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Interventions and Management

1. Test-Retest Reliability of a Static and Dynamic Motor Fatigability Protocol Using Grip and Pinch Strength in Children with Cerebral Palsy

Lieke Brauers, Rob Smeets, Peter Feys, Andrew M Gordon, Bertie Leij-Roelofsen, Caroline Bastiaenen, Eugene Rameckers, Katrijn Klingels

Phys Ther. 2022 Jul 6;pzac088. doi: 10.1093/ptj/pzac088. Online ahead of print.

Objective: The purpose of this study was to investigate the test-retest reliability, measurement error, and interpretability of new motor fatigability outcomes of grip and pinch strength for children with unilateral cerebral palsy (UCP). **Methods:** Motor fatigability during grip and pinch strength was measured twice (within 48 hours) in both hands of 50 children (mean age = 11 years 2 months; 14, 31, and 5 children with Manual Ability Classification System levels I, II, and III, respectively) using a 30-second static and dynamic maximum-exertion protocol. For static motor fatigability, the Static Fatigue Index (SFI) and mean force (Fmean) in the first (Fmean1) and last (Fmean3) 10 seconds were calculated. For dynamic motor fatigability, Fmean1, Fmean3, and the number of peaks in the first (Npeaks1) and last (Npeaks3) 10 seconds were calculated. **Results:** For static motor fatigability, the ICCs were moderate to high for Fmean1 and Fmean3 (0.56-0.88), and the SFI showed low to moderate reliability (ICC = 0.32-0.72). For dynamic motor fatigability, the ICCs were moderate to high for all outcomes (0.54-0.91). The standard error of measurement agreement and the smallest detectable difference agreement were large in all outcomes, except for the SFI in static motor fatigability. Details per age group are provided. In general, younger children (6-11 years old) showed lower reliability than older children (12-18 years old). **Conclusion:** Most outcome measures for static and dynamic motor fatigability of grip and pinch strength show moderate to high reliability in children with UCP, indicating that they can be used reliably to investigate the presence of motor fatigability in UCP, especially in older children. Standard Error of Measurement agreement and Smallest Detectable Difference agreement indicated that these outcome measures should be interpreted with caution when evaluating change.

PMID: [35793460](https://pubmed.ncbi.nlm.nih.gov/35793460/)

2. Characteristics of sit-to-stand movement are associated with trunk and lower extremity selective control in children with cerebral palsy: a cross-sectional study

Dilara Gunes, Evrim Karadag-Saygi, Esra Giray, Sefa Kurt

Int J Rehabil Res. 2022 Jul 4. doi: 10.1097/MRR.0000000000000541. Online ahead of print.

Even though the effect of several factors on sit-to-stand (STS) performance of children with CP has been previously explored, the potential role of lower extremity selective control, trunk control and sitting function on the performance of STS has not been examined. This study aimed to investigate the association of trunk control and lower extremity selective motor control

with STS performance in children with CP. We recruited 28 children with CP aged between 4 and 10 years whose Gross Motor Function Classification System levels were I and II and 32 age-matched typically developing (TP) children. Trunk control, sitting function, selective control of the lower extremities and STS were evaluated with Trunk Control Measurement Scale (TCMS), sitting section of Gross Motor Function Measure-88 (GMFM-88), Selective Control Assessment of the Lower Extremity (SCALE) and the STS outcomes of a force platform [weight transfer time, rising index, and center of gravity (COG) sway velocity], respectively. In all evaluations, children with CP demonstrated lower scores than TD children. A moderate correlation was found between total scores of TCMS, GMFM-88 sitting section scores and COG sway velocity during STS and a fair correlation between SCALE total scores and COG sway velocity in the CP group ($r = -0.51$, $r = -0.52$, $r = -0.39$, respectively). A fair correlation was found between SCALE total scores and the weight transfer time during STS in children with CP ($r = -0.39$). Based on these results, improving trunk and lower extremity selective control may enhance STS performance in children with CP.

PMID: [35777970](#)

3. A retrospective cohort study about hip luxation in non-ambulatory cerebral palsy patients: The point of no return

Silvia Faccioli, Silvia Sassi, Elena Corradini, Francesca Toni, Shaniko Kaleci, Francesco Lombardi, Maria Grazia Benedetti

J Child Orthop. 2022 Jun;16(3):227-232. doi: 10.1177/18632521221106361. Epub 2022 Jun 30.

Purpose: The migration percentage is a widely used criterion for surgery in displaced hips. Literature suggests that no hip can spontaneously improve if the migration percentage exceeds 45%, in a mixed population of cerebral palsy children. The aim of the present article was to identify the point of no return of the migration percentage in a selected sample of non-ambulatory cerebral palsy children, being the most exposed to hip luxation. **Methods:** This single-center retrospective cohort study included patients with spastic or dyskinetic cerebral palsy, Gross Motor Function Classification System level IV or V, age 0-18, having at least three pelvic radiographies, excluding radiographies relative to hips having previously undergone surgery. The following information was collected: sex, cerebral palsy subtype, Gross Motor Function Classification System level, presence of drug-resistant epilepsy, migration percentage, age at assessment, use of walking or standing assistive devices, previous botulinum injection, oral or intrathecal baclofen, and hip pain. Data were analyzed at the level of the individual hips. Descriptive statistics were presented. Receiver operating characteristic curve analysis was conducted to investigate which value of the migration percentage could be adopted as the "point of no return": that is, the cutoff value beyond which no migration percentage reduction, by more than 5%, could be expected. **Results:** The optimal cutoff value was identified as migration percentage $\geq 50\%$, with a sensitivity of 84.5% and a specificity of 100% (p -value < 0.001). **Conclusion:** Based on the present study, migration percentage $\geq 50\%$ is the "point of no return" for Gross Motor Function Classification System IV-V cerebral palsy patients, representing the cutoff value beyond which no spontaneous cerebral palsy reduction may be expected, unless addressing surgery. Level of evidence: level II-retrospective study.

PMID: [35800654](#)

4. Analysis of mechanical energy in thigh, calf and foot during gait in children with cerebral palsy

Wei Hua, Sadiq Nasir, Graham Arnold, Weijie Wang

Med Eng Phys. 2022 Jul;105:103817. doi: 10.1016/j.medengphy.2022.103817. Epub 2022 May 10.

Background: Many studies on children with cerebral palsy (CP) have focused on metabolic energy, however research on the mechanical energy in the lower limbs is sparse. **Research question:** What differences of mechanical energies in the lower limbs exist between the children with CP and typically developing (TD) children during gait? The purpose of this research was to analyse the mechanical energy changes of the lower limbs of children with CP during walking and compare them with TD children. **Methods:** Twelve children with CP including 8 diplegic and 4 hemiplegic without severity levels (aged 4-22 year old) and 14 TD participants (aged 5-15 year old) walked barefoot in a gait lab where a motion capture system collected marker data during walking. The translational and rotative kinetic energy and potential energy in the thigh, calf and foot were then calculated using the marker data. Gait parameters, e.g., stride frequency, pace, stride length, stride width, were also obtained. **Findings:** The results show that the children with CP had significantly lower values than the TD group in terms of kinetic energy and potential energy. This was especially seen in the thigh where the energy recovery coefficient in the children with CP was 31% compared with 43% in the TD group. In the calf and foot, the CP and TD groups had similar energy recovery to the TD group, i.e. not significantly different clinically. The gait parameters showed that children with CP had slower walking speed, shorter stride length, larger step width than TD but similar cadence to TD. **Interpretation:** The energy recovery

coefficient represents the efficiency of exchanges of kinetic and potential energies. The higher its value, the better the energy use during gait. Significance: This study concluded that CP gait is weaker in the use of energy than TD gait. To our best knowledge, this study is the first one to analyse mechanical energy changes in the lower limbs for CP and TD groups during gait.

PMID: [35781382](#)

5. Repetitive Peripheral Magnetic Stimulation to Improve Ankle Function and Gait in Cerebral Palsy at Adulthood: An open-label Case Study

Janie Provencher, Éva Marion Beaulieu-Guay, Sophy Desbiens Loranger, Cyril Schneider

Brain Res. 2022 Jun 30;147999. doi: 10.1016/j.brainres.2022.147999. Online ahead of print.

Repetitive peripheral magnetic stimulation (rPMS) is noninvasive and painless. It drives plasticity of the primary motor cortex (M1) in children with cerebral palsy (CP) and this improves the ankle function and gait. Our study explored whether rPMS of muscles could influence motricity in an adult CP case. A 30-year-old woman with mixed CP participated in four sessions (S1 to S4, one per week) where rPMS was applied bilaterally on leg and trunk muscles (tibialis anterior-TA, hamstrings, transverse abdominis, paraspinal multifidus). Clinical scores and M1 excitability (probed by transcranial magnetic stimulation) were tested at pre-rPMS at S1 (baseline) and S4, then 40 days later (follow-up). The active ankle dorsiflexion was significantly increased and the plantar flexors resistance to stretch reduced as compared to baseline. The improvement of the ankle function was carried-over to the quality of locomotor patterns. Changes persisted until follow-up and were paralleled by drastic changes of M1 excitability. These original findings of rPMS influence on M1 plasticity and motricity are promising for the functional improvement of adult people living with CP and should be replicated in larger-sampled studies.

PMID: [35780866](#)

6. PROMPT to improve speech motor abilities in children with cerebral palsy: a wait-list control group trial protocol

S Fiori, C Ragoni, I Podda, A Chilosi, C Amador, P Cipriani, A Guzzetta, G Sgandurra

BMC Neurol. 2022 Jul 6;22(1):246. doi: 10.1186/s12883-022-02771-6.

Background: Children with cerebral palsy (CP) often have communication impairments, including speech altered intelligibility. Multiple levels of disrupted speech have been reported in CP, which negatively impact on participation and quality of life, with increase of care needs. Augmentative Alternative Communication (AAC) is an option, with debated benefits and limitations, in particular for its functional use. This is supported by a substantial lack of defined evidences in favor of direct speech articulation intervention in CP. Motor learning-based interventions are effective in CP and are the basis of speech motor interventions such as PROMPT (Prompts for Restructuring Oral Muscular Phonetic Targets). The PROMPT speech motor treatment provides tactile-kinesthetic inputs to facilitate articulatory movements by dynamic modelling, resulting in more efficient motor patterns that can be integrated into speech and communication. In CP, exploratory evidences support the feasibility and preliminarily advantages on intelligibility of motor speech treatments, such as PROMPT, with increased speech motor control, also documented by kinematic analyses. **Methods:** A randomized waitlist-control trial will be conducted in children aged between 3- and 10-years having CP and dysarthria (estimated sample size = 60 children). Children will be allocated in the immediate intervention or in the waitlist control group. The intervention consists of an intensive 3 weeks period of twice-a-day administration of PROMPT. Standard care will be administered in the control (waitlist) group. After repeated baseline assessments (T0), the PROMPT treated group will undergo the experimental 3-week intervention period, with T1 assessment at the end. A further T2 assessment will be provided at medium term (3 months after the end of the intervention) for evaluating the stability of intervention. Primary and secondary speech clinical and kinematics outcome measures will be collected at T0, T1 and T2. **Discussion:** This paper describes the study protocol consisting of a RCT with two main objectives: (1) to evaluate the or short-term benefits of an intensive speech motor intervention on speech and intelligibility in children with CP and the stability of the intervention at medium term; (2) to describe the kinematic correlates of speech motor control modifications. Trial registration: Trial registration date 06/12/2019; ClinicalTrials.gov Identifier: NCT04189159.

PMID: [35794522](#)

7. Multimorbidities and quality of life in adult cerebral palsy over 40 years

Bilinc Dogruoz Karatekin, Afitap İcagasioglu, Seyma Nur Sahin, İsmail Hakan Akbulut, Ozge Pasin

Acta Neurol Belg. 2022 Jul 2. doi: 10.1007/s13760-022-01958-5. Online ahead of print.

Aim: This study aimed to describe the most common combinations of comorbidities and their relationship to quality of life in a sample of adults over 40 years of age with cerebral palsy. **Methods:** Patients who are 40 years or older and admitted to the hospital in the last 5 years and were diagnosed with cerebral palsy were included. Demographic data and comorbidities were both questioned through the Patient Information Management System and confirmed by asking the individual about their diseases. The patients' quality of life was evaluated with the EQ-5D-3L Telephone interview version. Principal component analysis was used to determine comorbidity combinations for multiple morbidity. **Results:** Comorbidity was found in 72.1% of the participants and multimorbidity was found in 47.5%. The 5 most common comorbidities were musculoskeletal diseases (34.4%), psychiatric diseases (21.3%), essential hypertension (21.3%), osteoporosis (18%) and hyperlipidemia (18%). As a result of principal component analysis, a total of five components are formed and this most common comorbidity combinations in the sample explained 66.78% of the total variance. **Conclusions:** New combinations of comorbidities have been demonstrated that may perhaps serve as a starting point for identifying new association of pathways. Future efforts are needed to identify modifiable factors for early intervention and prevention of chronic health problems in this population.

PMID: [35780206](#)

8. Effects of Augmented Reality Interventions on the Function of Upper Extremity and Balance in Children With Spastic Hemiplegic Cerebral Palsy: A Randomized Clinical Trial

Wardah Hussain Malick, Rizwana Butt, Waqar Ahmed Awan, Muhammad Ashfaq, Qamar Mahmood

Front Neurol. 2022 Jun 21;13:895055. doi: 10.3389/fneur.2022.895055. eCollection 2022.

Objective: To determine the effects of augmented reality (AR) interventions on the function of the upper extremity (UE) and balance in children with spastic hemiplegic cerebral palsy (SHCP). **Methods:** In total, 30 children with SHCP, aged 6 to 12 years, were randomly divided into three interventional groups. Each group received an AR game, i.e., Balance It, Bubble Pop, or Scoop'd (WonderTree, Pakistan). The UE function and balance were assessed at the baseline and after 8 weeks of intervention through the Disability of Arm, Shoulder, and Hand (DASH) questionnaire and Pediatric Balance Scale (PBS), respectively. The mixed ANOVA was used to determine the combined with-in and between-the-groups differences in the function of the upper extremity. The Wilcoxon sign ranked test was used for with-in group changes, while the Kruskal Wallis test with the bonferroni correction post-hoc analysis was used to compare the groups in terms of balance. The data were analyzed by using SPSS version 21 and the level of significance was set at $p < 0.05$. Paired sample t-test and Wilcoxon signed-rank test was used for analyzing the changes in the total DASH and PBS scores within the groups, respectively. One-way ANOVA was used to determine the differences between the groups in the total DASH and PBS scores, while the Kruskal Wallis test was used for the differences between the groups in the PBS items. The data were analyzed by using SPSS version 21. **Results:** All the groups improved significantly in the total DASH and PBS scores post-intervention. A significant difference was determined in standing with one foot in front between Bubble Pop and Balance It groups ($p = 0.03$). The total score of PBS also showed a significant difference between Bubble Pop and Balance It groups ($p = 0.02$). **Conclusion:** The AR interventions used in this study were found to be effective in improving the UE function and balance of children with SHCP. The Balance It game showed more promising results in improving the balance as compared with the other games, however, no significant difference was determined between the three AR games in terms of the UE function of the participants.

PMID: [35800080](#)

9. Application of Space Technologies Aimed at Proprioceptive Correction in Terrestrial Medicine in Russia

Eugenia Motanova, Maria Bekreneva, Ilya Rukavishnikov, Tatiana A Shigueva, Alina A Saveko, Elena S Tomilovskaya

Review Front Physiol. 2022 Jun 16;13:921862. doi: 10.3389/fphys.2022.921862. eCollection 2022.

Space technologies greatly contributed not only to space medicine but also to terrestrial medicine, which actively involves these technologies in everyday practice. Based on the existing countermeasures, and due to similarities of sensorimotor

alterations provoked by the weightlessness with various neurological disorders, a lot of work has been dedicated to adaptation and introduction of these countermeasures for rehabilitation of patients. Axial loading suit and mechanical stimulation of the soles' support zones are used in mitigation of stroke and traumatic brain injury consequences. They are also applied for rehabilitation of children with cerebral palsy. Complex application of these proprioceptive correction methods in neurorehabilitation programs makes it possible to effectively treat neurological patients with severe motor disturbances and significant brain damage.

PMID: [35784861](#)

10. The implementation of systematic monitoring of cognition in children with cerebral palsy in Sweden and Norway

Maja Knudsen, Kristine Stadskleiv, Elisabeth O'Regan, Ann I Alriksson-Schmidt, Guro L Andersen, Sandra Julsen Hollung, Åsa Korsfelt, Pia Ödman

Disabil Rehabil. 2022 Jul 6;1-10. doi: 10.1080/09638288.2022.2094477. Online ahead of print.

Purpose: Children with cerebral palsy (CP) are at risk of cognitive impairments and need to be cognitively assessed to allow for individualized interventions, if applicable. Therefore, a systematic protocol for the follow-up of cognition in children with CP, CPCog, with assessments offered at five/six and 12/13 years of age, was developed. This report presents and discusses assessment practices in Sweden and Norway following the introduction of CPCog and a quality improvement project in Norway aimed at increasing the number of children offered cognitive assessments. **Materials and methods:** A questionnaire investigating assessment practices was sent to pediatric habilitation centers in Sweden and Norway. In Norway, the habilitation centers also participated in a quality improvement project aimed at increasing adherence to the CPCog protocol. **Results:** Of the respondents, 64-70% report that they assess cognition in children with all degrees of motor impairment, and 70-80% assess at the ages recommended in CPCog. Following the quality improvement project in Norway, the percentage of children assessed increased from 34 to 62%. **Conclusions:** The findings illustrate that the provision of information is not sufficient to change practice. Implementation of new re/habilitation procedures is aided by targeting health care practices individually. **Implications for rehabilitation:** Children with cerebral palsy (CP) have increased risk of cognitive impairments that require intervention. Assessments of cognition should be offered to all children with CP because the nature of cognitive impairments may vary. Introducing a follow-up protocol of how and when to perform cognitive assessments is a step towards ensuring equal access to the services for all children with CP. A quality improvement project might be a viable method for implementing a protocol into everyday clinical practice.

PMID: [35793099](#)

11. Parental decisions to divorce and have additional children among families with children with cerebral palsy: Evidence from Swedish longitudinal and administrative data

Vibeke Müller, Ulf Gerdtham, Ann Alriksson-Schmidt, Johan Jarl

Health Econ. 2022 Jul 1. doi: 10.1002/hec.4567. Online ahead of print.

This study analyzes the relationship of having a child with the early-onset disability cerebral palsy (CP) and the parental decision to divorce and to have additional children. We use longitudinal matched case-control data from multiple linked Swedish National Population Registers between 2001 and 2015 and perform Cox proportional hazards regressions with interval-censoring. Although we do not find a general excess parental divorce risk on CP relative to the comparison group without CP, we find that having a child with CP increases the risk of divorce for parents with low education. We also find that having a child with CP reduces the likelihood of having additional children, especially for mothers in the older age range (maternal age at delivery >33 years) and parents with low education. The severity level of the disability, as indicated by gross motor function, is not related to the results. These findings should be understood in the Swedish context, which provides extensive welfare support (e.g., personal assistance). If future studies would find adverse results in countries with less social care and benefits, our results may indicate that it is possible to mitigate negative consequences for the family of a child with disability.

PMID: [35778857](#)

12. Sequence of flexion contracture development in the lower limb: a longitudinal analysis of 1,071 children with cerebral palsy

Erika Clodt, Anna Lindgren, Henrik Lauge-Pedersen, Elisabet Rodby-Bousquet

BMC Musculoskelet Disord. 2022 Jul 2;23(1):629. doi: 10.1186/s12891-022-05548-7.

Background: To prevent severe contractures and their impact on adjacent joints in children with cerebral palsy (CP), it is crucial to treat the reduced range of motion early and to understand the order by which contractures appear. The aim of this study was to determine how a hip-knee or ankle contracture are associated with the time to and sequence of contracture development in adjacent joints. **Methods:** This was a longitudinal cohort study of 1,071 children (636 boys, 435 girls) with CP born 1990 to 2018 who were registered before 5 years of age in the Swedish surveillance program for CP and had a hip, knee or ankle flexion contracture of $\geq 10^\circ$. The results were based on 1,636 legs followed for an average of 4.6 years (range 0-17 years). The Cox proportional-hazards model adjusted for Gross Motor Function Classification System (GMFCS) levels I-V was used to compare the percentage of legs with and without more than one contracture. **Results:** A second contracture developed in 44% of the legs. The frequency of multiple contractures increased with higher GMFCS level. Children with a primary hip or foot contracture were more likely to develop a second knee contracture. Children with a primary knee contracture developed either a hip or ankle contracture as a second contracture. **Conclusions:** Multiple contractures were associated with higher GMFCS level. Lower limb contractures appeared in specific patterns where the location of the primary contracture and GMFCS level were associated with contracture development in adjacent joints.

PMID: [35780097](#)

13. Access, use and satisfaction with physiotherapy services among adults with cerebral palsy living in the United Kingdom and Ireland

Manjula Manikandan, Elizabeth Cassidy, Gemma Cook, Cherry Kilbride, Claire Kerr, Aisling Walsh, Michael Walsh, Jennifer M Ryan

Disabil Rehabil. 2022 Jul 4;1-9. doi: 10.1080/09638288.2022.2087760. Online ahead of print.

Purpose: The aims of this study were to describe how and why adults with CP living in the UK and Ireland accessed and used physiotherapy services; to describe the type of physiotherapy accessed and satisfaction with physiotherapy services and to examine the associations between relevant factors. **Methods:** A cross-sectional semi-structured online survey was employed. Participants were adults with CP aged 18 and above living in the UK and Ireland; able to complete an online questionnaire in English independently or with technical or physical assistance. Data were collected from April 2019 to February 2020. **Results:** Participants (n = 162) were aged 18-74 years. The majority were female (75%) and lived in the UK (83%). Ninety percent of participants reported a need for physiotherapy but only 35% received physiotherapy services. The most common reason for visiting physiotherapy was mobility decline (62%). Satisfaction with the availability and quality of physiotherapy services were 21% and 27%, respectively. Adults with scoliosis and mobility decline were less likely to report that they received the physiotherapy they needed. **Conclusion:** Adults with CP did not receive the physiotherapy services that they perceived they needed. There is a need to develop physiotherapy services in collaboration with people living with CP. **Implications of rehabilitation:** Adults with cerebral palsy (CP) needed physiotherapy services, but were not receiving the physiotherapy services that they perceive they needed. Adults were not satisfied with the availability or quality of physiotherapy services received. Adults with scoliosis and mobility decline were less likely to report that they received the physiotherapy they needed. There is a need to develop physiotherapy services from a life-span perspective for adults living with CP.

PMID: [35786164](#)

14. Clinic Follow up and Neurological Disability in Children Following Pregnancies Complicated by Preterm Rupture of Membranes and Preeclampsia

Laura Paulson, Dianne Thornhill, Jennifer Armstrong

J Child Dev Disord. 2021;7(5):2. Epub 2021 May 31.

Context: Preeclampsia and preterm premature rupture of membranes (PPROM) have been associated with perinatal brain

injury. Despite a strong understanding of the relationships between preterm birth and neurologic deficits, and between PPROM and preeclampsia and preterm birth, the relationship between PPROM and preeclampsia and neurologic disability is not well characterized. Objective: We compared trends in neurologic deficits in children born to mothers with these conditions and described differences in patient characteristics among follow up visit attendance. Methods: We conducted a prospective cohort study of women with preeclampsia or PPROM. Neurologic deficits were assessed with the Pediatric Stroke Outcome Measure at follow up visits through age 10 years. Eighty nine of the 178 women enrolled completed at least one follow up. Results: Among children born >32 weeks, PPROM showed higher left and right sided sensorimotor deficits at initial follow (p=0.045, p=0.01). In children born ≤ 32 weeks, preeclampsia had higher language production deficits at 3 year follow up (p=0.05). Sensorimotor deficits were greater and sustained in PPROM. Language production deficits were predominant among after 2 years of age in preeclampsia. Racial disparities were found in clinic attendance rates, with Black families most affected. Conclusion: Differences in neurodevelopmental patterns suggest differences in underlying neuronal injuries. Neurologic assessment should occur routinely throughout early childhood to detect delayed deficits after PPROM and preeclampsia and ensure inclusion of underserved or at risk populations.

PMID: [35782107](#)

15. Verification of the ability of the new MRI classification system to predict neurodevelopmental outcome in very low-birth-weight infants

Masakazu Nishimoto, Katsumi Hayakawa, Koichi Tanda, Daisuke Kinoshita, Akira Nishimura, Zenro Kizaki, Kei Yamada

Brain Dev. 2022 Jul 4;S0387-7604(22)00106-1. doi: 10.1016/j.braindev.2022.06.005. Online ahead of print.

Background: Very low-birth-weight infants (VLBWI) are at high risk for adverse neurodevelopmental outcomes. A new, feasible and practical classification system for white matter injury has been reported by Martinez-Biarge et al. Therefore, we investigated the relationship between white matter injury and neurodevelopmental outcomes using this system. Materials and methods: We enrolled a consecutive series of VLBWI birth weights <1500 g between 2012 and 2015. Two radiologists evaluated the brain MRI obtained in the VLBWI at term-equivalent age. MRI findings were classified into six Grades (Grade 0, Ia, Ib, II, III, IV). The frequency of abnormalities in each Grade was examined. The neurodevelopmental outcome of the VLBWI was assessed at two years or older, and we investigated the presence of cerebral palsy (CP) and intellectual disability (ID), and other serious outcomes. We also calculated the simple kappa value before the raters were matched. Results: Among 167 VLBWI, 131 met the eligibility criteria. 114 was Grade 0 (87%), 11 was Grade I (8.4%), 3 was Grade II (2.3%), 1 was Grade III (0.8%), and 2 was Grade IV (1.5%). The frequency of any abnormalities of intelligence in Grade 0 was 24%. The frequency of CP in Grade I was 18%. All Grade III and Grade IV cases had mild CP and an ID. The simple kappa value was 0.95. Conclusion: The prognostic value of the MRI scoring tool was limited. However, all Grade III and Grade IV cases had mild CP and ID. The results demonstrated an excellent inter-rater correlation.

PMID: [35798636](#)

Prevention and Cure

16. Interleukin-1: an important target for perinatal neuroprotection?

Sharmony B Kelly, Elys Green, Rod W Hunt, Claudia A Nold-Petry, Alistair J Gunn, Marcel F Nold, Robert Galinsky

Review Neural Regen Res. 2023 Jan;18(1):47-50. doi: 10.4103/1673-5374.341044.

Perinatal inflammation is a significant risk factor for lifelong neurodevelopmental impairments such as cerebral palsy. Extensive clinical and preclinical evidence links the severity and pattern of perinatal inflammation to impaired maturation of white and grey matters and reduced brain growth. Multiple pathways are involved in the pathogenesis of perinatal inflammation. However, studies of human and experimental perinatal encephalopathy have demonstrated a strong causative link between perinatal encephalopathy and excessive production of the pro-inflammatory effector cytokine interleukin-1. In this review, we summarize clinical and preclinical evidence that underpins interleukin-1 as a critical factor in initiating and perpetuating systemic and central nervous system inflammation and subsequent perinatal brain injury. We also highlight the

important role of endogenous interleukin-1 receptor antagonist in mitigating interleukin-1-driven neuroinflammation and tissue damage, and summarize outcomes from clinical and mechanistic animal studies that establish the commercially available interleukin-1 receptor antagonist, anakinra, as a safe and effective therapeutic intervention. We reflect on the evidence supporting clinical translation of interleukin-1 receptor antagonist for infants at the greatest risk of perinatal inflammation and impaired neurodevelopment, and suggest a path to advance interleukin-1 receptor antagonist along the translational path for perinatal neuroprotection.

PMID: [35799507](#)

17. Perampanel Reduces Brain Damage via Induction of M2 Microglia in a Neonatal Rat Stroke Model

Hyo Jung Shin, Ka Young Lee, Joon Won Kang, Seung Gyu Choi, Dong Woon Kim, Yoon Young Yi

Int J Nanomedicine. 2022 Jun 27;17:2791-2804. doi: 10.2147/IJN.S361377. eCollection 2022.

Purpose: Ischemic stroke is a leading cause of death and disability worldwide. Additionally, neonatal ischemia is a common cause of neonatal brain injury, resulting in cerebral palsy with subsequent learning disabilities and epilepsy. However, there is currently a lack of effective treatments available for patients with perinatal ischemic stroke. In this study, we investigated the effect of perampanel (PER)-loaded poly lactic-co-glycolic acid (PLGA) by targeting microglia in perinatal stroke. **Methods:** After formation of focal ischemic stroke by photothrombosis in P7 rats, PER-loaded PLGA was injected intrathecally. Proinflammatory markers (TNF- α , IL-1 β , IL-6, COX2, and iNOS) and M2 polarization markers (Ym1 and Arg1) were evaluated. We investigated whether PER increased M2 microglial polarization in vitro. **Results:** PER-loaded PLGA nanoparticles decreased the pro-inflammatory cytokines compared to the control group. Furthermore, they increased M2 polarization. **Conclusion:** PER-loaded PLGA nanoparticles decreased the size of the infarct and increased motor function in a perinatal ischemic stroke rat model. Pro-inflammatory cytokines were also reduced compared to the control group. Finally, this development of a drug delivery system targeting microglia confirms the potential to develop new therapeutic agents for perinatal ischemic stroke.

PMID: [35782016](#)