

Monday 13 May 2019

Cerebral Palsy Alliance is delighted to bring you this free weekly bulletin of the latest published research into cerebral palsy. Our organisation is committed to supporting cerebral palsy research worldwide - through information, education, collaboration and funding. Find out more at research.cerebralpalsy.org.au

Professor Nadia Badawi AM

Macquarie Group Foundation Chair of Cerebral Palsy

[Subscribe to CP Research News](#)

Interventions and Management

1. Cross-cultural adaptation and measurement properties of the Arabic version of the ABILHAND-Kids scale.

Alnahdi AH, Alhusaini AA, Alshami A, Yousef B, Melam G.

Disabil Rehabil. 2019 May 8:1-8. doi: 10.1080/09638288.2018.1555622. [Epub ahead of print]

PURPOSE: To cross-culturally adapt the ABILHAND-Kids into Arabic and to examine its measurement properties in children with cerebral palsy. **MATERIALS AND METHODS:** The Cross-cultural adaption of the ABILHAND-Kids into Arabic language included forward translation, backward translation, expert committee followed by preliminary testing. Structural validity using Rasch analysis, internal consistency, test-retest reliability, measurement error, and construct validity of the Arabic ABILHAND-Kids were examined in children with cerebral palsy (N = 154; 54% male, mean age 7.4 years). **RESULTS:** Rasch analysis did not support the structural validity of the Arabic ABILHAND-Kids mainly due to response dependency. Removal of two items addressed the issue of the response dependency and resulted in a unidimensional scale meeting the requirement of the Rasch model. The scale had excellent internal consistency (Person Separation Index = 0.93) and excellent test-retest reliability (intraclass correlation coefficient = 0.98). The results supported 86% of the predefined hypotheses regarding correlation of the Arabic ABILHAND-Kids with the manual ability classification system, gross motor function classification system and the functional independence measure for children. **CONCLUSION:** The Arabic ABILHAND-Kids demonstrated adequate evidence supporting its structural validity as a unidimensional measure along with evidence supporting its internal consistency, test-retest reliability and construct validity as a measure of manual ability in children with cerebral palsy. Implications for rehabilitation The Arabic ABILHAND-Kids is a reliable and valid measure of manual ability in children with cerebral palsy. The Arabic ABILHAND-Kids can be used to quantify manual ability in children with cerebral palsy in clinical practice and for research purposes.

PMID: [31067144](#)

2. Influence of Visual Dependence on Inter-Segmental Coordination during Upright Stance in Cerebral Palsy.

Yu Y, Tucker CA, Lauer RT, Keshner EA.

J Mot Behav. 2019 May 7:1-13. doi: 10.1080/00222895.2019.1610860. [Epub ahead of print]

The presence of visual dependence as an influential factor on the development of functional stability in ambulatory individuals with cerebral palsy (CP) was studied in 22 adults with spastic bilateral CP, 11 of whom were considered visually dependent, and 18 healthy adults. Participants stood upright during pitch plane disturbances of the visual field and support surface. Intersegmental coordination behaviors were assessed by fitting trajectories of adjacent body segments to an ellipse. Mixed-model repeated measures ANOVAs were performed on ellipse orientation angle and area. Dissimilar stabilizing strategies adopted by the two groups with CP imply that visual dependence impacts postural control. Postural reorganization in response to visual flow in all groups indicates that we cannot ignore perceptual aspects of postural control when designing

therapeutic interventions.

PMID: [31063037](#)

3. Physical activity in non-ambulatory toddlers with cerebral palsy.

Orlando JM, Pierce S, Mohan M, Skorup J, Paremski A, Bochnak M, Prosser LA.

Res Dev Disabil. 2019 May 4;90:51-58. doi: 10.1016/j.ridd.2019.04.002. [Epub ahead of print]

BACKGROUND: Children with cerebral palsy are less likely to be physically active than their peers, however there is limited evidence regarding self-initiated physical activity in toddlers who are not able, or who may never be able, to walk. **AIMS:** The aim of this study was to measure self-initiated physical activity and its relationship to gross motor function and participation in non-ambulatory toddlers with cerebral palsy. **METHODS AND PROCEDURES:** Participants were between the ages of 1-3 years. Physical activity during independent floor-play at home was recorded using a wearable tri-axial accelerometer worn on the child's thigh. The Gross Motor Function Measure-66 and the Child Engagement in Daily Life, a parent-reported questionnaire of participation, were administered. **OUTCOMES AND RESULTS:** Data were analyzed from the twenty participants who recorded at least 90 min of floor-play (mean: 229 min), resulting in 4598 total floor-play minutes. The relationship between physical activity and gross motor function was not statistically significant ($r = 0.20$; $p = 0.39$), nor were the relationships between physical activity and participation ($r = 0.05-0.09$; $p = 0.71-0.84$). **CONCLUSIONS AND IMPLICATIONS:** The results suggest physical activity during floor-play is not related to gross motor function or participation in non-ambulatory toddlers with cerebral palsy. Clinicians and researchers should independently measure physical activity, gross motor function, and participation.

PMID: [31063871](#)

4. Duration of Treatment Effect of Extracorporeal Shock Wave on Spasticity and Subgroup-Analysis According to Number of Shocks and Application Site: A Meta-Analysis.

Oh JH, Park HD, Han SH, Shim GY, Choi KY.

Ann Rehabil Med. 2019 Apr;43(2):163-177. doi: 10.5535/arm.2019.43.2.163. Epub 2019 Apr 30.

OBJECTIVE: To investigate duration of the treatment effect of extracorporeal shockwave therapy (ESWT) on spasticity levels measured with Modified Ashworth Scale (MAS) regardless of the patient group (stroke, multiple sclerosis, and cerebral palsy) and evaluate its spasticity-reducing effect depending on the number of shocks and site of application. **METHODS:** PubMed, EMBASE, the Cochrane Library, and Scopus were searched from database inception to February 2018. Randomized controlled trials and cross-over trials were included. All participants had spasticity regardless of cause. ESWT was the main intervention and MAS score was the primary outcome. Among 122 screened articles, 9 trials met the inclusion criteria. **RESULTS:** The estimate of effect size showed statistically significant MAS grade reduction immediately after treatment (standardized mean difference [SMD]=-0.57; 95% confidence interval [CI], -1.00 to -0.13; $p=0.012$), 1 week after (SMD=-1.81; 95% CI, -3.07 to -0.55; $p=0.005$), 4 weeks after (SMD=-2.35; 95% CI, -3.66 to -1.05; $p<0.001$), and 12 weeks after (SMD=-1.07; 95% CI, -2.04 to -0.10; $p=0.03$). Meta-regression and subgroup analysis were performed for the 'immediately after ESWT application' group. The prediction equation obtained from metaregression was $-1.0824+0.0002^*$ (number of shocks), which was not statistically significant. Difference in MAS grade reduction depending on site of application was not statistically significant either in subgroup analysis (knee and ankle joints vs. elbow, wrist, and finger joints). **CONCLUSION:** ESWT effectively reduced spasticity levels measured with MAS regardless of patient group. Its effect maintained for 12 weeks. The number of shocks or site of application had no significant influence on the therapeutic effect of ESWT in reducing spasticity. Ongoing trials with ESWT are needed to address optimal parameters of shock wave to reduce spasticity regarding intensity, frequency, and numbers.

PMID: [31072083](#)

5. Use of botulinum toxin A in children with cerebral palsy.

Ross Raftemo AE, Mahendran A, Hollung SJ, Jahnsen RB, Lydersen S, Vik T, Andersen GL.

Tidsskr Nor Laegeforen. 2019 Apr 24;139(8). doi: 10.4045/tidsskr.18.0554. Print 2019 May 7. [Article in English, Norwegian]

BACKGROUND: For more than 20 years, intramuscular injections of botulinum toxin A have been an established treatment for spasticity in children with cerebral palsy. We investigated the proportion of children with cerebral palsy who receive such treatment in Norway and the guidelines that apply to the treatment. **MATERIAL AND METHOD:** Data from the five-year registration in the Cerebral Palsy Registry of Norway were used to investigate the proportion of children with cerebral palsy born in the period 1999-2010 treated with botulinum toxin A, and whether there were any variations in the proportion of children treated between the habilitation centres. We conducted an online survey to identify the treatment guidelines that were applied in all of the 21 habilitation centres. **RESULTS:** A total of 1 414 children (average age 6.3 years) were included, of whom 775 (55 %) had been treated with botulinum toxin A. The proportion of children who received treatment varied considerably between the habilitation centres (38-80 %; $p < 0.001$). The maximum dose of botulinum toxin A per treatment per patient was 200-600 units of Botox. Five centres reported to have written guidelines for the treatment indication. **INTERPRETATION:** The proportion of children with cerebral palsy who are treated with botulinum toxin A varies considerably between Norwegian habilitation centres.

PMID: [31062563](#)

6. Mirror Neuron System Activation in Children With Unilateral Cerebral Palsy During Observation of Actions Performed by a Pathological Model.

Errante A, Di Cesare G, Pinaridi C, Fasano F, Sghedoni S, Costi S, Ferrari A, Fogassi L.

Neurorehabil Neural Repair. 2019 May 10;1545968319847964. doi: 10.1177/1545968319847964. [Epub ahead of print]

BACKGROUND: Recent evidence suggested that Action Observation Therapy (AOT), based on observation of actions followed by immediate reproduction, could be a useful rehabilitative strategy for promoting functional recovery of children affected by unilateral cerebral palsy (UCP). AOT most likely exploits properties of the parieto-premotor mirror neuron system (MNS). This is more intensely activated when participants observe actions belonging to their own motor repertoire. **OBJECTIVE:** The aim of the present study was to investigate the issue of whether MNS of UCP children is better activated by actions performed by a paretic hand rather than a healthy one. **METHODS:** Using functional magnetic resonance imaging, we assessed brain activation in a homogeneous group of 10 right UCP children compared with that of 10 right-handed typically developing (TD) children, during observation of grasping actions performed by a healthy or a paretic hand. **RESULTS:** The results revealed a significant activation within the MNS in both UCP and TD children, more lateralized to the left hemisphere in the TD group. Most important, region of interest (ROI) analysis on parietal and premotor regions showed that, in UCP, the MNS was more strongly activated by observation of actions performed by the paretic hand, a motor model more similar to the observer's motor repertoire. **CONCLUSIONS:** This study shows that children affected by spastic UCP exhibit enhanced activation of the MNS during observation of goal-directed actions performed by a pathological model with respect to a healthy one.

PMID: [31072215](#)

7. Motor Learning Feeding Interventions for Infants at Risk of Cerebral Palsy: A Systematic Review.

Khamis A, Novak I, Morgan C, Tzannes G, Pettigrew J, Cowell J, Badawi N.

Dysphagia. 2019 May 8. doi: 10.1007/s00455-019-10016-x. [Epub ahead of print]

Feeding difficulties and dysphagia are common in cerebral palsy (CP) and can lead to deficiencies of development and aspiration pneumonia; a leading cause of death in CP. Motor learning interventions have shown positive results in other clinical areas and may be beneficial for this population. This systematic review appraises research that addresses the question: are motor learning-based interventions more effective than compensatory strategies alone in treating dysphagia in infants with, or at risk of, CP?. Systematic searches were conducted in nine electronic databases. All levels of evidence, with at least one infant between 37 weeks post-menstrual age and 12 months corrected age who were at risk of, or diagnosed with CP, implemented interventions which aimed to improve oropharyngeal function for feeding, and aligned with at least two motor learning principles, were included. Studies were appraised by two independent reviewers using the Cho & Bero Instrument and GRADE. One historical case-control study and four case series met inclusion criteria. All involved a combination of motor learning interventions and compensatory strategies, which do not traditionally align with motor learning principles. All studies reported improvements in oral feeding outcomes, however, only three reported statistical analysis. The best available evidence collectively demonstrated a very weak positive effect for motor learning-based interventions for feeding difficulties in infants with, or at risk of, CP.

PMID: [31069491](#)

8. The forgotten sixth sense in cerebral palsy: do we have enough evidence for proprioceptive treatment?

Yardımcı-Lokmanoğlu BN, Bingöl H, Mutlu A.

Disabil Rehabil. 2019 May 6:1-10. doi: 10.1080/09638288.2019.1608321. [Epub ahead of print]

PURPOSE: The aim of this study was to evaluate the proprioception treatment approaches as well as to investigate the effect of these approaches in individuals with Cerebral Palsy. **MATERIALS AND METHODS:** A systematic review was performed using American Academy of Cerebral Palsy and Developmental Medicine Methodology. PubMed, PEDro, ScienceDirect, The Cochrane Library, Scopus and Web of Science database were searched. All the articles included were evaluated based on their level of evidence and conduct. **RESULTS:** Five articles met the inclusion criteria, children and adults with Cerebral Palsy. The effectiveness of different approaches has been examined in all studies and some studies showed effectiveness of treatment on proprioception or on motor performance. However, there was no superiority in between treatment approaches.

CONCLUSIONS: The reasons that limits the studies analyzed in this review were small sample sizes and insufficient heterogeneity of groups included. Because of the significance of proprioception on movement and motor performance, it should be included in the evaluation and treatment programs of individuals with Cerebral Palsy. Implications for rehabilitation It has been found that the various treatment methods applied appear to have a positive effect on proprioception with children and adults Cerebral Palsy. No treatment appears to be superior to the others. Treatment was found to be better as Gross Motor Function Classification System level severity decreased in adults with Cerebral Palsy. Treatments used in children with Cerebral Palsy were shown to have effects especially on gait parameters associated with proprioception improvement.

PMID: [31056965](#)

9. Peer support interventions for individuals with acquired brain injury, cerebral palsy, and spina bifida: a systematic review.

Levy BB, Luong D, Perrier L, Bayley MT, Munce SEP.

BMC Health Serv Res. 2019 May 8;19(1):288. doi: 10.1186/s12913-019-4110-5.

BACKGROUND: Neurological disorders may negatively impact community integration and/or quality of life. Peer support has emerged as a potential strategy to enhance patients' efficacy in managing their own health. This review examines the key characteristics and impact of peer support interventions for adults with acquired brain injury, cerebral palsy, and spina bifida on community integration and quality of life. **METHODS:** Eligible studies reported on peer support interventions for adults (16 years of age or older) with acquired brain injury, cerebral palsy, or spina bifida. Only randomized controlled trials published in English in the last 10 years were included. MEDLINE, EMBASE, PsycINFO, and CINAHL were used to conduct the literature search. Two reviewers independently screened studies, abstracted data, and evaluated the risk of bias (for individual study elements and overall) using the Cochrane Risk of Bias Tool. **RESULTS:** The systematic review included 6 trials reporting on acquired brain injury only. Of these studies, 4 reported on stroke and 2 reported on traumatic brain injury. Two studies found significant improvements in quality of life following peer support. No studies reported significant results on community integration. Considerable heterogeneity existed in the key characteristics of interventions. **CONCLUSIONS:** There are a limited number of studies on the impact of peer support interventions for adults with acquired brain injury, cerebral palsy, or spina bifida on community integration and quality of life. Standardization of key intervention characteristics may aid the global adoption of peer support as a formalized, evidence-based practice.

PMID: [31068184](#)

10. Childhood factors predict participation of young adults with cerebral palsy in domestic life and interpersonal relationships: a prospective cohort study.

van Gorp M, E Roebroek M, van Eck M, M Voorman J, Twisk JWR, J Dallmeijer A, van Wely L.

Disabil Rehabil. 2019 May 6:1-10. doi: 10.1080/09638288.2019.1585971. [Epub ahead of print]

PURPOSE: To determine childhood predictors of participation in domestic life and interpersonal relationships of young adults with cerebral palsy (CP). **MATERIALS AND METHODS:** This 13-year follow-up of an existing cohort (baseline age 9-13 years) included 67 young adults with CP (age 21-27 years). The Vineland adaptive behavior scales (VABS) and Life Habits questionnaire were used to assess attendance and difficulty in participation in domestic life and interpersonal relationships. Baseline factors were categorised according to the international classification of functioning, disability, and health. Stepwise multiple linear regression analyses determined significant predictors ($p < 0.05$). **RESULTS:** Lower manual ability, intellectual

disability (ID), epilepsy and lower motor capacity predicted decreased future participation in domestic life, and/or interpersonal relationships (explained variance $R^2 = 67-87\%$), whereas no association was found with environmental and personal factors. Extending models with baseline fine motor skills, communication, and interpersonal relationships increased R^2 to 79-90%. **CONCLUSIONS:** Childhood factors account for 79-90% of the variation in young adult participation in domestic life and interpersonal relationships of individuals with CP. Children with limited motor capacity, low manual ability, ID, or epilepsy are at risk for restrictions in participation in young adulthood. Addressing fine motor, communication, and social skills in paediatric rehabilitation might promote young adult participation. Implications for rehabilitation Childhood risk factors for limited participation in domestic life and interpersonal relationships as a young adult with CP are ID, epilepsy, low manual ability, low motor capacity, and low activity & participation levels. In line with current practice, this study confirms the importance of addressing gross and fine motor skills in children with CP for their future participation in domestic life. In addition, results suggest that addressing communication and social skills during paediatric rehabilitation may optimise future participation in interpersonal relationships.

PMID: [31060408](#)

11. Is Cerebral Palsy Spectrum Disorder Changing in High Resource Settings? Data From the Quebec Cerebral Palsy Registry.

Hadjinicolaou A, Ng P, Zhang X, Koclas L, Lamarre C, Malouin F, Pigeon N, Richards CL, Shevell M, Oskoui M.

J Child Neurol. 2019 May 10:883073819845272. doi: 10.1177/0883073819845272. [Epub ahead of print]

Advances in maternal and perinatal care in developed countries have led to improved health outcomes for children. These changes may have impacted the profile of children with a cerebral palsy spectrum disorder (CP) and groups at risk for CP over time. Using data from the Canadian CP Registry, the objectives of this retrospective cohort study were to describe the profile of children with CP in Quebec born between 1999 and 2010 and identify possible temporal variation in CP risk factors and phenotypic profile. Our sample consisted of 662 children with CP in Quebec. No change in profile or associated risk factors was observed across the birth cohorts 1999 to 2010. Prematurity remains the largest risk factor for CP in Quebec, and children with CP have multiple comorbidities that contribute to overall CP burden. CP registries offer a unique platform to study spectrum disorders and their longitudinal changes over time.

PMID: [31074324](#)

12. The Perception of Disability Among Mothers Living With a Child With Cerebral Palsy in Saudi Arabia.

Mohamed Madi S, Mandy A, Aranda K.

Glob Qual Nurs Res. 2019 Apr 28;6:2333393619844096. doi: 10.1177/2333393619844096. eCollection 2019 Jan-Dec.

The purpose of this study was to explore the perceptions of disability among Saudi mothers and to understand the implication of the meaning for the mothers of children with disability. A critical ethnographic approach was employed using focus groups and follow-up interviews with the mothers. Three primary themes were identified that specifically influenced and affected the mothers' experiences: (a) culture and religion, (b) motherhood and disability, and (c) community stigma and discrimination. The study reveals much-needed knowledge and sheds light on a topic, the details of which are rarely available in research literature from the Middle East. The findings further endorse the need for clinicians to listen to the mothers to consider their beliefs and the impact of these beliefs on their experiences. This, in turn, may provide a valuable conceptual lens for health care practitioners to use the family-centered model when working with cerebral palsy children.

PMID: [31065572](#)

13. The Pros and Cons of Operating Early Versus Late in the Progression of Cerebral Palsy Scoliosis.

Hollenbeck SM, Yaszay B, Sponseller PD, Bartley CE, Shah SA, Asghar J, Abel MF, Miyajima F, Newton PO.

Spine Deform. 2019 May;7(3):489-493. doi: 10.1016/j.jspd.2018.09.002.

STUDY DESIGN: Retrospective review of prospective data. **OBJECTIVE:** To delineate a curve threshold where further delay of surgery significantly increased the risks for patients with cerebral palsy (CP) scoliosis. **SUMMARY OF BACKGROUND DATA:** Two approaches exist in the management of CP scoliosis: a proactive one where surgery is recommended once there is

a risk of progression (Cobb > 50°) and a reactive one where surgery is recommended after the patient/caregiver may have significant challenges caused by a large deformity. **METHODS:** A prospectively collected CP scoliosis surgical registry was queried for patients with minimum two years of follow-up. Three groups were delineated based on the distribution of curve magnitudes: <70° (proactive), 70°-90°, and >90° (reactive). Radiographic, surgical, and quality of life outcome data were compared between the groups using analysis of variance and chi-square analyses. **RESULTS:** There were 38 patients in the <70° group, 44 in the 70°-90° group, and 42 in the >90° group. They were similar in age. The >90° group had significantly longer operative time ($p < .001$), a higher percentage of anterior/posterior procedures (31% vs 5%), and a higher infection rate requiring I&D (16.7%) than the other groups (<70°: 5.3%; 70°-90°: 6.8%; $p < .05$). The percentage blood volume loss was significantly higher in the >90° group compared to <70°. There were no differences in length of hospitalization or intensive care unit stay. Preoperatively, the Caregiver Priorities and Child Health Index of Life with Disabilities (CPchild) QOL score was significantly higher for the <70° group. At two years, the <70° and 70°-90° groups reached similar QOL scores, whereas the >90° trended toward a lower postoperative QOL. **CONCLUSIONS:** Being proactive (Cobb <70°) has no advantage in terms of decreasing risks or improving outcomes compared to curves 70°-90°. However, delaying surgery to a curve greater than 90° increases the risk of infection, blood loss, and the need for anterior/posterior procedures. Ideally, surgery should be recommended for curves less than 90°.

PMID: [31053320](#)

14. Incidence of osteoarthritis, osteoporosis and inflammatory musculoskeletal diseases in adults with cerebral palsy: A population-based cohort study.

O'Connell NE, Smith KJ, Peterson MD, Ryan N, Liverani S, Anokye N, Victor C, Ryan JM.

Bone. 2019 May 7. pii: S8756-3282(19)30170-X. doi: 10.1016/j.bone.2019.05.007. [Epub ahead of print]

BACKGROUND: People with cerebral palsy (CP) may be at increased risk of musculoskeletal conditions due to various factors including malnutrition and abnormal levels of skeletal loading. This study aimed to compare the incidence of osteoporosis, osteoarthritis and inflammatory musculoskeletal diseases between adults with and without CP. **METHODS:** A population based cohort study was conducted using data from the Clinical Practice Research Datalink collected between 1987 and 2015. Adults with CP were matched to adults without CP for age, sex and general practice. Cox models, stratified by matched set and adjusted for potential confounders, were fitted to compare the risk of osteoporosis, osteoarthritis and inflammatory musculoskeletal diseases. **RESULTS:** 1705 adults with CP were matched to 5115 adults without CP. Adults with CP had an increased risk of osteoporosis in unadjusted (Hazard Ratio (HR) 3.67, 95% Confidence Interval (CI) 2.32 to 5.80, $p < 0.001$) and adjusted (HR 6.19, 95% CI 3.37 to 11.39, $p < 0.001$) analyses. No evidence of increased risk of inflammatory musculoskeletal diseases was observed in unadjusted or adjusted analyses. For osteoarthritis no evidence of increased risk was seen in the unadjusted analysis, but evidence of an increased risk was seen when the analysis was adjusted for alcohol consumption, smoking status, and mean yearly general practice (GP) visits (HR 1.54, 95% CI 1.17 to 2.02, $p < 0.001$). **CONCLUSIONS:** After accounting for potential confounding variables, we found that CP is associated with increased risk of osteoporosis and osteoarthritis. These findings provide the strongest epidemiological evidence to date for increased risk of osteoporosis and osteoarthritis in people with CP, and highlight need for clinical awareness of such conditions in this population.

PMID: [31075418](#)

15. Pregnancy, Birth, Neonatal, and Postnatal Neurological Outcomes After Pregnancy With Migraine.

Skajaa N, Szépligeti SK, Xue F, Sørensen HT, Ehrenstein V, Eisele O, Adelborg K.

Headache. 2019 May 8. doi: 10.1111/head.13536. [Epub ahead of print]

BACKGROUND: Prevalence of migraine is high during the reproductive age. Although migraine often improves during pregnancy, the risk of adverse pregnancy, birth, neonatal, and neurological outcomes in mother and offspring remains poorly understood. **OBJECTIVE:** To investigate the associations between maternal migraine and risks of adverse pregnancy outcomes in the mother, and birth, neonatal and postnatal outcomes in the offspring. **METHODS:** We used Danish population registries to assemble a cohort of pregnancies among women with migraine and an age- and conception year-matched comparison cohort of pregnancies among women without migraine. The study period was 2005-2012. We computed adjusted prevalence ratios (aPRs) for pregnancy and birth outcomes and adjusted risk ratios (aRRs) for neonatal and postnatal outcomes, adjusting for age, preconception medical history, and preconception reproductive history. **RESULTS:** We identified 22,841 pregnancies among women with migraine and 228,324 matched pregnancies among women without migraine. Migraine was associated with an increased risk of pregnancy-associated hypertension disorders (aPR: 1.50 [95% confidence interval (CI): 1.39-1.61]) and miscarriage (aPR: 1.10 [95% CI: 1.05-1.15]). Migraine was associated with an increased prevalence of low birth weight

(aPR: 1.14 [95% CI: 1.06-1.23]), preterm birth (aPR: 1.21 [95% CI: 1.13-1.30]) and cesarean delivery (aPR: 1.20 [95% CI: 1.15-1.25]), but not of small for gestational age offspring (aPR: 0.94 [95% CI: 0.88-0.99]) and birth defects (aPR: 1.01 [95% CI: 0.93-1.09]). Offspring prenatally exposed to maternal migraine had elevated risks of several outcomes in the neonatal and postnatal period, including intensive care unit admission (aRR: 1.22 [95% CI: 1.03-1.45]), hospitalization (aRR: 1.12 [95% CI: 1.06-1.18]), dispensed prescriptions (aRR: 1.34 [95% CI: 1.24-1.45]), respiratory distress syndrome (aRR: 1.20 [95% CI: 1.02-1.42]), and febrile seizures (aRR: 1.27 [95% CI: 1.03-1.57]), but not of death (aRR: 0.67 [95% CI: 0.43-1.04]) and cerebral palsy (aRR: 1.00 [95% CI: 0.51-1.94]). **CONCLUSIONS:** Women with migraine and their offspring have greater risks of several adverse pregnancy outcomes than women without migraine.

PMID: [31069791](#)

16. Glutamate Transport and Preterm Brain Injury.

Pregolato S, Chakkarapani E, Isles AR, Luyt K.

Front Physiol. 2019 Apr 24;10:417. doi: 10.3389/fphys.2019.00417. eCollection 2019.

Preterm birth complications are the leading cause of child death worldwide and a top global health priority. Among the survivors, the risk of life-long disabilities is high, including cerebral palsy and impairment of movement, cognition, and behavior. Understanding the molecular mechanisms of preterm brain injuries is at the core of future healthcare improvements. Glutamate excitotoxicity is a key mechanism in preterm brain injury, whereby the accumulation of extracellular glutamate damages the delicate immature oligodendrocytes and neurons, leading to the typical patterns of injury seen in the periventricular white matter. Glutamate excitotoxicity is thought to be induced by an interaction between environmental triggers of injury in the perinatal period, particularly cerebral hypoxia-ischemia and infection/inflammation, and developmental and genetic vulnerabilities. To avoid extracellular build-up of glutamate, the brain relies on rapid uptake by sodium-dependent glutamate transporters. Astrocytic excitatory amino acid transporter 2 (EAAT2) is responsible for up to 95% of glutamate clearance, and several lines of evidence suggest that it is essential for brain functioning. While in the adult EAAT2 is predominantly expressed by astrocytes, EAAT2 is transiently upregulated in the immature oligodendrocytes and selected neuronal populations during mid-late gestation, at the peak time for preterm brain injury. This developmental upregulation may interact with perinatal hypoxia-ischemia and infection/inflammation and contribute to the selective vulnerability of the immature oligodendrocytes and neurons in the preterm brain. Disruption of EAAT2 may involve not only altered expression but also impaired function with reversal of transport direction. Importantly, elevated EAAT2 levels have been found in the reactive astrocytes and macrophages of human infant post-mortem brains with severe white matter injury (cystic periventricular leukomalacia), potentially suggesting an adaptive mechanism against excitotoxicity. Interestingly, EAAT2 is suppressed in animal models of acute hypoxic-ischemic brain injury at term, pointing to an important and complex role in newborn brain injuries. Enhancement of EAAT2 expression and transport function is gathering attention as a potential therapeutic approach for a variety of adult disorders and awaits exploration in the context of the preterm brain injuries.

PMID: [31068830](#)

17. GLUT1 Deficiency in a Patient Diagnosed as Cerebral Palsy: Is NGS a Valuable Tool to Be Considered in All Cases of CP to Detect Underlying Genetic Disorders?

Méneret A, Roze E.

Mov Disord Clin Pract. 2019 Mar 28;6(4):277-279. doi: 10.1002/mdc3.12754. eCollection 2019 Apr.

PMID: [31061833](#)

Prevention and Cure

18. Novel interventions to reduce oxidative-stress related brain injury in neonatal asphyxia.

Al S, Gm S, P-Y C.

Free Radic Biol Med. 2019 Apr 27. pii: S0891-5849(18)32359-1. doi: 10.1016/j.freeradbiomed.2019.04.028. [Epub ahead of print]

Perinatal asphyxia-induced brain injury may present as hypoxic-ischemic encephalopathy in the neonatal period, and disability including cerebral palsy in the long term. The brain injury is secondary to both the hypoxic-ischemic event and the reoxygenation-reperfusion following resuscitation. Early events in the cascade of brain injury can be classified as either inflammation or oxidative stress through the generation of free radicals. The objective of this paper is to present efforts that have been made to limit the oxidative stress associated with hypoxic-ischemic encephalopathy. In the acute phase of ischemia/hypoxia and reperfusion/reoxygenation, the outcomes of asphyxiated infants can be improved by optimizing the initial delivery room stabilization. Interventions include limiting oxygen exposure, and shortening the time to return of spontaneous circulation through improved methods for supporting hemodynamics and ventilation. Allopurinol, melatonin, noble gases such as xenon and argon, and magnesium administration also target the acute injury phase. Therapeutic hypothermia, N-acetylcysteine-2-iminobiotin, remote ischemic postconditioning, cannabinoids and doxycycline target the subacute phase. Erythropoietin, mesenchymal stem cells, topiramate and memantine could potentially limit injury in the repair phase after asphyxia. To limit the injurious biochemical processes during the different stages of brain injury, determination of the stage of injury in any particular infant remains essential. Currently, therapeutic hypothermia is the only established treatment in the subacute phase of asphyxia-induced brain injury. The effects and side effects of oxidative stress reducing/limiting medications may however be difficult to predict in infants during therapeutic hypothermia. Future neuroprotection in asphyxiated infants may indeed include a combination of therapies. Challenges include timing, dosing and administration route for each neuroprotectant.

PMID: [31039399](#)