Cerebral Palsy ALLIANCE

NEWS
Cerebral Palsy Research

Monday 29 October 2018

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. Adult Head and Neck Health Care Needs for Individuals with Complex Chronic Conditions of Childhood.
Mixter S, Stewart RW.

Med Clin North Am. 2018 Nov;102(6):1055-1061. doi: 10.1016/j.mcna.2018.06.007.

Millions of adults in the United States are currently living with what is termed chronic childhood conditions-childhood-onset conditions, about which adult providers often receive minimal training-and another half million youths with special health care needs enter adulthood each year and will undergo transition from pediatric to adult care. Here, the authors review the important otolaryngologic manifestations of several of these chronic childhood conditions, including autism spectrum disorder, cerebral palsy, and Down syndrome, as well as the primary care providers' role in caring for transitioning tracheostomy-dependent patients.

PMID: 30342608

2. Corticospinal Tract Wiring and Brain Lesion Characteristics in Unilateral Cerebral Palsy: Determinants of Upper Limb Motor and Sensory Function.
Simon-Martinez C, Jaspers E, Mailleux L, Ortibus E, Klingels K, Wenderoth N, Feys H.

Neural Plast. 2018 Sep 13;2018:2671613. doi: 10.1155/2018/2671613. eCollection 2018.

Brain lesion characteristics (timing, location, and extent) and the type of corticospinal tract (CST) wiring have been proposed as determinants of upper limb (UL) motor function in unilateral cerebral palsy (uCP), yet an investigation of the relative combined impact of these factors on both motor and sensory functions is still lacking. Here, we first investigated whether structural brain lesion characteristics could predict the underlying CST wiring and we explored the role of CST wiring and brain lesion characteristics to predict UL motor and sensory functions in uCP. Fifty-two participants with uCP (mean age (SD): 11 y and 3 m (3 y and 10 m)) underwent a single-pulse Transcranial Magnetic Stimulation session to determine CST wiring between the motor cortex and the more affected hand (n = 17 contralateral, n = 19 ipsilateral, and n = 16 bilateral) and an MRI to determine lesion timing (n = 34 periventricular (PV) lesion, n = 18 corticosubcortical (CSC) lesion), location, and extent. Lesion location and extent were evaluated with a semiquantitative scale. A standardized protocol included UL motor (grip strength, unimanual capacity, and bimanual performance) and sensory measures. A combination of lesion locations (damage to the PLIC and frontal lobe) significantly contributed to differentiate between the CST wiring groups, reclassifying the participants in their original group with 57% of accuracy. Motor and sensory functions were influenced by each of the investigated neurological factors. However, multiple regression analyses showed that motor function was predicted by the CST wiring (more preserved in individuals with contralateral CST ($p < 0.01$)), lesion extent, and damage to the basal ganglia and thalamus. Sensory function was predicted by the combination of a large and later lesion and an ipsilateral or bilateral CST wiring, which led to increased sensory deficits ($p < 0.05$). These novel insights contribute to a better understanding of the

underlying pathophysiology of UL function and may be useful to delineate individualized treatment strategies.

PMID: 30344602

3. The Effect of Two Attending Surgeons on the Outcomes of Posterior Spine Fusion in Children With Cerebral Palsy.
Shrader MW, Wood W, Falk M, Segal LS, Boan C, White G.

Spine Deform. 2018 Nov - Dec;6(6):730-735. doi: 10.1016/j.jspd.2018.03.002.

BACKGROUND: Posterior spinal fusion (PSF) in children with cerebral palsy (CP) carries a high risk of complications and morbidity. The purpose of this study is to investigate the impact of using two attending surgeons on blood loss, operative time, and complications in this fragile population. METHODS: This was a prospective, matched cohort analysis of patients with CP who underwent PSF with two attending surgeons. These were matched with a control group that had a single-surgeon team, assisted by a senior resident or PA. The groups were compared using paired Student t tests and chi-square tests. RESULTS: 50 patients were included in the study (25 study and 25 matched controls), determined by our power analysis. There was no statistical difference in the mean age, preoperative major curve angle, major curve angle correction, or use of antifibrinolytics. The two-surgeon group decreased surgical time from 5.25 to 3.3 hours (p = .000002), and estimated blood loss from 1,238 to 865 mL (p = .009). The complication rate decreased from 33% to 8% (p=.034). Length of stay was also decreased from 6.5 days to 5.35 (p = .02). CONCLUSIONS: Although confounding variables were present, this study demonstrates that the use of a two-surgeon team during spinal surgery for patients with cerebral palsy could have a role in reducing operative time, blood loss, complication rates, and hospital length of stay. Overall, these factors and any improved operating room efficiencies may lead to lasting improved patient outcomes. LEVEL OF EVIDENCE: Level III, retrospective, comparative study.

PMID: 30348351

4. Multi-joint gait clustering for children and youth with diplegic cerebral palsy.
Kuntze G, Nettel-Aguirre A, Ursulak G, Robu I, Bowal N, Goldstein S, Emery CA.

PLoS One. 2018 Oct 24;13(10):e0205174. doi: 10.1371/journal.pone.0205174. eCollection 2018.

BACKGROUND: Clinical management of children and youth with cerebral palsy (CP) is increasingly supported by computerized gait analysis. Methods have been developed to reduce the complexity of interpreting biomechanical data and quantify meaningful movement patterns. However, few methods are inclusive of multiple joints and planes of motion, and consider the entire duration of gait phases; potentially limiting insight into this heterogeneous pathology. The objective of this study was to assess the implementation of k-means clustering to determine clusters of participants with CP based on multi-joint gait kinematics. METHODS: Barefoot walking kinematics were analyzed for a historical cohort (2007-2015) of 37 male and female children and youth with spastic diplegic CP [male n = 21; female n = 16; median age = 12 (range 5-25) years; Gross Motor Function Classification System Level I n = 17 and Level II n = 20]. Mean stance phase hip (sagittal, coronal, transverse), knee (sagittal), and ankle (sagittal) kinematics were time (101 data points), mean and range normalized. Normalized kinematics data vectors (505 data points) for all participants were then combined in a single data matrix M (37x505 data points). K-means clustering was conducted 10 times for all data in M (2-5 seeds, 50 repetitions). Cluster quality was assessed using the mean Silhouette value ([Formula: see text]) and cluster repeatability. The mean kinematic patterns of each cluster were explored with respect to a dataset of normally developing (ND) children using Statistical Parametric Mapping (SPM, alpha 0.05). Differences in potentially confounding variables (age, height, weight, walking speed) between clusters (C) were assessed individually in SPSS (IBM, USA) using Kruskal-Wallis H tests (alpha 0.05). RESULTS: Four clusters (n1 = 5, n2 = 12, n3 = 12, n4 = 8) provided the largest possible data separation based on high cluster repeatability (96.8% across 10 repetitions) and comparatively greater cluster quality [[Formula: see text] (SD), 0.275 (0.152)]. Participant data with low cluster quality values displayed a tendency toward lower cluster allocation repeatability. Distinct kinematic differences between clusters and ND data were observable. Specifically, C1 displayed a unique continuous hip abduction and external rotation pattern. In contrast, participants in C2 moved from hip adduction (loading response) to abduction (mid to terminal stance) and featured a unique ankle plantarflexor pattern during pre-swing. C3 was characterized by gait deviations in the sagittal plane of the hip, knee and ankle only. C4 displayed evidence for the most substantial hip and knee extension, and ankle plantarflexion deficit from midstance to pre-swing. DISCUSSION: K-means clustering enabled the determination of up to four kinematic clusters of individuals with spastic diplegic CP using multi-joint angles without a priori data reduction. A cluster boundary effect was demonstrated by the Silhouette value, where data with values approaching zero were more likely to change cluster allocation. Exploratory analyses using SPM revealed significant differences across joints and between clusters indicating the formation of clinically meaningful clusters. Further work is needed to determine the effects of including further topographical classifications of CP, additional biomechanical data, and the sensitivity to clinical interventions to assess the potential for informing clinical decision-making.

PMID: 30356242

5. Effects of an underwear-type hip abduction orthosis on sitting balance and sit-to-stand activities in children with spastic cerebral palsy.
Kusumoto Y, Matsuda T, Fujii K, Miyamoto K, Takaki K, Nitta O.

J Phys Ther Sci. 2018 Oct;30(10):1301-1304. doi: 10.1589/jpts.30.1301. Epub 2018 Oct 12.

[Purpose] Hip dislocation and subluxation are common in patients with cerebral palsy (CP). Hip abduction orthoses are used to prevent and treat these problems. This study investigated the effects of an underwear-type hip abduction orthosis on sitting balance and sit-to-stand (STS) activity in children with spastic CP. [Participants and Methods] This trial had a cross-over design. Eight children aged 6 to 18 years old with spastic CP and Gross Motor Function Classification level III and IV were randomly allocated to groups with or without use of the underwear-type hip orthosis. The trunk impairment scale (TIS) score was evaluated and the 5-times sit-to-stand test (FTSST) was conducted with and without the underwear. [Results] The dynamic sitting balance scores in the TIS and FTSST showed significant improvement with use of the orthotic underwear. [Conclusion] The dynamic sitting balance scores of the TIS and FTSST were higher, thus indicating better stability, when wearing the orthosis underwear. Thus, it was suggested that underwear-type hip abduction orthoses are effective for promoting sitting balance and STS activities in children with spastic CP.

PMID: 30349168

6. Strength Training Effects on Muscle Forces and Contributions to Whole-Body Movement in Cerebral Palsy.
Hegarty AK, Kurz MJ, Stuberg W, Silverman AK1.

J Mot Behav. 2018 Oct 23:1-15. doi: 10.1080/00222895.2018.1519691. [Epub ahead of print]

Strength training is often prescribed for children with cerebral palsy (CP); however, links between strength gains and mobility are unclear. Nine children (age 14 ± 3 years; GMFCS I-III) with spastic CP completed a 6-week strength-training program. Musculoskeletal gait simulations were generated for four children to assess training effects on muscle forces and function. There were increases in isometric joint strength, but no statistical changes in fast-as-possible walking speed or endurance after training. The walking simulations revealed changes in muscle forces and contributions to body center of mass acceleration, with greater forces from the hip muscles during walking most commonly observed. A progressive strength-training program can result in isometric and dynamic strength gains in children with CP, associated with variable mobility outcomes.

PMID: 30351246

7. Effect of ankle foot orthoses on motor performance in cerebral palsy.
Degelaen M.

Dev Med Child Neurol. 2018 Oct 22. doi: 10.1111/dmcn.14069. [Epub ahead of print]

PMID: 30346033

8. Measuring change in gait performance of children with motor disorders: assessing the Functional Mobility Scale and the Gillette Functional Assessment Questionnaire walking scale.
Ammann-Reiffer C, Bastiaenen CHG, Van Hedel HJA.

Dev Med Child Neurol. 2018 Oct 19. doi: 10.1111/dmcn.14071. [Epub ahead of print]

AIM: To examine the responsiveness and minimal important change (MIC) of two gait performance measures, the Functional Mobility Scale (FMS) and the Gillette Functional Assessment Questionnaire walking scale (FAQ), in a paediatric inpatient setting. METHOD: Sixty-four children and adolescents with a motor disorder, including cerebral palsy, traumatic brain injury, or stroke (25 females, 39 males; mean age [SD] 12y 6mo [3y 2mo], range 6-18y 6mo), were recruited. Physiotherapists scored the FMS and FAQ at the start and end of active gait rehabilitation. Change scores were compared with changes in gait capacity tests, the walking item of the Functional Independence Measure for Children, and a global rating scale (GRS) on the physiotherapists' perceived change of the child's functional mobility. The GRS was also used to define the MIC. RESULTS: Change scores of the FMS and FAQ correlated between 0.35 and 0.49 with those of the capacity tests, 0.54 to 0.76 with the

Functional Independence Measure for Children walking item change scores, and 0.57 to 0.76 with the GRS. The MIC values for the FMS and FAQ were 0.5 and 1.5 respectively. INTERPRETATION: FMS and FAQ can illustrate change in inpatient gait performance of children and adolescents with motor disorders. An improvement of one level in the FMS and two levels in the FAQ is considered as a clinically meaningful change. WHAT THIS PAPER ADDS: The Functional Mobility Scale (FMS) can detect change in children's inpatient gait performance. The Gillette Functional Assessment Questionnaire walking scale (FAQ) can also detect change in children's inpatient gait performance. A one-level improvement in the FMS is clinically relevant. A two-level improvement in the FAQ is clinically relevant.

PMID: 30341775

9. Dance and rehabilitation in cerebral palsy: a systematic search and review.
López-Ortiz C, Gaebler-Spira DJ, Mckeeman SN, Mcnish RN, Green D.

Dev Med Child Neurol. 2018 Oct 23. doi: 10.1111/dmcn.14064. [Epub ahead of print]

AIM: To conduct a review of research literature on the use of dance and movement with music (rhythmic auditory stimulation [RAS]) in the neurorehabilitation of children and adults with cerebral palsy (CP). METHOD: We conducted a systematic search and quality appraisal of the research literature on dance and RAS in CP. Additionally, we linked the research outcomes to the International Classification of Functioning, Disability and Health (ICF) framework. RESULTS: Studies showed preliminary evidence of the benefits of dance and RAS on body functions, particularly balance, gait, walking, and cardiorespiratory fitness for individuals with CP. Research gaps are evident across all domains of the ICF, particularly in the participation and environment domains. INTERPRETATION: To facilitate translation of quantitative research outcomes to the clinical classification of the ICF, a table was constructed that links traditional areas of quantitative rehabilitation research with the ICF categories highlighting areas of research strengths and areas where increased rigor is desirable. The potential for dance and RAS to have positive impacts on body functions, emotional expression, social participation, and attitudinal change are indicated areas for consideration in future research. WHAT THIS PAPER ADDS: The potential for dance and movement to music help balance, gait, and walking in children and adults with cerebral palsy. Research gaps are evident across International Classification of Functioning, Disability and Health domains, particularly participation and environment domains.

PMID: 30350851

10. Developmental trajectory of self-care in children with cerebral palsy with different manual abilities.
Chen CL.

Dev Med Child Neurol. 2018 Oct 22. doi: 10.1111/dmcn.14078. [Epub ahead of print]

PMID: 30346035

11. Effect of prebiotic and probiotic supplementation on neurodevelopment in preterm very low birth weight infants: findings from a meta-analysis.
Upadhyay RP, Taneja S, Chowdhury R, Strand TA, Bhandari N.

Pediatr Res. 2018 Oct 18. doi: 10.1038/s41390-018-0211-9. [Epub ahead of print]

BACKGROUND: Preterm very low birth weight (VLBW) infants are at risk of gut dysbiosis and neurodevelopmental deficits. Prebiotics and probiotics may modulate gut microbiota and influence brain functions. This review synthesizes literature on effect of prebiotic and/or probiotic supplementation in preterm VLBW on their neurodevelopmental outcomes. METHODS: Search was done using PubMed and CENTRAL. Randomized controlled trials (RCTs) in preterm infants (<37 weeks gestation) and/or infants with birth weight <1500 g that evaluated the effect of prebiotic and/or probiotic supplementation on neurodevelopmental outcomes were included. Weighted mean difference in cognitive and motor scores; pooled relative risks for cognitive and motor impairment, cerebral palsy, hearing, and visual impairment were estimated. Quality of evidence was assessed using the GRADE criteria. RESULTS: Out of 275 articles identified, seven were included for review. All, except one, were done in preterms <33 weeks of gestation. Age of assessment of outcomes was ≥18-22 months of corrected age in five studies. Interventions did not decrease or increase the risk of cognitive and motor impairment, cerebral palsy, visual, and hearing impairment. Quality of evidence was "low" to "very low." CONCLUSIONS: Limited evidence from RCTs does not demonstrate a difference in neurodevelopmental outcomes between prebiotic/probiotic treated and untreated control groups.

PMID: 30353041

12. Evaluation of the effectiveness of a custom-made toothbrush in maintaining oral hygiene and gingival health in cerebral palsy patients.
Rai T, Ym K, Rao A, P AN, Natarajan S, Joseph RM.

Spec Care Dentist. 2018 Oct 23. doi: 10.1111/scd.12334. [Epub ahead of print]

AIM: To evaluate and compare the efficacy of customized toothbrushes in maintenance of oral hygiene and gingival health with that of conventional toothbrushes in children with cerebral palsy. METHODS: Thirty patients with cerebral palsy in the age group of 6 to 18 years were randomly divided into two groups-group I (normal toothbrush) and group II (customized toothbrush). Common oral hygiene instructions were given to both the groups. Before beginning the study, plaque index (PI) and modified gingival index (MGI) were recorded, following which patients were made to practice their routine twice a day brushing with either normal toothbrush or custom-made toothbrush for 3 weeks. At the end of 3 weeks, PI and MGI were rerecorded. The subjects belonging to group II were also made to perform muscle exercises using the modified brush head. RESULTS: Significantly high percentage drop between the pre- and post-PI as well as MGI (31.55% and 30.23%, respectively) was observed in the custom-made toothbrush group, while the percentage drop of only 8.34% (PI) and 14.51% (MGI) was seen in the normal toothbrush group. CONCLUSIONS: Custom-made tooth brushes increased the efficiency of maintaining oral hygiene and gingival health of individuals with cerebral palsy.

PMID: 30350870

13. Constipation and fecal incontinence in children with cerebral palsy. Overview of literature and flowchart for a stepwise approach.
Vande Velde S, Van Renterghem K, Van Winkel M, De Bruyne R, Van Biervliet S.

Acta Gastroenterol Belg. 2018 Jul-Sep;81(3):415-418.

BACKGROUND AND STUDY AIMS: Constipation and fecal incontinence are common problems in neurologically impaired children. This paper aims to give an overview on bowel problems in cerebral palsy children and to suggest a stepwise treatment approach. A pubmed search was performed looking at studies during the past 20 years investigating bowel problems in neurologically disabled children. RESULTS: The search revealed 15 articles. Prevalence and presentation was the subject of 8 papers, confirming the importance of the problem in these children. The other papers studied the results of different treatment modalities. No significant differences between treatment modalities could be demonstrated due to small studied cohorts. Therefore, no specific treatment strategy is currently available. An experienced based stepwise approach is proposed starting with normalization of fiber intake. The evaluation of the colon transit time could help in deciding whether desimpaction and eventually laxatives including both osmotic (lactulose, macrogol) as well as stimulant laxatives might be indicated. Or, in case of fast transit loperamide or psyllium can be tried. Surgery should be a last resort option. CONCLUSION: Studies investigating constipation and continence in neurologically impaired children are scarce, making it difficult to choose for the optimal treatment. A stepwise treatment approach is proposed, measuring the colon transit time to guide treatment choices.

PMID: 30350531

14. Mental health disorders and physical risk factors in children with cerebral palsy: a cross-sectional study.
Whitney DG, Warschausky SA, Peterson MD.

Dev Med Child Neurol. 2018 Oct 26. doi: 10.1111/dmcn.14083. [Epub ahead of print]

AIM: To examine the prevalence of mental health disorders among children with and without cerebral palsy (CP), and to examine how physical risk factors in children with CP might mitigate any elevated risk of mental health disorders in this population. METHOD: Children from 6 years to 17 years of age with (n=111) and without (n=29 909) CP from the 2016 National Survey of Children's Health were included in this cross-sectional study. Mental health disorders included depression, anxiety, behavior/conduct problems, and attention deficit disorder/attention-deficit/hyperactivity disorder (ADHD). Physical risk factors included physical activity (number of active days ≥60min), sleep duration, and pain. RESULTS: Adjusting for sociodemographics, children with CP had higher odds of mental health disorders (odds ratio [OR]=2.7-7.1, $p<0.05$) except for attention deficit disorder/ADHD (OR=2.5; 95% confidence interval [CI]=0.9-7.1). Further adjusting for physical factors, the odds of depression were no longer increased (i.e. attenuated) in children with CP (OR=1.0; 95% CI=0.3-3.3); however, the odds of anxiety (OR=3.8; 95% CI=1.9-7.8) and behavior/conduct problems (OR=3.8; 95% CI=1.3-11.1) remained elevated. Assessed individually, low physical activity and pain attenuated the odds of depression in children with CP (OR=1.9; 95%

CI=0.7-5.3; OR=1.4; 95% CI=0.6-3.8 respectively). INTERPRETATION: Children with CP have an elevated prevalence of mental health disorders even after accounting for physical risk factors. Low physical activity and pain partially accounts for the association between CP and depression. WHAT THIS PAPER ADDS: Children with cerebral palsy (CP) have an elevated risk of developing mental health disorders. Physical factors do not fully account for higher mental health disorder prevalence. Physical activity partially accounts for the relationship between CP and depression. Pain partially accounts for the relationship between CP and depression.

PMID: 30362114

15. Depressive Symptoms in Parents of Children With Chronic Health Conditions: A Meta-Analysis.
Pinquart M.

J Pediatr Psychol. 2018 Oct 19. doi: 10.1093/jpepsy/jsy075. [Epub ahead of print]

OBJECTIVE: Caring for children with chronic health conditions is associated with stressors that may impair mental health. The goal of our meta-analysis was to analyze depressive symptoms among parents who care for a child or adolescent with chronic physical disease and/or sensory disability and/or physical disability compared with parents of healthy children or test norms. METHODS: A systematic search through electronic databases identified 460 relevant studies that were included in a random-effects meta-analysis. RESULTS: Parents of children with chronic conditions showed small to moderate elevations of depressive symptoms compared with parents of healthy/nondisabled children and test norms (g = .46 SD units). Twelve studies using structured clinical interviews provided a weighted mean depression rate of 20.9%. The highest elevations were found among parents of young people with neuromuscular disorders, cancer, and cerebral palsy. Elevations of depressive symptoms were greater in cases with shorter durations of the chronic condition, in mothers compared with fathers, and in parents from economically less developed countries rather than developed countries. CONCLUSIONS: Parents of children with chronic conditions, particularly parents of children with neuromuscular disorders, cancer, and cerebral palsy, should be screened for depression and receive psychosocial services aimed at reducing these symptoms, if needed.

PMID: 30346613

16. Cerebral palsy and maternal obesity.
Dolin CD.

Dev Med Child Neurol. 2018 Oct 23. doi: 10.1111/dmcn.14079. [Epub ahead of print]

PMID: 30350854

17. Neurodevelopmental outcomes among extremely premature infants with linear growth restriction.
Meyers JM, Tan S, Bell EF, Duncan AF, Guillet R, Stoll BJ, D'Angio CT; Eunice Kennedy Shriver National Institute of Child Health and Human Development Neonatal Research Network.

J Perinatol. 2018 Oct 23. doi: 10.1038/s41372-018-0259-8. [Epub ahead of print]

OBJECTIVE: To compare neurodevelopmental outcomes in linear growth-restricted (LGR) infants born <29 weeks with and without weight gain out of proportion to linear growth. STUDY DESIGN: We compared 2-year neurodevelopmental outcomes between infants with and without LGR and between LGR infants with and without weight gain out of proportion to linear growth. The outcomes were Bayley-III cognitive, motor, and language scores, cerebral palsy, Gross Motor Function Classification System (GMFCS) level ≥ 2, and neurodevelopmental impairment. RESULT: In total, 1227 infants were analyzed. LGR infants were smaller and less mature at birth, had higher BMI, and had lower Bayley-III language scores (82.3 vs. 85.0, $p < 0.05$). Among infants with LGR, infants with high BMI had lower language scores compared with those with low-to-normal BMI (80.8 vs. 83.3, $p < 0.05$), and were more likely to have GMFCS level ≥2 and neurodevelopmental impairment. CONCLUSION: Among infants with LGR, weight gain out of proportion to linear growth was associated with poorer neurodevelopmental outcomes.

PMID: 30353080

18. Neuromotor performance in infants before and after early open-heart surgery and risk factors for delayed development at 6 months of age.
Campbell MJ, Ziviani JM, Stocker CF, Khan A, Sakzewski L.

Cardiol Young. 2018 Oct 24:1-10. doi: 10.1017/S1047951118001622. [Epub ahead of print]

BACKGROUND: Early identification of infants with CHD at heightened risk of developmental delays can inform surveillance priorities. This study investigated pre-operative and post-operative neuromotor performance in infants undergoing open-heart surgery, and their developmental status at 6 months of age, to identify risk factors and inform care pathways. METHODS: Infants undergoing open-heart surgery before 4 months of age were recruited into a prospective cohort study. Neuromotor performance was assessed pre-operatively and post-operatively using the Test of Infant Motor Performance and Prechtl's Assessment of General Movements. Development was assessed at 6 months of age using the Ages and Stages Questionnaire third edition. Pre-operative and post-operative General Movements performance was compared using McNemar's test and test of infant motor performance z-scores using Wilcoxon's signed rank test. Risk factors for delayed development at 6 months were explored using logistic regression. RESULTS: Sixty infants were included in this study. In the 23 (38%) infants. A total of 60 infants were recruited. In the 23 (38%) infants assessed pre-operatively, there was no significant difference between pre- and post-operative performance on the GMs (p=0.63) or TIMP (p=0.28). At discharge, 15 (26%) infants presented with abnormal GMs, and the median TIMP z-score was -0.93 (IQR: -1.4 to -0.69). At 6 months, 28 (52.8%) infants presented with gross motor delay on the ASQ-3, significantly negatively associated with gestational age (p=0.03), length of hospital stay (p=0.04) and discharge TIMP score (p=0.01). CONCLUSIONS: Post-operative assessment using the GMs and TIMP may be useful to identify infants requiring individualised care and targeted developmental follow-up. Long-term developmental surveillance beyond 6 months of age is recommended.

PMID: 30352635

19. Changes in long-term prognosis with increasing postnatal survival and the occurrence of postnatal morbidities in extremely preterm infants offered intensive care: a prospective observational study.
Cheong JLY, Lee KJ, Boland RA, Spittle AJ, Opie GF, Burnett AC, Hickey LM, Roberts G, Anderson PJ, Doyle LW; Victorian Infant Collaborative Study Group.

Lancet Child Adolesc Health. 2018 Oct 22. pii: S2352-4642(18)30287-6. doi: 10.1016/S2352-4642(18)30287-6. [Epub ahead of print]

BACKGROUND: Decisions regarding provision of intensive care and post-discharge follow-up for infants born extremely preterm (<28 weeks' gestation) are based on the risks of mortality and neurodevelopmental disability. We aimed to elucidate the changes in probability of three outcomes (death, survival with major disability, and survival without major disability) with postnatal age in extremely preterm infants offered intensive care, and the effect of postnatal events on the probability of survival without major disability. METHODS: In this prospective observational study, we used data from three geographical cohorts composed of all extremely preterm livebirths offered intensive care at birth during three distinct periods (1991-92, 1997, and 2005) in Victoria, Australia. Participants were assessed at 8 years' corrected age for major neurodevelopmental disability, defined as moderate or severe cerebral palsy, general intelligence more than 2 SDs below term-born control means, blindness, or deafness. Probabilities of outcomes conditional on survival to different postnatal ages were calculated by logistic regression. Multivariable logistic regression was used to assess factors predictive of survival with major disability. FINDINGS: 751 (82%) of 915 extremely preterm livebirths free of lethal anomalies were offered intensive care, of whom 546 (73%) survived to age 8 years. Of the 499 survivors assessed, 86 (17%) had a major disability. With increasing gestational age at birth or days of postnatal survival, the probability of death decreased and of survival without major disability increased. By contrast, the probability of survival with major disability varied little with gestational age or postnatal survival. In survivors, major disability was associated with the occurrence of four important postnatal events: grade 3 or 4 intraventricular haemorrhage (odds ratio 2·61 [95% CI 1·11-6·15]), cystic periventricular leukomalacia (9·17 [3·57-23·53]), postnatal corticosteroid use (1·99 [1·03-3·85]), and surgery (2·78 [1·51-5·13]). 241 survivors (48%) had no major postnatal events during the newborn period, and had the lowest prevalence of major disability (17 participants [7%]). The probability of survival without major disability decreased with increasing number of major events (0·93 [0·89-0·96] for no events vs 0·31 [0·11-0·59] for three or more events). INTERPRETATION: Long-term prognosis in terms of death and major neurodevelopmental disability changes rapidly after birth for extremely preterm infants. Counselling of families and post-discharge planning should be individualised to changing circumstances following birth. FUNDING: National Health and Medical Research Council of Australia.

PMID: 30361130

20. Longitudinal trajectories and reference centiles for the impact of health conditions on daily activities of children with cerebral palsy.
Bartlett DJ, Gorter JW, Jeffries LM, Avery L, Hanna SE; On Track Study Team.

Dev Med Child Neurol. 2018 Oct 23. doi: 10.1111/dmcn.14080. [Epub ahead of print]

AIM: First, to describe the impact of health conditions on daily activities over time in children with cerebral palsy (CP) and to create age-specific reference centiles. Second, to determine the amount of change typical over a 1-year period, across Gross Motor Function Classification System (GMFCS) levels. METHOD: A prospective, cohort design, with five assessments over 2 years, involved 708 children with a confirmed diagnosis of CP participating in the On Track Study (396 males, 312 females; mean age 6y [SD 2y 7mo]; range 18mo-12y at first assessment; 32.1% in GMFCS level I, 22.7% in GMFCS level II, 11.2% in GMFCS level III, 18.2% in GMFCS level IV, 15.7% in GMFCS level V). The impact of health conditions on daily activities was assessed using the Child Health Conditions Questionnaire. Data were analyzed using mixed-effects models and quantile regression. RESULTS: Linear longitudinal trajectories describe the relatively stable impact of health conditions over time for each functional level for children aged 2 years to 12 years, with the lowest scores (least impact) in GMFCS level I and the highest scores (highest impact) in GMFCS level V. Centiles were created for children in each GMFCS level. A system to interpret the magnitude of change over time in centiles was developed. INTERPRETATION: Longitudinal trajectories of co-occurring health conditions assist with understanding children's prognoses. Centiles assist in understanding a child's experience relative to children in similar GMFCS levels. Guidelines are provided to determine if children are progressing 'as expected', 'better than expected' or 'more poorly than expected' in regard to the impact of health conditions on daily activities. WHAT THIS PAPER ADDS: For children with cerebral palsy, the mean impact of health conditions on daily activities is relatively stable. Significant intraindividual and interindividual variability for the impact of health conditions exists, which complicates prognosis. Centiles enable interpretation of the impact of health conditions relative to Gross Motor Function Classification System level.

PMID: 30353544

21. Immunisation status of children with cerebral palsy in rural Bangladesh: results from the Bangladesh Cerebral Palsy Register (BCPR).
May P, Smithers-Sheedy H, Muhit M, Cumming R, Jones C, Booy R, Badawi N, Khandaker G.

Infect Disord Drug Targets. 2018 Oct 23. doi: 10.2174/1871526518666181024101002. [Epub ahead of print]

BACKGROUND: Cerebral palsy (CP) is the most common cause of physical disability in childhood, with an estimated 17 million cases worldwide. There is limited data concerning the general health of this population and the immunisation status of children with CP is largely unknown. OBJECTIVE: We aimed to assess the immunisation status of children with CP in rural Bangladesh and determine the predictors of non-immunisation. METHODS: This study is part of the Bangladesh CP Register (BCPR) study; a population based CP register commenced in January 2015 in the Shahjadpur sub-district of Bangladesh. As part of BCPR registration, all children with CP in the catchment area were assessed by a paediatrician and their clinical and immunisation history were collected. RESULTS: Between January and December 2015, 615 children with CP were registered on the BCPR. The median age of the children was 7.5 years, and 38.5% were female. 91.7% of those children had a BCG vaccine scar (as an objective marker for immunisation at birth). However, only 43.2% reported to have received the rubella vaccine during the 2014 national rubella immunisation campaign. Timing of CP diagnosis was found to be an independent predictor for immunisation uptake; those diagnosed after the age of 3 were more likely to have received the rubella vaccine (95% confidence interval [CI] 1.6 - 4.3, odds ratio [OR] 2.6, p <0.0001). CONCLUSIONS: To the best of our knowledge, this is the first paper to use a formal CP register to examine the relationship between CP and immunisation status in a low or middle income country like Bangladesh. Our data suggest that more than two thirds of children with CP in rural Bangladesh did not receive immunisation during a recent national campaign.

PMID: 30360749

22. Cerebral palsy in Moldova: subtypes, severity and associated impairments.
Gincota Bufteac E, Andersen GL, Torstein V, Jahnsen R.

BMC Pediatr. 2018 Oct 19;18(1):332. doi: 10.1186/s12887-018-1305-6.

BACKGROUND: Moldova is ranked as one of the countries in Europe with the lowest income per capita and with a relatively

high infant and maternal mortality rate. Information on neurodisabilities in general is limited, and regarding cerebral palsy (CP) in particular, it is completely lacking. The aim of this study was therefore to make a crude estimate of the prevalence of CP and to describe subtypes and the severity of motor impairments and associated problems in this country. METHODS: Children with CP born 2009-2010, attending the National Hospital Institute of Mother and Child, the reference hospital for ~ 75% of children in Moldova with neurological disabilities, were identified from medical records. RESULTS: Among 207 children with CP (estimated prevalence 3.4 per 1000 live births), 185 (mean age 7.3 years; 36% girls) had detailed information. Thirty seven (20%) children had spastic unilateral, 113 (61%) spastic bilateral, 22 (12%) dyskinetic and 9 (5%) children had ataxic CP. The subtype was unclassified in four children. Among all children, 93 (51%) had epilepsy, 109 (59%) intellectual disability, 42 (23%) severe vision and 10 (5%) hearing impairments while 84 (45%) children had severe speech impairments. Fifty-two (28%) children were born prematurely, and 46 (25%) had Apgar scores below 7 at five minutes. CONCLUSION: Compared to other European studies, the distribution of CP subtypes was different in Moldova. Moreover, the estimated prevalence, the proportions with severe motor and associated impairments and of children born at term were higher in Moldova while the proportion with low Apgar did not differ. The findings may suggest different etiological pathways causing CP in Moldova than in other European countries. A national register is warranted for quality assurance and improvement.

PMID: 30340478

Prevention and Cure

23. Nesting Environment Provides Sex-Specific Neuroprotection in a Rat Model of Neonatal Hypoxic-Ischemic Injury.
Mason B, Rollins LG, Asumadu E, Cange C, Walton N, Donaldson ST.

Front Behav Neurosci. 2018 Oct 2;12:221. doi: 10.3389/fnbeh.2018.00221. eCollection 2018.

Hypoxic-ischemic (HI) encephalopathy is a devastating injury that occurs when the fetal brain is deprived of oxygen and blood to a degree that may lead to neurological damage, seizing and cerebral palsy. In rodents, early environmental enrichment that promotes maternal care-taking behavior (mCTB) can improve neurobehavioral outcomes and protect against neurological decline. We hypothesized that an enhanced nesting environment would improve mCTB as measured by pup weight gain, and support greater HI recovery in developing rats. Pregnant dams (E15-16) were introduced to either control Standard Facility (SF) housing or closed nestbox (CN) conditions and maintained in larger cages through pup weaning. On postnatal day (PND) 7, male and female Long-Evans rat pups (N = 73) were randomly sorted into one of two surgical conditions: control and HI. HI pups received isoflurane anesthesia and right carotid artery ligation, a 2-h rest followed by 90 min exposure to a moist hypoxic (92% N, 8% O2) chamber. Pups (PND 8) were weighed daily, and tested on the Morris Water Maze (MWM) task (PND 35-50). Results demonstrate significant differences afforded to male and female pups based on weight measure, where CN-rearing modifies pre-weaning adolescent weights in females and increases post-weaning weights in males and females by an average of 10 g. Following successful MWM training and acquisition (PND 35-37), both male and female CN-raised animals demonstrated faster latency to find the hidden platform (HP) during HP trials (PND 38-42) and appeared to freely explore the MWM pool during an additional probe trial (PND 43). Moreover, after sacrifice (PND 60), CN rearing created sex-specific alterations in brain-derived neurotrophic factor (BDNF), glial-derived neurotrophic factor (GDNF) immunopositive cell staining of the dorsomedial striatum and CA1 of the hippocampus. CN-rearing afforded HI males higher BDNF levels in the striatum and produced greater GDNF levels in the hippocampus of HI-injured females. These results suggest that early life environmental enrichment positively modifies nesting environment, increases weight gain, as well as spatial learning and memory in a sex-specific directionality. Our findings also implicate correlative changes in corticolimbic neurotrophin protein levels in the CN-reared animals that may contribute to these benefits.

PMID: 30356904