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NEWS
Cerebral Palsy Research

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Interventions and Management

1. Efficacy of a home-based platform for child-to-child interaction on hand motor function in unilateral cerebral palsy.
Nuara A, Avanzini P, Rizzolatti G, Fabbri-Destro M.

Dev Med Child Neurol. 2019 May 21. doi: 10.1111/dmcn.14262. [Epub ahead of print]

AIM: To evaluate the feasibility and effectiveness of an action observation treatment (AOT) home-based platform promoting child-to-child interaction to improve hand motor function in unilateral cerebral palsy (CP). METHOD: Twenty children (14 males, six females; mean age 6y 7mo, standard deviation 1y 7mo; range 5y 1mo-10y 6mo) with unilateral CP underwent 20 sessions where they had to observe and then imitate a wizard performing dexterity-demanding magic tricks; a child-to-child live video-session to practise the same exercise then took place. We assessed hand-motor skills with the Besta Scale, neurological motor impairment with Fugl-Meyer Assessment for upper extremity, as well as spasticity, muscle strength, visual analogue scale, and global impression of change 1-month before (T-1), at baseline (T0), and at the end of treatment (T1). RESULTS: We observed a T0 to T1 improvement in global hand-motor and bimanual skills, and a significant correlation between motor improvement and difference in hand motor skills relative to the peer (r=-0.519). INTERPRETATION: AOT associated with child-to-child interaction effectively improves hand motor function in unilateral CP. This improvement is linked to differences in hand motor ability among peers, suggesting that children should observe others with superior motor skills to their own. This study extends traditional AOT toward novel socially-enriched scenarios, where children might simultaneously be recipients and leaders within a motor learning process. WHAT THIS PAPER ADDS: Home-based action observation treatment (AOT) based on child-to-child interaction improves hand motor function in children with unilateral cerebral palsy. Interaction with a more capable peer increases the chances of positive outcome in child-to-child AOT.

PMID: 31115046

2. Patterns of hip migration in non-ambulant children with cerebral palsy: A prospective cohort study.
Poirot I, Laudy V, Rabilloud M, Roche S, Iwaz J, Kassaï B, Vuillerot C.

Ann Phys Rehabil Med. 2019 May 20. pii: S1877-0657(19)30064-8. doi: 10.1016/j.rehab.2019.04.008. [Epub ahead of print]

BACKGROUND: In children with cerebral palsy (CP), we have little information on when hip migration (HM) starts, what causes hip displacement, how HM changes over time, and how to halt this migration to avoid surgery. OBJECTIVES: We aimed to estimate the prevalence of HM percentage (HMP)>40% in a homogeneous population of non-ambulant children with CP and model the changes in HMP over a 2.6-year mean follow-up. METHODS: From September 2009 to September 2015, this observational, prospective, multicenter cohort study recruited 235 children from 51 centers who were 3 to 10 years old and had levels IV and V of the Gross Motor Function Classification System for CP. The outcomes were yearly HMP measurements by the Reimers index. Only children with at least one hip with HMP≤40% at baseline were included in trajectory modeling. Comparisons of chidren's characteristics between trajectory groups were adjusted by the false discovery

rate method. RESULTS: The prevalence of children with at least one hip with HMP>40% was estimated at 24.3% (95% confidence interval 18.6-30.0). Pelvic obliquity was observed in 51.4% and 24.4% of children with asymmetric and symmetric HMP (P=0.002). The trajectory modelling identified 3 types of MP changes over time. Many children (67.4% and 79.3% for the right and left hip) could be assigned to the "stable" trajectory group. CONCLUSIONS: In non-ambulant children with CP, the prevalence of HM requiring surgery is low and most hips remain practically stable over time.

PMID: 31121332

3. Can altered muscle synergies control unimpaired gait?
Mehrabi N, Schwartz MH, Steele KM.

J Biomech. 2019 May 8. pii: S0021-9290(19)30314-8. doi: 10.1016/j.jbiomech.2019.04.038. [Epub ahead of print]

Recent studies have postulated that the human motor control system recruits groups of muscles through low-dimensional motor commands, or muscle synergies. This scheme simplifies the neural control problem associated with the high-dimensional structure of the neuromuscular system. Several lines of evidence have suggested that neurological injuries, such as stroke or cerebral palsy, may reduce the dimensions that are available to the motor control system, and these altered dimensions or synergies are thought to contribute to impaired walking patterns. However, no study has investigated whether impaired low-dimensional control spaces necessarily lead to impaired walking patterns. In this study, using a two-dimensional model of walking, we developed a synergy-based control framework that can simulate the dynamics of walking. The simulation analysis showed that a synergy-based control scheme can produce well-coordinated movements of walking matching unimpaired gait. However, when the dimensions available to the controller were reduced, the simplified emergent pattern deviated from unimpaired gait. A system with two synergies, similar to those seen after neurological injury, could not produce an unimpaired walking pattern. These findings provide further evidence that altered muscle synergies can contribute to impaired gait patterns and may need to be directly addressed to improve gait after neurological injury.

PMID: 31101431

4. Longitudinal Growth in Single Word Intelligibility Among Children With Cerebral Palsy From 24 to 96 Months of Age: Predicting Later Outcomes From Early Speech Production.
Hustad KC, Sakash A, Natzke PEM, Broman AT, Rathouz PJ2.

J Speech Lang Hear Res. 2019 May 20:1-15. doi: 10.1044/2018_JSLHR-S-18-0319. [Epub ahead of print]

Purpose Children with cerebral palsy (CP) are at risk for significant communication problems. Reduced speech intelligibility is common, even for those who do not have speech motor deficits. Development of intelligibility has not been comprehensively quantified in children with CP; as a result, we are currently unable to predict later speech outcomes. Such information would advance treatment decision making. We sought to examine growth in speech intelligibility among children with CP using a prospective longitudinal design, with a focus on age of crossing target intelligibility thresholds, age of greatest intelligibility growth, and how well intelligibility at 36 months predicted intelligibility at 96 months. Method Sixty-nine children with CP were followed longitudinally between 24 and 96 months of age. A total of 566 time points were examined across children (M = 8.2 time points per child, SD = 2.6). We fitted a nonlinear random effects model for longitudinal observations and then used the fitted model trajectories to generate descriptive analyses of growth. We used results of the model to generate a set of simulations, which we analyzed to determine how well 36-month intelligibility data predicted 96-month data. Results Half of children crossed 25% and 50% intelligibility thresholds at 36 and 49 months of age, respectively. Slightly more than half of children did not reach 75% intelligibility by 96 months of age. Age of crossing 25%, 50%, and 75% intelligibility thresholds was highly negatively correlated with intelligibly at 96 months. Children had the steepest intelligibility growth at 36 months, followed by 48 and 60 months. Intelligibility at 36 months was highly predictive of intelligibility at 96 months. Conclusions The developmental window from 3 to 5 years constitutes a time of rapid growth in speech intelligibility in children with CP. Children who cross intelligibility thresholds of 25%, 50%, and 75% at earlier ages have better outcomes when they are older; early performance is highly predictive of later speech intelligibility outcomes. Children with CP as a group have delayed speech intelligibility development but are still growing through 96 months of age.

PMID: 31112444

5. Unsuccessful submandibular duct surgery for anterior drooling: Surgical failure or parotid gland salivation?
Delsing CPA, Bekkers S, van Hulst K, Erasmus CE, van den Hoogen FJA.

Int J Pediatr Otorhinolaryngol. 2019 Apr 30;123:132-137. doi: 10.1016/j.ijporl.2019.04.036. [Epub ahead of print]

OBJECTIVES: To evaluate if drooling recurrence after surgery of the submandibular ducts is due to surgical failure or other variables. METHODS: Historic cohort with prospective collected data of all patients with severe drooling who underwent unsuccessful submandibular duct surgery with subsequent re-intervention between 2003 and 2018. A reference cohort was used for comparison of clinical variables. RESULTS: Six males and 4 females were included (cerebral palsy n = 8, neurodevelopmental disorders n = 2). All patients underwent submandibular gland surgery as a primary intervention (duct ligation n = 8, submandibular duct relocation n = 2) followed by re-intervention (submandibular gland excision n = 7, parotid duct ligation n = 3). One patient underwent tertiary surgery (parotid duct ligation after re-intervention by submandibular gland excision). Three patients were successful after re-intervention. No difference was found between both re-intervention techniques. There was significantly more severe dental malocclusion (50% vs. 21%, P value = 0.047) and severe speech disorders (80% vs. 42%, P value = 0.042) in the current cohort when compared to the reference cohort. CONCLUSION: Recurrence of drooling surgery is most likely not caused by surgical failure of the primary intervention, because re-intervention (submandibular gland excision) did not lead to more success. Dysarthria and dental malocclusion might negatively influence treatment outcome.

PMID: 31102967

6. The Impact of Dysarthria on Laypersons' Attitudes towards Adults with Cerebral Palsy.
Schölderle T, Staiger A, Schumacher B, Ziegler W.

Folia Phoniatr Logop. 2019 May 22:1-12. doi: 10.1159/000493916. [Epub ahead of print]

OBJECTIVE: This study investigated laypersons' attitudes towards adults with dysarthria due to cerebral palsy (CP). We aimed to explore the impact of the overall severity and of specific symptoms of dysarthria on laypersons' evaluations. PATIENTS AND METHODS: Eighteen adults with dysarthria due to CP and 6 nondysarthric controls participated as speakers. The individuals with CP underwent dysarthria assessment based on a standardized tool. The results were compared to those of a listening experiment with 20 laypersons. A text passage spoken by all speakers was presented to the listeners, who provided their evaluations using rating scales specifically developed for this study. The tool addressed 3 dimensions of attitudes: (1) estimation of a speaker's cognitive-linguistic abilities; (2) attribution of personality and social characteristics, and (3) listeners' emotions and behavioral tendencies towards the speaker. RESULTS: Severity of dysarthria was strongly correlated with the overall attitudes. Regression analyses identified different symptoms as predictors of the listeners' judgements. CONCLUSION: Severity of dysarthria seems to have a major impact on laypersons' attitudes. Results suggest that speech symptoms may have a very specific influence on laypersons' evaluations. This may be important for clinical care, since symptoms with the most negative impact should be focused on in treatment.

PMID: 31117109

7. Ease of Caregiving for Children: Re-Validation of Psychometric Properties of the Measure for Children with Cerebral Palsy up to 11 Years of Age.
Alghamdi MS, Chiarello LA, Avery L, Palisano RJ.

Dev Neurorehabil. 2019 May 20:1-10. doi: 10.1080/17518423.2019.1616844. [Epub ahead of print]

PURPOSE: To re-validate stability and hierarchal ordering of items, test-retest reliability, and construct validity of the Ease of Caregiving for Children measure for parents of children with cerebral palsy (CP) up to 11 years of age. METHODS: Participants were 613 parents of children with CP between 1.5 and 11 years of age. Parents completed Ease of Caregiving for Children and both parents and therapists classified children's levels of gross motor, manual and communication functions. RESULTS: Rasch analysis indicated acceptable fit of items, stable item calibration, and logical ordering of items by difficulty. Test-retest reliability was good: ICC = 0.69 (95% CI 0.52-0.81). For construct validity, ease of caregiving was higher for parents of children with higher functioning compared to parents of children with lower functioning, $p < .001$. CONCLUSIONS: Ease of Caregiving for Children is a unidimensional, reliable and valid measure of physical caregiving for parents of children with CP 1.5-11 years.

PMID: 31107128

8. Corrigendum: Cross-Cultural Validation of Children's Assessment of Participation and Enjoyment Portuguese Version.
Vila-Nova F, Oliveira R, Cordovil R.

Front Pediatr. 2019 Apr 30;7:167. doi: 10.3389/fped.2019.00167. eCollection 2019.

This corrects the article DOI: 10.3389/fped.2019.00033. Erratum for Cross-Cultural Validation of Children's Assessment of Participation and Enjoyment Portuguese Version. [Front Pediatr. 2019]

PMID: 31114773

9. Facilitating the transition of young people with long-term conditions through health services from childhood to adulthood: the Transition research programme.
Editors: Colver A, Rapley T, Parr JR, McConachie H, Dovey-Pearce G, Le Couteur A, McDonagh JE, Bennett C, Hislop J, Maniatopoulos G, Mann KD, Merrick H, Pearce MS, Reape D, Vale L.

Source: Southampton (UK): NIHR Journals Library; 2019 May. Programme Grants for Applied Research.

BACKGROUND: As young people with long-term conditions move from childhood to adulthood, their health may deteriorate and their social participation may reduce. ‘Transition’ is the ‘process’ that addresses the medical, psychosocial and educational needs of young people during this time. ‘Transfer’ is the ‘event’ when medical care moves from children’s to adults’ services. In a typical NHS Trust serving a population of 270,000, approximately 100 young people with long-term conditions requiring secondary care reach the age of 16 years each year. As transition extends over about 7 years, the number in transition at any time is approximately 700. OBJECTIVES: Purpose – to promote the health and well-being of young people with long-term conditions by generating evidence to enable NHS commissioners and providers to facilitate successful health-care transition. Objectives – (1) to work with young people to determine what is important in their transitional health care, (2) to identify the effective and efficient features of transitional health care and (3) to determine how transitional health care should be commissioned and provided. DESIGN, SETTINGS AND PARTICIPANTS: Three work packages addressed each objective. Objective 1. (i) A young people’s advisory group met monthly throughout the programme. (ii) It explored the usefulness of patient-held health information. (iii) A ‘Q-sort’ study examined how young people approached transitional health care. Objective 2. (i) We followed, for 3 years, 374 young people with type 1 diabetes mellitus (150 from five sites in England), autism spectrum disorder (118 from four sites in England) or cerebral palsy (106 from 18 sites in England and Northern Ireland). We assessed whether or not nine proposed beneficial features (PBFs) of transitional health care predicted better outcomes. (ii) We interviewed a subset of 13 young people about their transition. (iii) We undertook a discrete choice experiment and examined the efficiency of illustrative models of transition. Objective 3. (i) We interviewed staff and observed meetings in three trusts to identify the facilitators of and barriers to introducing developmentally appropriate health care (DAH). We developed a toolkit to assist the introduction of DAH. (ii) We undertook a literature review, interviews and site visits to identify the facilitators of and barriers to commissioning transitional health care. (iii) We synthesised learning on ‘what’ and ‘how’ to commission, drawing on meetings with commissioners. MAIN OUTCOME MEASURES: Participation in life situations, mental well-being, satisfaction with services and condition-specific outcomes. STRENGTHS: This was a longitudinal study with a large sample; the conditions chosen were representative; non-participation and attrition appeared unlikely to introduce bias; the research on commissioning was novel; and a young person’s group was involved. LIMITATIONS: There is uncertainty about whether or not the regions and trusts in the longitudinal study were representative; however, we recruited from 27 trusts widely spread over England and Northern Ireland, which varied greatly in the number and variety of the PBFs they offered. The quality of delivery of each PBF was not assessed. Owing to the nature of the data, only exploratory rather than strict economic modelling was undertaken. RESULTS AND CONCLUSIONS: (1) Commissioners and providers regarded transition as the responsibility of children’s services. This is inappropriate, given that transition extends to approximately the age of 24 years. Our findings indicate an important role for commissioners of adults’ services to commission transitional health care, in addition to commissioners of children’s services with whom responsibility for transitional health care currently lies. (2) DAH is a crucial aspect of transitional health care. Our findings indicate the importance of health services being commissioned to ensure that providers deliver DAH across all health-care services, and that this will be facilitated by commitment from senior provider and commissioner leaders. (3) Good practice led by enthusiasts rarely generalised to other specialties or to adults’ services. This indicates the importance of NHS Trusts adopting a trust-wide approach to implementation of transitional health care. (4) Adults’ and children’s services were often not joined up. This indicates the importance of adults’ clinicians, children’s clinicians and general practitioners planning transition procedures together. (5) Young people adopted one of four broad interaction styles during transition: ‘laid back’, ‘anxious’, ‘wanting autonomy’ or ‘socially oriented’. Identifying a young person’s style would help personalise communication with them. (6) Three PBFs of transitional health care were significantly associated with better outcomes: ‘parental involvement, suiting parent and young person’, ‘promotion of a young person’s confidence in managing their health’ and ‘meeting the adult team before transfer’. (7) Maximal service uptake would be achieved by services encouraging appropriate parental involvement with young

people to make decisions about their care. A service involving 'appropriate parental involvement' and 'promotion of confidence in managing one's health' may offer good value for money. FUTURE WORK: How might the programme's findings be implemented by commissioners and health-care providers? What are the most effective ways for primary health care to assist transition and support young people after transfer? STUDY REGISTRATION: This study is registered as UKCRN 12201, UKCRN 12980, UKCRN 12731 and UKCRN 15160. FUNDING: The National Institute for Health Research Programme Grants for Applied Research programme.

PMID: 31116547

10. Effect of aspiration on the lungs in children: a comparison using chest computed tomography findings.
Tanaka N, Nohara K, Ueda A, Katayama T, Ushio M, Fujii N, Sakai T.

BMC Pediatr. 2019 May 22;19(1):162. doi: 10.1186/s12887-019-1531-6.

BACKGROUND: Detecting and addressing aspiration early in children with dysphagia, such as those with cerebral palsy, is important for preventing aspiration pneumonia. The current gold standards for assessing aspiration are swallowing function tests, such as fiberoptic endoscopic evaluation of swallowing (FEES) and videofluorographic swallowing study; however, the relationship between aspiration of secretion vs aspiration of foodstuff and pulmonary injury is unclear. To clarify this relationship, we examined the correlations between pneumonia findings from chest computed tomography (CT) and the presence or absence of aspiration detected by FEES. METHODS: Eighty-five children (11 years 2 months ±7 years 2 months) underwent FEES and chest CT. Based on the FEES findings, the participants were divided into groups: with and without food aspiration, and with and without saliva aspiration. Correlations between chest CT findings of pneumonia and the presence or absence of each type of aspiration were then examined. RESULTS: No significant correlations were observed between food aspiration and chest CT findings of pneumonia, whereas saliva aspiration and chest CT findings of pneumonia were significantly correlated. In addition, saliva aspiration was significantly associated with bronchial wall thickening ($p < 0.01$) and atelectasis ($p < 0.05$). CONCLUSIONS: Our findings in children suggest that: (1) the presence or absence of food aspiration detected by FEES evaluation has little correlation with pneumonia, and (2) the presence or absence of saliva aspiration may be an indicator of aspiration pneumonia risk.

PMID: 31117982

11. Nutritional Status and Cardiometabolic Risk Factors in Institutionalized Adults with Cerebral Palsy.
Norte A, Alonso C, Martínez-Sanz JM, Gutierrez-Hervas A, Sospedra I.

Medicina (Kaunas). 2019 May 17;55(5). pii: E157. doi: 10.3390/medicina55050157.

Background and Objectives: Cerebral palsy (CP) is a set of permanent disorders that limit physical activity and increase the risk of developing other diseases, such as metabolic syndrome (MS). Adequate nutrition can contribute to the prevention of associated symptoms. The main objective of this study is to evaluate the nutritional status and the prevalence of cardiometabolic risk factors in adults with CP and Gross Motor Function Classification System (GMFCS) levels between IV and V. Materials and Methods: A sample of 41 adults with CP and GMFCS levels from IV to V were studied. The variables used in the study were age, sex, weight, height, mean age, and GMFCS level range. To evaluate nutritional status, body mass index and the Mini Nutritional Assessment (MNA), a nutritional screening tool, were used. To assess cardiometabolic risk, data on obesity, central obesity, blood pressure, fasting plasma glucose, total cholesterol, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, and triglycerides were collected. Results: More than 80% of the population studied was malnourished or at risk of malnutrition, according to the MNA tool classification ranges, and around 35% of the studied population was within the underweight range. Regarding cardiometabolic risk factors, only one adult with CP was diagnosed with MS. Conclusions: The studied population of adults with CP and GMFCS levels between IV and V is not a population at risk of MS; however, the high prevalence of malnutrition, as well as some of the most prevalent cardiovascular risk factors, should be taken into consideration.

PMID: 31108986

12. Emerging evidence for accelerated aging cardiovascular disease in individuals with cerebral palsy.
McPhee PG, MacDonald MJ, Cheng JL, Dunford EC, Gorter JW.

J Rehabil Med. 2019 May 23. doi: 10.2340/16501977-2564. [Epub ahead of print]

OBJECTIVE: To examine longitudinal changes in traditional and non-traditional risk factors for cardiovascular disease in individuals with cerebral palsy and to investigate relationships between age, Gross Motor Function Classification System (GMFCS) and risk of cardiovascular disease. METHODS: Individuals with cerebral palsy (n = 28 of 53 eligible participants; GMFCS levels I-V; follow-up mean age 35.1 years (standard deviation (SD) 14.4)) participated in a longitudinal cohort study with 4.0 years (SD 1.2) follow-up. Traditional risk factors included waist circumference and systolic blood pressure. Non-traditional risk factors included carotid artery intima media thickness and distensibility, carotid-femoral pulse wave velocity, and flow-mediated dilation. RESULTS: Absolute (0.31 mm (SD 0.13) vs 0.22 mm (SD 0.08), p = 0.045, 95% confidence interval (95% CI) 0.040, 0.151) and relative flow-mediated dilation (9.9% (SD 4.7) vs 7.5% (SD 2.6), p = 0.049, 95% CI 0.464, 4.42) decreased, while carotid artery intima media thickness (0.52 mm (SD 0.17 vs 0.67 mm (SD 0.33), p = 0.041, 95% CI -0.242, -0.074) increased from baseline to follow-up. No other risk factor changed significantly. Age at baseline was a significant independent predictor of carotid artery intima media thickness change (R-squared = 0.261, p = 0.031). CONCLUSION: Individuals with cerebral palsy experience significant changes in non-traditional risk factors for cardiovascular disease over 4 years, in the face of no changes in traditional risk factors. Compared with findings in the literature from the general population, these risk factors progress at a faster rate and at a younger age in individuals with cerebral palsy.

PMID: 31120542

13. Baclofen Toxicity Responsive to Hemodialysis in a Pediatric Patient with Acute Kidney Injury.
Gee SW, Outsen S, Becknell B, Schwaderer AL.

J Pediatr Intensive Care. 2016 Mar;5(1):37-40. doi: 10.1055/s-0035-1568151. Epub 2015 Nov 21.

Background Baclofen (para-chlorophenyl-gamma-aminobutyric acid) is widely used for its therapeutic effect of providing muscle relaxation from the persistent muscle spasms and posturing often related to spinal and central nervous system injuries. However, baclofen is also a potent neuronal depressant which is most evident in cases of toxicity. In severe toxicity, respiratory failure and obtundation may occur. Case-diagnosis/treatment We present the case of a neurologically devastated 16-year-old on chronic baclofen therapy for bilateral spastic cerebral palsy (Gross Motor Function Classification System level V) who presented with fever, leukocytosis, and hypotension. Initial management with fluid resuscitation and antimicrobials for presumed infection did initially improve the patient's mental status; however, he subsequently became comatose later during the same hospitalization. Comprehensive diagnostic studies and infectious work-up did not reveal an etiology. Upon further examination of history, acute kidney injury from chronic nonsteroidal use and complicated by vancomycin toxicity was suspected to cause acute baclofen toxicity. The patient underwent a single run of hemodialysis with resultant neurologic improvement and later laboratory-confirmed toxic baclofen levels. Conclusion Clinicians should consider possible acute baclofen toxicity in patients with impaired renal function who present with neurologic depression. Respiratory failure and mechanical ventilation, with its associated intensive care costs and complications, may be avoided with prompt treatment using hemodialysis.

PMID: 31110881

14. Influence of Combined Transcranial Direct Current Stimulation and Motor Training on Corticospinal Excitability in Children With Unilateral Cerebral Palsy.
Nemanich ST, Rich TL, Chen CY, Menk J, Rudser K, Chen M, Meekins G, Gillick BT.

Front Hum Neurosci. 2019 Apr 24;13:137. doi: 10.3389/fnhum.2019.00137. eCollection 2019.

Combined non-invasive brain stimulation (NIBS) and rehabilitation interventions have the potential to improve function in children with unilateral cerebral palsy (UCP), however their effects on developing brain function are not well understood. In a proof-of-principle study, we used single-pulse transcranial magnetic stimulation (TMS) to measure changes in corticospinal excitability and relationships to motor performance following a randomized controlled trial consisting of 10 days of combined constraint-induced movement therapy (CIMT) and cathodal transcranial direct current stimulation (tDCS) applied to the contralesional motor cortex. Twenty children and young adults (mean age = 12 years, 9 months, range = 7 years, 7 months, 21

years, 7 months) with UCP participated. TMS testing was performed before, after, and 6 months after the intervention to measure motor evoked potential (MEP) amplitude and cortical silent period (CSP) duration. The association between neurophysiologic and motor outcomes and differences in excitability between hemispheres were examined. Contralesional MEP amplitude decreased as hypothesized in five of five participants receiving active tDCS immediately after and 6 months after the intervention, however no statistically significant differences between intervention groups were noted for MEP amplitude [mean difference = -323.9 μV, 95% CI = (-989, 341), p = 0.34] or CSP duration [mean difference = 3.9 ms, 95% CI = (-7.7, 15.5), p = 0.51]. Changes in corticospinal excitability were not statistically associated with improvements in hand function after the intervention. Across all participants, MEP amplitudes measured in the more-affected hand from both contralesional (mean difference = -474.5 μV) and ipsilesional hemispheres (-624.5 μV) were smaller compared to the less-affected hand. Assessing neurophysiologic changes after tDCS in children with UCP provides an understanding of long-term effects on brain excitability to help determine its potential as a therapeutic intervention. Additional investigation into the neurophysiologic effects of tDCS in larger samples of children with UCP are needed to confirm these findings.

PMID: 31105541

15. Neurodevelopmental Outcomes in Preterm Infants with White Matter Injury Using a New MRI Classification.
Martinez-Biarge M, Groenendaal F, Kersbergen KJ, Benders MJNL, Foti F, van Haastert IC, Cowan FM, de Vries LS.

Neonatology. 2019 May 20:1-9. doi: 10.1159/000499346. [Epub ahead of print]

OBJECTIVE: The aim of this study was to evaluate whether a new MRI scoring system for preterm non-haemorrhagic white matter injury (WMI), derived from the analysis of the natural evolution of WMI throughout the neonatal period until term-equivalent age, can be used for outcome prediction. METHODS: Eighty-two infants <36 weeks gestation with WMI diagnosed from sequential cranial ultrasound and confirmed on neonatal MRI were retrospectively included. WMI was classified in four grades of severity. Neurodevelopmental data at a median age of 24 months were analysed. RESULTS: In 74 surviving children WMI severity was strongly associated with the presence and severity of cerebral palsy (CP) and other neurodevelopmental impairments (Spearman's rank correlation 0.88, p < 0.001). Only 3 children with grade I WMI (9%) developed CP (all ambulant) and their developmental scores were not different to those from the controls, although they started walking significantly later (p = 0.036). Of the 6 children with grade II, 83% developed CP (mild in most), whereas 91% of the 34 children with grade III had CP (moderate-severe in 76%) and all had some degree of neurodevelopmental impairment. Three children with grade III WMI did not develop CP; their imaging showed, in contrast to children who developed CP, that the cysts did not affect the corticospinal tracts; also, myelin in the posterior limb of the internal capsule appeared normal in 2 children and suboptimal in 1. CONCLUSIONS: This MRI scoring system for preterm WMI can be used to predict neurodevelopmental outcomes. Individualized assessment of the site of lesions and the progression of myelination improves prognostic accuracy.

PMID: 31108490

16. White matter changes follow low-frequency repetitive transcranial magnetic stimulation plus intensive occupational therapy for motor paralysis after stroke: a DTI study using TBSS.
Ueda R, Yamada N, Abo M, Senoo A.

Acta Neurol Belg. 2019 May 21. doi: 10.1007/s13760-019-01150-2. [Epub ahead of print]

Intervention that combines low-frequency repetitive transcranial magnetic stimulation (rTMS) and intensive occupational therapy (OT) may improve brain function in post-stroke patients with motor paralysis. We aimed to clarify the brain region involved in motor function improvement following chronic stroke. We recruited 25 patients hospitalized for 15 days with post-stroke upper extremity paralysis to receive 12 sessions of low-frequency rTMS over the non-lesioned hemisphere and occupational therapy. In this study, 72% of the patients had suffered from intracranial haemorrhage. Imaging analysis was performed using diffusion tensor imaging (DTI) to assess changes in white matter after intervention. We investigated white matter change before and after intervention and the relationship between white matter structure and motor function recovery using tract-based spatial statistics. The intra-voxel directional coherence was significantly increased in the anterior limb of the internal capsule and anterior thalamic radiation on the lesional side following intervention. Mean diffusivity and radial diffusivity values of clusters in the superior corona radiata on the lesional side were negatively correlated with motor function recovery. White matter nerve fibre structures are involved in motor function improvement following rTMS and OT interventions. Our results show novel findings regarding the relationship between stroke neurorehabilitation and cerebral nerve structure.

PMID: 31115787

17. Predictive model of proficiency in powered mobility of children and young adults with motor impairments.
Gefen N, Rigbi A, Weiss PL.

Dev Med Child Neurol. 2019 May 21. doi: 10.1111/dmcn.14264. [Epub ahead of print]

AIM: To identify variables that can predict proficiency in powered mobility use for children in young adults. METHOD: Participants included 80 children and young adults (42 males, 38 females; mean age 10y 2mo, [SD 5y 1mo]; range: 2-22y) with cerebral palsy, neuromuscular disease, and spinal cord injury who participated in the ALYN Hospital Powered Mobility Lending Program from 2009 to 2016. Data were collected and compared before and after participation in the program and powered mobility levels were determined by the Israeli Ministry of Health (MOH) Powered Mobility Proficiency Test. Multivariate logistic regression analysis followed by a bootstrapping procedure that was based on 1000 samples were used to determine if the variables were predictive of success on the Israeli MOH Powered Mobility Proficiency Test. RESULTS: Significant variables for predicting success were identified: manual wheelchair propulsion, go-stop voluntarily upon request, and using a joystick. The model was able to correctly identify 80% of the children. INTERPRETATION: Children and young adults with the ability to go-stop upon request, propel a manual wheelchair short distances, and use a joystick to activate the powered wheelchair had a higher chance of becoming proficient. In countries where wheelchair proficiency is a requirement for powered wheelchair procurement, these findings may support policy changes, as they did in Israel. WHAT THIS PAPER ADDS: Using powered wheelchairs offers children earlier and more natural practice to determine driving proficiency. Manual wheelchair propulsion, go-stop voluntarily upon request, and using a joystick were predictors of powered mobility proficiency. More than 80% of children use a joystick with their hand to activate a powered wheelchair.

PMID: 31115048

18. Ultracompact Multielectrode Array for Neurological Monitoring.
Cheng MY, Damalerio RB, Chen W, Rajkumar R, Dawe GS.

Sensors (Basel). 2019 May 17;19(10). pii: E2286. doi: 10.3390/s19102286.

Patients with paralysis, spinal cord injury, or amputated limbs could benefit from using brain-machine interface technology for communication and neurorehabilitation. In this study, a 32-channel three-dimensional (3D) multielectrode probe array was developed for the neural interface system of a brain-machine interface to monitor neural activity. A novel microassembly technique involving lead transfer was used to prevent misalignment in the bonding plane during the orthogonal assembly of the 3D multielectrode probe array. Standard microassembly and biopackaging processes were utilized to implement the proposed lead transfer technique. The maximum profile of the integrated 3D neural device was set to 0.50 mm above the pia mater to reduce trauma to brain cells. Benchtop tests characterized the electrical impedance of the neural device. A characterization test revealed that the impedance of the 3D multielectrode probe array was on average approximately 0.55 MΩ at a frequency of 1 KHz. Moreover, in vitro cytotoxicity tests verified the biocompatibility of the device. Subsequently, 3D multielectrode probe arrays were implanted in rats and exhibited the capability to record local field potentials and spike signals.

PMID: 31108970

19. Engaging children with cerebral palsy in interactive computer play-based motor therapies: theoretical perspectives.
Biddiss E, Chan-Viquez D, Cheung ST, King G.

Disabil Rehabil. 2019 May 19:1. doi: 10.1080/09638288.2019.1613681. [Epub ahead of print]

PURPOSE: To provide a theoretically grounded understanding of engagement in interactive computer play-based motor therapies by children with cerebral palsy in home settings. METHODS: A motivational framework for engagement and its relationship with three contemporary theories (self-determination theory, expectancy-value theory, social cognitive theory of self-regulation) was overviewed. A scoping review was conducted to understand how engagement is influenced by features of the technology and intervention design that impact intrinsic and extrinsic motivation, child and parent values and expectancies, and the processes of self-regulation. Multiple reviewers screened and extracted data from 26 articles describing home-based clinical trials of interactive computer play-based motor interventions for children with cerebral palsy. A narrative synthesis framework was used for analysis. RESULTS: Features of the technology and the intervention influence feelings of autonomy (e.g., personalization), competence (e.g., calibration), and relatedness (e.g., social play, virtual therapist/coach). There may be multiple and differently valued goals in interactive computer play-based interventions (e.g., game- and therapy-focused) that, if disconnected or unmet, negatively impact engagement. Multiplayer interactions, real-time feedback and progress tracking

provide information that influences self-regulation and engagement over time. CONCLUSIONS: Optimizing engagement in interactive computer play-based motor interventions requires closer alignment with client-led values/goals; design of technologies and interventions that sustain intrinsic motivation; and feedback that informs/builds self-efficacy. Implications for rehabilitation The decision to prescribe an interactive computer play-based motor intervention should be guided by client-led goals and an informed understanding of the capacity of the interactive computer play-based intervention to meet individual client values/expectancies. Sustaining intrinsic motivation in interactive computer play-based motor therapies is greatly influenced by features of the technology (e.g., calibration, feedback, personalization) and the intervention (e.g., interactions with therapists, social play). Increased effort should be directed towards ensuring that interactive computer play-based interventions and technologies reward and reinforce efforts towards therapy goals.

PMID: 31104517

Prevention and Cure

20. Survey on use of antenatal magnesium sulphate for fetal neuroprotection prior to preterm birth in Australia and New Zealand - Ongoing barriers and enablers.
Gatman K, May R, Crowther C.

Aust N Z J Obstet Gynaecol. 2019 May 22. doi: 10.1111/ajo.12981. [Epub ahead of print]

BACKGROUND: Clinical practice guidelines recommend the use of antenatal magnesium sulphate for fetal neuroprotection before preterm birth at <30 weeks' gestation. AIMS: This survey assessed the use of antenatal magnesium sulphate for fetal neuroprotection to determine if use has changed since the previous survey in 2012, and to evaluate enablers and barriers to use. MATERIALS AND METHODS: A questionnaire was sent to clinical leaders at 29 hospitals with a neonatal intensive care unit in Australia and New Zealand asking at what gestational ages magnesium sulphate was given, if use was audited and any enablers and barriers to use. RESULTS: Responses were received for 24 (83%) hospitals. The use of magnesium sulphate for fetal neuroprotection was reported as 89% (IQR 80-90%), an increase from 80% (IQR 53-90%) from the earlier survey. The majority of health professionals were reported as using magnesium sulphate at <30 weeks' gestation. The top enablers for use of magnesium sulphate were availability of pamphlets, posters, case record stickers and PowerPoint presentations. The main reasons as to why eligible women did not receive magnesium sulphate were imminent birth, the hospital being short staffed and the patient declined. The use of antenatal magnesium sulphate has been or is being audited in 11 (46%) of the hospitals. CONCLUSIONS: Clinical leaders at institutions in Australia and New Zealand report that uptake in the use of magnesium sulphate for fetal neuroprotection has continued to increase since the earlier, bi-national survey in 2012. Barriers to the use of magnesium sulphate identified have institutional and consumer implications.

PMID: 31119725

21. [Combined therapy in neonatal hypoxic-ischaemic encephalopathy].
Cánovas-Ahedo M, Alonso-Alconada D.

An Pediatr (Barc). 2019 May 17. pii: S1695-4033(19)30173-0. doi: 10.1016/j.anpedi.2019.04.007. [Epub ahead of print] [Article in Spanish]

Neonatal hypoxic-ischaemic encephalopathy due to the lack of oxygen at birth can have severe neurological consequences, such as cerebral palsy, or even the death of the asphyxiated newborn. Hypothermia is currently the only therapy included in intensive care neonatal units. This shows a clinical benefit in neonates suffering from hypoxic-ischaemic encephalopathy, mainly because of its ability to decrease the accumulation of excitatory amino acids and its anti-inflammatory, antioxidant, and anti-apoptotic effects. However, hypothermia is not effective in half of the cases, making it necessary to search for new, or to optimize current therapies, with the aim on reducing asphyxia-derived neurological consequences, either as single treatments or in combination with cooling. Within current potential therapies, melatonin, allopurinol, and erythropoietin stand out among the others, with clinical trials on the way. While, stem cells, N-acetylcysteine and noble gases have obtained promising pre-clinical results. Melatonin produces a powerful antioxidant and anti-inflammatory effect, acting as free radical scavenger and regulating pro-inflammatory mediators. Through the inhibition of xanthine oxidase, allopurinol can decrease oxidative stress. Erythropoietin has cell death and neurogenesis as its main therapeutic targets. Keeping in mind the whole scenario of current therapies, management of neonates suffering from neonatal asphyxia could rely on the combination of one or some of these treatments, together with therapeutic hypothermia.

PMID: 31109785

22. Intranasal Delivery of Mesenchymal Stromal Cells Protects against Neonatal Hypoxic-Ischemic Brain Injury.
McDonald CA, Djuliannisaa Z, Petraki M, Paton MCB, Penny TR, Sutherland AE, Castillo-Melendez M, Novak I, Jenkin G, Fahey MC, Miller SL.

Int J Mol Sci. 2019 May 17;20(10). pii: E2449. doi: 10.3390/ijms20102449.

Cerebral palsy (CP) is a permanent motor disorder that results from brain injury and neuroinflammation during the perinatal period. Mesenchymal stromal cells (MSCs) have been explored as a therapy in multiple adult neuroinflammatory conditions. Our study examined the therapeutic benefits of intranasal delivery of human umbilical cord tissue (UC) derived-MSCs in a rat model of neonatal hypoxic-ischemic (HI) brain injury. To do this, HI was performed on postnatal day 10 Sprague-Dawley rat pups via permanent ligation of the left carotid artery, followed by a hypoxic challenge of 8% oxygen for 90 min. A total of 200,000 UC-MSCs (10 million/kg) were administered intranasally 24 h post-HI. Motor control was assessed after seven days, followed by post-mortem. Analysis included brain immunohistochemistry, gene analysis and serum cytokine measurement. Neonatal HI resulted in brain injury with significant loss of neurons, particularly in the hippocampus. Intranasal administration of UC-MSCs significantly reduced the loss of brain tissue and increased the number of hippocampal neurons. HI significantly upregulated brain inflammation and expression of pro-inflammatory cytokines, while intranasal UC-MSCs significantly reduced markers of neuroinflammation. This study demonstrated that a clinically relevant dose (10 million/kg) of UC-MSCs was neuroprotective following HI by restoring neuronal cell numbers and reducing brain inflammation. Therefore, intranasal delivery of UC-MSCs may be an effective therapy for neonatal brain injury.

PMID: 31108944

23. Autologous cord blood in children with cerebral palsy: a review.
Boruczkowski D, Pujal JM, Zdolińska-Malinowska I.

Int J Mol Sci. 2019 May 16;20(10). pii: E2433. doi: 10.3390/ijms20102433.

The aim of this narrative review is to report on the current knowledge regarding the clinical use of umbilical cord blood (CB) based on articles from PubMed and clinical trials registered on ClinicalTrials.gov. An increasing amount of evidence suggests that CB may be used for both early diagnostics and treatment of cerebral palsy. The acidity of CB and its biochemical parameters, including dozens of cytokines, growth factors, and other metabolites (such as amino acids, acylcarnitines, phosphatidylcholines, succinate, glycerol, 3-hydroxybutyrate, and O-phosphocholine) are predictors of future neurodevelopment. In addition, several clinical studies confirmed the safety and efficacy of CB administration in both autologous and allogeneic models, including a meta-analysis of five clinical trials involving a total of 328 participants. Currently, nine clinical trials assessing the use of autologous umbilical CB in children diagnosed with hypoxic-ischemic encephalopathy or cerebral palsy are in progress. The total population assessed in these trials exceeds 2500 patients.

PMID: 31100943