation was higher in the severe motor dysfunction group, and the difference was statistically significant ($p = 0.029$).Conclusion: Children with CP had lower immunization rates and incomplete immunization programs. Clinicians must ensure children with CP receive the same preventative health measures as healthy children, including vaccines. What is Known: • Health authorities have defined chronic neurological diseases as high-risk conditions for influenza and pneumococcal infections, and they recommend vaccines against these infections. • Children with CP have a high risk of incomplete and delayed immunization, a significant concern given to their increased healthcare needs and vulnerability to infectious diseases. What is New: • Influenza vaccination was recommended for patients hospitalized due to pneumonia at a higher rate, and patients were administered influenza vaccine more commonly. • Children with CP who had higher levels of motor dysfunction (levels 4 and 5) were more likely to be overdue immunizations.

PMID: 34355277

20. Mutation in ZDHHC15 Leads to Hypotonic Cerebral Palsy, Autism, Epilepsy, and Intellectual Disability
Sara A Lewis, Somayeh Bakhtiari, Jennifer Heim, Patricia Cornejo, James Liu, Aris Huang, Andrew Musmacker, Sheng Chih Jin, Kaya Bilguvar, Sergio R Padilla-Lopez, Michael C Kruer

Neurol Genet. 2021 Jul 29;7(4):e602. doi: 10.1212/NXG.0000000000000602. eCollection 2021 Aug.

Objective: To determine whether mutations reported for ZDHHC15 can cause mixed neurodevelopmental disorders, we performed both functional studies on variant pathogenicity and ZDHHC15 function in animal models. Methods: We examined protein function of 4 identified variants in ZDHHC15 in a yeast complementation assay and locomotor defects of loss-of-function genotypes in a Drosophila model. Results: Although we assessed multiple patient variants, only 1 (p.H158R) affected protein function. We report a patient with a diagnosis of hypotonic cerebral palsy, autism, epilepsy, and intellectual disability associated with this bona fide damaging X-linked variant. Features include tall forehead with mild brachycephaly, down-slanting palpebral fissures, large ears, long face, facial muscle hypotonia, high-arched palate with dental crowding, and arachnodactyly. The patient had mild diminished cerebral volume, with left-sided T2/FLAIR hyperintense periatrial ovoid lesion. We found that loss-of-function mutations in orthologs of this gene cause flight and coordinated movement defects in Drosophila. Conclusions: Our findings support a functional expansion of this gene to a role in motor dysfunction. Although ZDHHC15 mutations represent a rare cause of neurodevelopmental disability, candidate variants need to be carefully assessed before pathogenicity can be determined.

PMID: 34345675

21. Push versus gravity for intermittent bolus gavage tube feeding of preterm and low birth weight infants
Jennifer A Dawson, Ravinder Summan, Nadia Badawi, Jann P Foster

Review Cochrane Database Syst Rev. 2021 Aug 4;8:CD005249. doi: 10.1002/14651858.CD005249.pub3.

Background: Many small, sick, and preterm infants are unable to co-ordinate sucking, swallowing, and breathing, and therefore require gavage feeding. In gavage feeding, milk feeds are delivered through a tube passed via the nose or the mouth into the stomach. Intermittent bolus milk feeds may be administered by a syringe to gently push milk into the infant's stomach (push feed). Alternatively, milk can be poured into a syringe attached to the tube and allowed to drip in by gravity (gravity feed). Objectives: To determine whether use of push feeding compared with gravity feeding results in more rapid establishment of full gavage feeds without increasing adverse events among preterm or low birth weight infants, or both, who require intermittent bolus tube feeding. Search methods: We used the standard search strategy of Cochrane Neonatal to search the

Cochrane Central Register of Controlled Trials (CENTRAL; 2020, Issue 7), in the Cochrane Library; Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Daily and Versions(R); and the Cumulative Index to Nursing and Allied Health Literature (CINAHL), on 30 July 2020. We also searched clinical trials databases and the reference lists of retrieved articles for randomised controlled trials (RCTs) and quasi-RCTs. Selection criteria: We included RCTs and quasi-RCTs comparing push versus gravity intermittent gavage tube feeding in preterm (less than 37 weeks' gestation) or low birth weight (less than 2500 grams) infants, or both. Data collection and analysis: We assessed the methods of trials regarding blinding of randomisation and outcome measurement. We evaluated treatment effects with a fixed-effect model using risk ratio (RR), relative risk reduction, risk difference (RD), and number needed to treat for an additional beneficial outcome (NNTB) for categorical data; and using mean, standard deviation, and mean difference (MD) for continuous data. We analysed outcomes measured as count data, for example, frequency of apnoea, bradycardia, and episodes of pulse oximeter oxygen (SpO_2) desaturation, by comparing rates of events and the rate ratio. We evaluated heterogeneity to help determine the suitability of pooling results. We used the GRADE approach to assess the certainty of evidence. Main results: One small cross-over trial (31 infants) met the criteria for inclusion in this review. The certainty of evidence for all outcomes was very low due to imprecision of estimates, wide confidence intervals, and unclear risk of bias. The primary outcome - time taken to establish full gavage feeding (days) and feeding intolerance (number of episodes per day) - was not reported in the included study. The evidence is very uncertain about the effects of push versus gravity intermittent gavage tube feeding on all other outcomes. Investigators reported respiratory rate (breaths per minute) at completion of feeding (MD 0.58, 95% confidence interval (CI) -5.97 to 7.13; 1 study, 31 participants; very low-certainty evidence); respiratory rate (breaths per minute) 10 to 30 minutes after completion of feeding (MD 3.1, 95% CI -3.43 to 9.63; 1 study, 31 participants; very low-certainty evidence); heart rate (beats per minute) at completion of feeding (MD 2.6, 95% CI -9.71 to 4.51; 1 study, 31 participants; very low-certainty evidence); and heart rate (beats per minute) 10 to 30 minutes after completion of feeding (MD 2.4, 95% CI -9.16 to 4.36; 1 study, 31 participants; very low-certainty evidence). We are very uncertain of the effects of push versus gravity intermittent gavage feeding on respiratory rate during and after feeding. Authors' conclusions: We do not have sufficient evidence to determine the effects of intermittent bolus gavage feeding for preterm and low birth weight infants. The single small study of 31 infants comparing effects of push versus gravity bolus gavage feeding did not report the primary outcome identified in this review. Thus, evidence is insufficient to show whether use of push compared with gravity gavage feeding results in more rapid establishment of full gavage feeds without increasing adverse events in preterm or low birth weight infants who receive intermittent bolus gavage feeding. In addition, the included study was too small to measure potential adverse events that can occur during gavage tube feeding, for example, episodes of oxygen desaturation, apnoea, or bradycardia.

PMID: 34346056

22. Haematological issues in neonates with neonatal encephalopathy treated with hypothermia
Eman Isweisi, Carmel Maria Moore, Tim Hurley, Martha Sola-Visner, Naomi McCallion, Fionnuala Ni Ainle, Zunera Zareen, Deirdre U Sweetman, Anna E Curley, Eleanor J Molloy, Newborn Brain Society Guidelines and Publications Committee

Review Semin Fetal Neonatal Med. 2021 Jul 22;101270. doi: 10.1016/j.siny.2021.101270. Online ahead of print.

Neonatal encephalopathy (NE) is associated with abnormality of neurological function and involves multiorgan dysfunction. There are long-term complications such as cerebral palsy and developmental delay. Cardiac, renal, neurological and other organ dysfunctions are well described. Haematological dysfunction is relatively common and includes anaemia, thrombocytopenia, monocyte and neutrophil activation, hypofibrinogenemia and coagulopathy. There is a lack of consensus definitions of hematological parameters and optimal levels for intervention due to the lack of interventional studies in term neonates and the lack of knowledge of the optimal values during therapeutic hypothermia. However, derangements in hematological values are also associated with neurodevelopmental outcomes. This article outlines the different hematological complications associated with NE and therapeutic hypothermia and suggests a framework for management.

PMID: 34330681

23. Standardized Neurodevelopmental Surveillance of High-risk Infants Using Telehealth: Implementation Study during COVID-19
Nathalie L Maitre, Kristen L Benninger, Mary Lauren Neel, Jennifer A Haase, Lindsay Pietruszewski, Katelyn Levengood, Kathleen Adderley, Nancy Batterson, Kaleigh Hague, Megan Lightfoot, Sarah Weiss, Dennis J Lewandowski, Heather Larson

Pediatr Qual Saf. 2021 Jul 28;6(4):e439. doi: 10.1097/pq9.0000000000000439. eCollection Jul-Aug 2021.

Introduction: Neurodevelopmental surveillance is critical for high-risk infants following neonatal intensive care discharge and

is traditionally performed in-person. COVID-19 interruption of regular surveillance necessitated a rapid development of telehealth models for effective and standardized care. Methods: We used implementation science and lean methodologies to develop an effective telehealth neurodevelopmental surveillance program for high-risk infants. Interventions included reorganization of visit flow processes and a telehealth toolkit for standardized neurological and developmental assessments. We tested and improved our intervention through plan-do-study-act cycles, value-added analysis, and parent- and provider-satisfaction questionnaires. Process metrics (standard elements, subspecialty referrals, diagnostic tests, and prescriptions ordered) were compared in group-level analyses between telehealth patients (N = 97) March 16, 2020-July 1, 2020 and a matched in-person cohort at the same period the previous year. Run charts examined shifts in balancing measures (provider efficiency and missed visits) over 8 weeks before and after implementation. Results: Primary outcomes were visit completion (100%), patient parent satisfaction (>90% strongly agreed or agreed telehealth procedures were valuable and easy to use) and ability to accurately diagnose cerebral palsy (no statistical difference with comparison visits). Providers (N = 6) rated telehealth experiences favorably. Process metrics indicated no differences between telehealth and in-person visits (all P > 0.05). Following telehealth implementation, provider efficiency increased to near baseline (median 88.9% versus 91.7%) and median missed visits decreased to 0% from 20% (in-person). Conclusions: Implementation of telehealth for neurodevelopmental surveillance in a tertiary high-risk infant follow-up clinic successfully provided standardized and timely care during stay-at-home orders; broader telehealth applications may overcome access barriers in this field.

PMID: 34345752

24. Feasibility of Early Intervention Through Home-Based and Parent-Delivered Infant Massage in Infants at High Risk for Cerebral Palsy

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Front Pediatr. 2021 Jul 19;9:673956. doi: 10.3389/fped.2021.673956. eCollection 2021.

Infant massage (IM) can be considered an early intervention program that leads to the environmental enrichment framework. The effectiveness of IM to promote neurodevelopment in preterm infants has been proved, but studies on infants with early brain damage are still lacking. The main aim of this study was to assess the feasibility, acceptability and usability of IM, carried out by parents at home, on infants at high risk for Cerebral Palsy. An IM daily diary and an ad hoc questionnaire, called Infant Massage Questionnaire Parent-Infant Experiences (IMQPE), were developed. IMQPE consisted of a total of 30 questions, divided into 5 areas. The parents were trained to carry out the IM with a home-based course, conducted by an expert therapist. The intensive IM program was set according to a defined daily length of at least 20 min, with a frequency of at least 5 days per week for a total of 8 weeks. Data collection consisted in the selection of the variables around the characteristics, both of the infants and the mothers, IM dosage and frequency, different body parts of the infants involved and IMQPE scores. Variable selection was carried out by minimizing the Bayesian Information Criteria (BIC) over all possible variable subsets. Nineteen high-risk infants, aged 4.83 ± 1.22 months, received IM at home for 8 weeks. The massage was given by the infants' mothers with a mean daily session dose of 27.79 ± 7.88 min and a total of 21.04 ± 8.49 h. 89.74% and 100% of mothers performed the IM for the minimum daily dosage and the frequency recommended, respectively. All the families filled in the IMQPE, with a Total mean score of 79.59% and of 82.22% in General Information on IM, 76.30% in Infant's intervention-related changes, 76.85% in IM Suitability, 79.07% in Infant's acceptance and 83.52% in Time required for the training. Different best predictors in mothers and in infants have been found. These data provide evidence of the feasibility of performing IM at home on infants at high risk for CP. Study registration: www.clinicaltrial.com (NCT03211533 and NCT03234959).

PMID: 34350144

25. Operationalization, measurement, and health indicators of sedentary behavior in individuals with cerebral palsy: a scoping review

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Disabil Rehabil. 2021 Jul 31;1-12. doi: 10.1080/09638288.2021.1949050. Online ahead of print.

Purpose: To explore the operationalization and measurement of sedentary behavior (SB) in individuals with cerebral palsy (CP). Materials and methods: We searched five databases from 2011 to 2020 for primary studies of experimental, qualitative, longitudinal, or observational designs measuring SB or postures typically characterized as sedentary (sitting, reclining, lying). Results: We screened 1112 citations and selected 47 studies. SB was operationalized through muscle activation, energy

expenditure or oxygen consumption in typically sedentary postures (n = 9), and through thresholds and postures used by accelerometers, activity monitors, and a questionnaire to measure time spent in SB (n = 25). Seven out of the eight studies that measured energy expenditure found ≤1.5 metabolic equivalents of task (METs) for sitting and lying. While different accelerometer thresholds were used to measure SB, the behavior (SB) was consistently operationalized as sitting and lying. Little consistency existed in the subpopulation, instruments and cut-points for studies on validity or reliability of tools for measuring SB (n = 19). Conclusions: Sitting and lying are considered sedentary postures, which is defined as ≤1.5 METs in individuals with CP. There is variability in the tools used to measure SB in individuals with CP. Therefore, consensus on the definition and reporting of SB is needed. Implications for rehabilitation: Although sedentary behavior (SB) is increased in individuals with cerebral palsy (CP) compared to the typically developing population, there is no standard definition for SB for these individuals; this makes it difficult to synthesize data across studies. Sitting and lying are ≤1.5 METs in individuals with CP, suggesting we only need to measure posture to show change in SB. The commonly used accelerometer cut-point in the typically developing population of ≤100 counts per minute generally has excellent reliability across multiple devices in ambulatory children with CP.

PMID: 34334077

26. Group A Streptococcal Septic Hip Arthritis in a Child With Spastic Triplegic Cerebral Palsy
Supriya Singh, Jacob Davidson, Timothy Carey, Michelle Barton Forbes, Megan Cashin

J Am Acad Orthop Surg Glob Res Rev. 2021 Aug 5;5(8). doi: 10.5435/JAAOSGlobal-D-20-00228.

Reports of septic hip arthritis in children with cerebral palsy are exceedingly rare. This case report describes a 10-year-old boy with spastic triplegic cerebral palsy (Gross Motor Functional Classification System), who presented with fever and irritability. This case highlights the difficulties in diagnosing septic joint arthritis in patients with cerebral palsy who are nonverbal and have limited mobility. A high index of suspicion is necessary in this population when presented with fever and new limitations in mobility.

PMID: 34351876

27. Risk Assessment for Postoperative Pneumonia in Children Living With Neurologic Impairments
Christian Mpody, Seth Hayes, Nathan Rusin, Joseph D Tobias, Olubukola O Nafiu

Pediatrics. 2021 Aug 4;e2021050130. doi: 10.1542/peds.2021-050130. Online ahead of print.

Background: Approximately one-third of all pediatric hospital charges are attributable to the care for children living with neurologic comorbidities. These children often require various surgical procedures and may have an elevated risk of lower respiratory infections because of poor neuromuscular coordination, poor cough, uncoordinated swallowing, and poor oral hygiene. Our objective was to evaluate the risk of pneumonia in children presenting with neurologic comorbidities. Methods: We performed a retrospective study of children (<18 years) who underwent inpatient surgery between 2012 and 2018 in hospitals participating in the National Surgical Quality Improvement Program. Our primary outcome was the time to incident pneumonia within the 30 days after surgery. Results: We identified 349 163 children, of whom 2191 developed pneumonia (30-day cumulative incidence: 0.6%). The presence of a preoperative neurologic comorbidity conferred approximately twofold higher risk of postoperative pneumonia (hazard ratio [HR]: 1.91, 95% confidence interval [CI]: 1.73-2.11). We explored the risk of pneumonia conferred by the components of neurologic comorbidity: cerebral palsy (HR: 3.92, 95% CI: 3.38-4.56), seizure disorder (HR: 2.93, 95% CI: 2.60-3.30), neuromuscular disorder (HR: 2.63, 95% CI: 2.32-2.99). The presence of a neurologic comorbidity was associated with a longer length of hospital stay (incidence rate ratio: 1.26, 95% CI: 1.25-1.28). Conclusions: The risk of postoperative pneumonia was almost twofold higher in children with neurologic comorbidity. The magnitude of these associations underscores the need to identify areas of research and preventive strategies to reduce the excess risk of pneumonia in children with preoperative neurologic conditions.

PMID: 34349030

28. Megalencephaly Polymicrogyria Polydactyly Hydrocephalus (MPPH): A Case Report and Review of Literature
Juan Fernando Ortiz, Samir Ruxmohan, Mahika Khurana, Jessica Hidalgo, Ivan Mateo Alzamora, Amrapali Patel

Case Reports Cureus. 2021 Jul 3;13(7):e16132. doi: 10.7759/cureus.16132. eCollection 2021 Jul.

Megacephaly polymicrogyria, polydactyly, hydrocephalus (MPPH) is an extremely rare condition caused by a defect in the AKT3, CCND2, or PIKR2 genes. Although the prevalence of the syndrome is very low, there is a significant clinical and radiological variation in the syndrome. We present a case with MPPH admitted to the hospital due to an increase in seizure frequency. The patient had a history of cerebral palsy, global developmental delay, spasticity, and hypoglycemic episodes. MRI findings revealed ventriculomegaly, polymicrogyria, abnormal encephalon, and pachygyria. The addition of clobazam and alprazolam diminished the seizures' frequency and the patient's spasticity, respectively. To highlight the clinical and radiological variation of the syndrome, we review cases of MPPH with clinical and radiological variants. Pachygyria and cerebral palsy are new associations not previously described before in MPPH. Pachygyria and cerebral palsy could be worsening the seizures and the global delay in this patient. Hypoglycemic episodes are probably related to the AKT3 gene, promoting more glucose consumption. Spasticity is most probably related to an upper motor sign due to the patient's cerebral palsy. This case highlights the clinical and radiological variation of the syndrome. More cases of MPPH need to be described to consolidate the knowledge and have a better understanding of the clinical and radiological variation of the syndrome.

PMID: 34354878

29. Neonatal Anoxia Increases Nociceptive Response in Rats: Sex Differences and Lumbar Spinal Cord and Insula Alterations
Ammir Yacoub Helou, Daniel Oliveira Martins, Bruna Petrucelli Arruda, Matheus Cerussi de Souza, Natalia Andrea Cruz Ochoa, Maria Inês Nogueira, Marucia Chacur

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Neonatal anoxia is a well-known world health problem which results in neurodevelopmental deficits, such as sensory alterations that are observed in patients with cerebral palsy and autism disorder, for which oxygen deprivation is a risk factor. Nociceptive response, as part of the sensory system, has been reported as altered in these patients. To determine whether neonatal oxygen deprivation alters nociceptive sensitivity and promotes medium- and long-term inflammatory feedback in the central nervous system, Wistar rats of around 30 h old were submitted to anoxia (100% nitrogen flux for 25 min) and evaluated on PND23 (postpartum day) and PND90. The nociceptive response was assessed by mechanical, thermal and tactile tests in the early postnatal and adulthood periods. The lumbar spinal cord (SC -L4-L6) motor neurons (MNs) and the posterior insular cortex neurons were counted and compared with their respective controls after anoxia. In addition, we evaluated the possible effect of anoxia on the expression of astrocytes in the spinal cord at adulthood. The results showed increased nociceptive responses in both males and females submitted to anoxia, although these responses were different according to the nociceptive stimulus. A decrease in MNs in adult anoxiated females and an upregulation of GFAP expression in the SC were observed. In the insular cortex, a decrease in the number of cells of anoxiated males was observed in the neonatal period. Our findings suggest that oxygen-deprived nervous systems in rats may affect their response at the sensorimotor pathways and respective controlling centers with sex differences, which were related to the used stimulus.

PMID: 34342028