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NEWS
Cerebral Palsy Research

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Interventions and Management

1. Dev Med Child Neurol. 2013 May;55(5):418-26. doi: 10.1111/dmcn.12140.

A systematic review of tests to predict cerebral palsy in young children.

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AIM: This systematic review evaluates the accuracy of predictive assessments and investigations used to assist in the diagnosis of cerebral palsy (CP) in preschool-age children (<5y). METHOD: Six databases were searched for studies that included a diagnosis of CP validated after 2 years of age. The validity of the studies meeting the criteria was evaluated using the Standards for Reporting Diagnostic Accuracy criteria. Where possible, results were pooled and a meta-analysis was undertaken. RESULTS: Nineteen out of 351 studies met the full inclusion criteria, including studies of general movements assessment (GMA), cranial ultrasound, brain magnetic resonance imaging (MRI), and neurological examination. All studies assessed high-risk populations including preterm (gestational range 23-41wks) and low-birthweight infants (range 500-4350g). Summary estimates of sensitivity and specificity of GMA were 98% (95% confidence interval [CI] 74-100%) and 91% (95% CI 83-93%) respectively; of cranial ultrasound 74% (95% CI 63-83%) and 92% (95% CI 81-96%) respectively; and of neurological examination 88% (95% CI 55-97%) and 87% (95% CI 57-97%) respectively. MRI performed at term corrected age (in preterm infants) appeared to be a strong predictor of CP, with sensitivity ranging in individual studies from 86 to 100% and specificity ranging from 89 to 97% There was inadequate evidence for the use of other predictive tools. SUMMARY: This review found that the assessment with the best evidence and strength for predictive accuracy is the GMA. MRI has a good predictive value when performed at term-corrected age. Cranial ultrasound is as specific as MRI and has the advantage of being readily available at the bedside. Studies to date have focused on high-risk infants. The accuracy of these tests in low-risk infants remains unclear and requires further research.

PMID: 23574478 [PubMed - in process]

2. Dev Med Child Neurol. 2013 May;55(5):397-8. doi: 10.1111/dmcn.12097.

High and variable prevalence does matter in reviews of diagnostic accuracy in cerebral palsy.

Hanna SE.

Department of Clinical Epidemiology and Biostatistics, McMaster University, Hamilton, ON, Canada.

PMID: 23574477 [PubMed - in process]

3. Brain Struct Funct. 2013 Apr 10. [Epub ahead of print]

Interhemispheric and intrahemispheric connectivity and manual skills in children with unilateral cerebral palsy.

Weinstein M, Green D, Geva R, Schertz M, Fattal-Valevski A, Artzi M, Myers V, Shiran S, Gordon AM, Gross-Tsur V, Bashat DB.

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This study investigated patterns of motor brain activation, white matter (WM) integrity of inter- and intrahemispheric connectivity and their associations with hand function in children with unilateral cerebral palsy (CP-U). Fourteen CP-U (mean age 10.6 ± 2.7 years) and 14 typically developing children (TDC) underwent magnetic resonance imaging. CP-U underwent extensive motor evaluation. Pattern of brain activation during a motor task was studied in 12 CP-U and six TDC, by calculating laterality index (LI) and percent activation in the sensorimotor areas (around the central sulcus), and quantifying the activation in the supplementary motor area (SMA). Diffusivity parameters were measured in CP-U and eight other TDC for the corpus callosum (CC), affected and less affected cortico-spinal tracts (CST), and posterior limb of the internal capsule (PLIC). Abnormal patterns of brain activation were detected in areas around the central sulcus in 9/12 CP-U, with bilateral activation and/or reduced percent activation. More activation in areas around the central sulcus of the affected hemisphere was associated with better hand function. CP-U demonstrated more activation in the SMA when moving the affected hand compared to the less affected hand. CP-U displayed reduced WM integrity compared to TDC, in the midbody and splenium of the CC, affected CST and affected PLIC. WM integrity in these tracts was correlated with hand function. While abnormal pattern of brain activation was detected mainly when moving the affected hand, the integrity of the CC was correlated with function of both hands and bimanual skills. This study highlights the importance of interhemispheric connectivity for hand function in CP-U, which may have clinical implications regarding prognosis and management.

PMID: 23571779 [PubMed - as supplied by publisher]

4. BMJ Open. 2013 Apr 10;3(4). pii: e002853. doi: 10.1136/bmjopen-2013-002853. Print 2013.

Move it to improve it (Mitii): study protocol of a randomised controlled trial of a novel web-based multimodal training program for children and adolescents with cerebral palsy.

Boyd RN, Mitchell LE, James ST, Ziviani J, Sakzewski L, Smith A, Rose S, Cunnington R, Whittingham K, Ware RS, Comans TA, Scuffham PA.

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INTRODUCTION: Persons with cerebral palsy require a lifetime of costly and resource intensive interventions which are often limited by equity of access. With increasing burden being placed on health systems, new methods to deliver intensive rehabilitation therapies are needed. Move it to improve it (Mitii) is an internet-based multimodal programme comprising upper-limb and cognitive training with physical activity. It can be accessed in the client's home at their convenience. The proposed study aims to test the efficacy of Mitii in improving upper-limb function and motor planning. Additionally, this study hopes to further our understanding of the central neurovascular mechanisms underlying the proposed changes and determine the cost effectiveness of Mitii. METHODS AND

ANALYSIS: Children with congenital hemiplegia will be recruited to participate in this waitlist control, matched pairs, single-blind randomised trial. Children be matched at baseline and randomly allocated to receive 20 weeks of 30 min of daily Mitii training immediately, or waitlisted for 20 weeks before receiving the same Mitii training (potential total dose=70 h). Outcomes will be assessed at 20 weeks after the start of Mitii, and retention effects tested at 40 weeks. The primary outcomes will be the Assessment of Motor and Process Skills (AMPS), the Assisting Hand Assessment (AHA) and unimanual upper-limb capacity using the Jebsen-Taylor Test of Hand Function (JTTHF). Advanced brain imaging will assess use-dependant neuroplasticity. Measures of body structure and functions, activity, participation and quality of life will be used to assess Mitii efficacy across all domains of the International Classification of Functioning, Disability and Health framework. ETHICS AND DISSEMINATION: This project has received Ethics Approval from the Medical Ethics Committee of The University of Queensland (2011000608) and the Royal Children's Hospital Brisbane (HREC/11/QRCH/35). Findings will be disseminated widely through conference presentations, seminars and peer-reviewed scientific journals.

TRIAL REGISTRATION: ACTRN12611001174976.

PMID: 23578686 [PubMed] Free full text

5. Phys Ther. 2013 Apr 11. [Epub ahead of print]

Evaluating Exercise Intensity Levels in Children With Cerebral Palsy Playing the Wii.

Robert M, Ballaz L, Hart R, Lemay M.

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BACKGROUND: Children with cerebral palsy (CP) are prone to secondary complications related to physical inactivity and poor cardiorespiratory capacity. This problem could be greatly attenuated through the use of video games that incorporate physical activity because video games already represent an important component of leisure time in younger people and such games can lead to a high level of exercise intensity in healthy individuals. OBJECTIVES: To evaluate exercise intensity in children with spastic diplegic CP and children who are typically developing while playing the Wii Fit active video game console. DESIGN: Cross-sectional study. METHODS: Ten children (7-12 years old) with spastic diplegic CP (Gross Motor Function Classification System level I or II) and 10 age-matched children who are typically developing were evaluated in the movement analysis laboratory. Four games were played on the Wii Fit (jogging, bicycling, snowboarding and skiing) for a total of 40 minutes. Heart rate was recorded during the whole playing period with a heart rate belt monitor. Game intensity was defined as the percentage of heart rate reserve (HRR). Lower extremity motion analysis was also carried out on the final minute of the playing period for the jogging and bicycling games. RESULTS: No difference between groups was observed for any variables ($p > 0.05$). A main effect of games was observed for the amount of time spent at an intensity greater than 40% of HRR. Specifically, > 50% of the playing time for the jogging game and > 30% of the playing time for the bicycling game was spent over 40% of HRR. In addition, the jogging game produced a larger range of motion than the bicycling game. CONCLUSIONS: For all four games, similar exercise intensity was observed for children who are typically developing and children with CP suggesting that children with CP could obtain similar exercise-related benefits as children without CP while playing on the Wii Fit.

PMID: 23580626 [PubMed - as supplied by publisher]

16. Phys Ther. 2013 Apr 11. [Epub ahead of print]

Reproducibility and Validity of the 10-Meter Shuttle Ride Test in Wheelchair-Bound Children and Adolescents With Cerebral Palsy.

Verschuren O, Zwinkels M, Ketelaar M, Reijnder-van Son F, Takken T.

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BACKGROUND: For children with cerebral palsy (CP) who are able to walk or run, the 10-meter shuttle run test is currently the test of choice to assess cardiorespiratory fitness. This test, however, has not yet been examined in wheelchair-bound youth with CP. OBJECTIVE: To investigate the test-retest reproducibility and validity of the Shuttle Ride Test (SRiT) in youth with CP. DESIGN: Repeated measures of the SRiT were obtained. METHODS: Twenty-three participants with spastic CP (mean (SD) age of 13.3 (3.6 years); 18 boys, 5 girls) using a manual wheelchair for at least part of the day participated in this study. During the study, all subjects performed 1 graded arm exercise test (GAET) and 2 identical SRiTs within 2 weeks. Peak oxygen uptake (VO2peak), peak heart rate (HRpeak), and Respiratory Exchange Ratio (RER) were recorded. Intraclass correlation coefficients (ICC2,1), the smallest detectable difference (SDD) and the limits of agreement (LOA) were calculated. The association between the results of the SRiT and GAET was tested using the Pearson correlation coefficients. RESULTS: Intra Class Correlation Coefficients (0.99; range 95% CI, 0.98-1.0) for all variables indicated highly acceptable reproducibility. LOA analysis revealed satisfactory levels of agreement. The SRiT variables demonstrated strong significant positive correlations for VO2peak values obtained during SRiT and GAET (PP: $r = 0.84$, $p < 0.01$). LIMITATIONS: Although considered as gold standard, the cardio-respiratory demand during the GAET was significantly lower compared to the SRiT. Future studies should determine whether GAET can still be accepted as the gold standard for upper extremity exercise. CONCLUSIONS: The SRiT is a reproducible and valid test for measuring cardiorespiratory fitness in youth with spastic CP who self-propel a manual wheelchair.

PMID: 23580630 [PubMed - as supplied by publisher]

9. Eur J Phys Rehabil Med. 2013 Feb;49(1):67-91.

Treadmill interventions with partial body weight support in children under six years of age at risk of neuromotor delay: a report of a Cochrane systematic review and meta-analysis.

Valentin-Gudiol M, Bagur-Calafat C, Girabent-Farrés M, Hadders-Algra M, Mattern-Baxter K, Angulo-Barroso R.

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Delayed motor development may occur in children with Down syndrome, cerebral palsy or children born preterm, which in turn may limit the child's opportunities to explore the environment. Neurophysiologic and early intervention literature suggests that task-specific training facilitates motor development. Treadmill intervention is a good example of locomotor task-specific training. Aim: The aim of this paper was to assess the effectiveness of treadmill intervention on locomotor motor development in pre-ambulatory infants and children under six years of age who are at risk for neuromotor delay. Design: A Cochrane systematic review with meta-analysis. Methods: We employed a comprehensive search strategy. We included randomised, quasi-randomised and controlled clinical trials that evaluated the effect of treadmill intervention in children up to six years of age with delays in gait development or the attainment of independent walking or who were at risk of neuromotor delay. We searched CENTRAL, MEDLINE, EMBASE, PsycINFO, CINAHL, Science Citation Index, PEDro, CPCI-S and LILACS; and also ICTRP, ClinicalTrials.gov, mRCT and CenterWatch. Four authors independently extracted the data using standardized forms. Results: We included five studies, which reported on treadmill intervention in 139 children. Of the 139 children, 73 were allocated to treadmill intervention groups. The studies varied in the type of population studied, the type of comparison, the time of evaluation and the parameters assessed. Due to the diversity of the studies, we were only able to use data from three studies in meta-analyses and these were limited to two outcomes: age of onset of independent walking and gross motor function. Evidence suggested that treadmill intervention could lead to earlier onset of independent walking when compared to no treadmill intervention (effect estimate -1.47; 95% CI: -2.97, 0.03), though these trials studied two different populations: Down syndrome and children at risk of neuromotor disabilities. Children with Down syndrome seemed to benefit while it was not clear if this was the case for children at high risk of neuromotor disabilities. Two other studies, both in children with Down syndrome, compared different types of treadmill intervention (high versus low intensity training). Both were inconclusive regarding the impact of these different protocols on the age at which children started to walk. There is insufficient evidence to determine whether treadmill intervention improves gross motor function (effect estimate 0.88; 95% CI: -4.54, 6.30). Conclusion: The current review provided only limited evidence of the efficacy of treadmill intervention in children up to six years of age. Few studies have assessed treadmill interventions in young children using an appropriate control group. The available evidence indicates that treadmill intervention may accelerate the development of independent walking in children with Down syndrome. Further research is needed to confirm this and should also address whether intensive treadmill intervention can accelerate walking onset in young children with cerebral palsy and high risk infants, and whether treadmill intervention has a general effect on gross motor development in the

various subgroups of young children at risk for developmental delay.

PMID: 23575201 [PubMed - in process]

12. J Orthop Sci. 2013 Apr 12. [Epub ahead of print]

Rotational osteotomy with submuscular plating in skeletally immature patients with cerebral palsy.

Lee HJ, Oh CW, Song KS, Kim JW, Jung JW, Park BC, Kim JY.

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BACKGROUND: In cerebral palsy, intoeing gait with increased femoral anteversion is not uncommon and often requires surgical intervention. Although several conventional methods have been used, complications are common. We applied a new technique of rotational osteotomy with submuscular plating in skeletally immature patients with cerebral palsy. METHODS: Eighteen patients (26 femora, 8 bilateral) with a mean age of 8.7 years (range, 6-16) were prospectively treated with this technique. The anatomic distribution of patients was hemiplegia (n = 7), diplegia (n = 8), and asymmetric diplegia (n = 3). Percutaneous osteotomy was performed at the middle of the femoral shaft. After rotational correction, submuscular plating was done using a locking compression plate. Femoral anteversion was evaluated by a trochanteric prominence angle test (TPAT) and computed tomography. RESULTS: In all cases, each osteotomy healed in an average of 12 weeks (range, 10-14). The mean femoral anteversion by TPAT improved to 12° (range, 5°-30°) after surgery from 44° (range, 30°-65°) ($p < 0.001$). There were no complications of deep infection, implant failure, or limb length discrepancy over 1 cm. CONCLUSIONS: In skeletally immature patients with cerebral palsy, femoral anteversion can be safely corrected using submuscular plating with a locking compression plate.

PMID: 23579357 [PubMed - as supplied by publisher]

13. Dev Med Child Neurol. 2013 May;55(5):396. doi: 10.1111/dmcn.12137.

Comorbidities of cerebral palsy need more emphasis - especially pain.

Baxter P.

Editor in Chief.

PMID: 23574476 [PubMed - in process]

14. Eur Arch Otorhinolaryngol. 2013 Apr 12. [Epub ahead of print]

Auditory profile and high resolution CT scan in autism spectrum disorders children with auditory hypersensitivity.

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Autism is the third most common developmental disorder, following mental retardation and cerebral palsy. ASD children have been described more often as being preoccupied with or agitated by noise. The aim of this study was to evaluate theprevalence and clinical significance of semicircular canal dehiscence detected on CT images in ASD children with intolerance to loud sounds in an attempt to find ananatomical correlate with hyperacusis.14 ASD children with auditory hypersensitivity and 15 ASD children without auditoryhypersensitivity as control group age and gender matched were submitted to historytaking, otological examination, tympanometry and acoustic reflex thresholdmeasurement. ABR was done to validate normal peripheral hearing and integrity ofauditory brain stem pathway. High resolution CT scan petrous and temporal bone imaging was performed to all participated children. All

participants had normal hearing sensitivity in ABR testing. Absolute ABR peak waves of I and III showed no statistically significant difference between the two groups, while absolute wave V peak andinterpeak latencies I-V and III-V were shorter in duration in study group whencompared to the control group. CT scans revealed SSCD in 4 out of 14 of the studygroup (29 %), the dehiscence was bilateral in one patient and unilateral in threepatients. None of control group showed SSCD. In conclusion, we have reported evidence that apparent hypersensitivity to auditory stimuli (short conduction time in ABR) despite the normal physiological measures in ASD children with auditory hypersensitivity can provide a clinical clue of a possible SSCD.

PMID: 23580033 [PubMed - as supplied by publisher]

15. Neuropediatrics. 2013 Apr 6. [Epub ahead of print]

Language Comprehension in Young People with Severe Cerebral Palsy in Relation to Language Tracts: A Diffusion Tensor Imaging Study.

Harlaar L, Pouwels P, Geytenbeek J, Oostrom K, Barkhof F, Vermeulen RJ.

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Patients with severe cerebral palsy (CP) often have poor speech ability but potentially better language comprehension. The arcuate fasciculus and the extreme capsule are two important language tracts between the Wernicke and Broca areas. Using diffusion tensor imaging, we visualized language tracts and pyramidal tracts in both hemispheres in 10 controls (5 to 18 years) and 5 patients (5 to 23 years) with severe CP. Language comprehension was assessed with a recently designed instrument (the Computer-Based instrument for Low motor Language Testing [C-BiLLT]). The language tracts were visualized in all control children and in four CP patients. In one CP patient without any objective language comprehension skills, no language tract could be visualized. Both language and pyramidal tracts were smaller in patients than in controls. These preliminary data indicate a relation between language tracts and language skills. Further research is necessary to study the value of structural integrity of language tracts in predicting language comprehension in CP patients.

Georg Thieme Verlag KG Stuttgart. New York.

PMID: 23564318 [PubMed - as supplied by publisher]

16. J Paediatr Child Health. 2013 Apr;49(4):E349-50. doi: 10.1111/jpc.12144.

Vitamin d status in Tasmanian children with cerebral palsy.

Ware T, Whitelaw C, Flett P, Parameswaran V.

Children's Neuroscience Centre, Royal Children's Hospital, Melbourne, Victoria; Royal Hobart Hospital, Hobart, Tasmania, Australia; Calvary Rehabilitation Service (now St Giles Southern Services), Hobart, Tasmania, Australia.

PMID: 23574565 [PubMed - in process]

17. Phys Occup Ther Pediatr. 2013 May;33(2):170-3. doi: 10.3109/01942638.2013.780421.

Evidence to Practice Commentary New Evidence in Developmental Coordination Disorder (DCD).

Novak I.

Cerebral Palsy Alliance, School of Medicine, University of Notre Dame, Darlinghurst, NSW, Australia.

PMID: 23574479 [PubMed - in process]

Prevention and Cure

18. BMC Pregnancy Childbirth. 2013 Apr 9;13(1):91. [Epub ahead of print]

Magnesium sulphate at 30 to 34 weeks' gestational age: neuroprotection trial (MAGENTA) - study protocol.

Crowther CA, Middleton PF, Wilkinson D, Ashwood P, Haslam R.

BACKGROUND: Magnesium sulphate is currently recommended for neuroprotection of preterm infants for women at risk of preterm birth at less than 30 weeks' gestation, based on high quality evidence of benefit. However there remains uncertainty as to whether these benefits apply at higher gestational ages. The aim of this randomised controlled trial is to assess whether giving magnesium sulphate compared with placebo to women immediately prior to preterm birth between 30 and 34 weeks' gestation reduces the risk of death or cerebral palsy in their children at two years' corrected age. Methods/design DESIGN: Randomised, multicentre, placebo controlled trial. Inclusion criteria: Women, giving informed consent, at risk of preterm birth between 30 to 34 weeks' gestation, where birth is planned or definitely expected within 24 hours, with a singleton or twin pregnancy and no contraindications to the use of magnesium sulphate. Trial entry & randomisation: Eligible women will be randomly allocated to receive either magnesium sulphate or placebo. Treatment groups: Women in the magnesium sulphate group will be administered 50 ml of a 100 ml infusion bag containing 8 g magnesium sulphate heptahydrate [16 mmol magnesium ions]. Women in the placebo group will be administered 50 ml of a 100 ml infusion bag containing isotonic sodium chloride solution (0.9%). Both treatments will be administered through a dedicated IV infusion line over 30 minutes.Primary study outcome: Death or cerebral palsy measured in children at two years' corrected age. Sample size: 1676 children are required to detect a decrease in the combined outcome of death or cerebral palsy, from 9.6% with placebo to 5.4% with magnesium sulphate (two-sided alpha 0.05, 80% power, 5% loss to follow up, design effect 1.2). DISCUSSION: Given the magnitude of the protective effect in the systematic review, the ongoing uncertainty about benefits at later gestational ages, the serious health and cost consequences of cerebral palsy for the child, family and society, a trial of magnesium sulphate for women at risk of preterm birth between 30 to 34 weeks' gestation is both important and relevant for clinical practice globally. Trial registration: Australian New Zealand Clinical Trials Registry - ACTRN12611000491965.

PMID: 23570677 [PubMed - as supplied by publisher]

19. Dev Neurosci. 2013 Apr 3. [Epub ahead of print]

Human Amnion Epithelial Cells Reduce Fetal Brain Injury in Response to Intrauterine Inflammation.

Yawno T, Schuilwerve J, Moss TJ, Vosdoganes P, Westover AJ, Afandi E, Jenkin G, Wallace EM, Miller SL.

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Intrauterine infection, such as occurs in chorioamnionitis, is a principal cause of preterm birth and is a strong risk factor for neurological morbidity and cerebral palsy. This study aims to examine whether human amnion epithelial cells (hAECs) can be used as a potential therapeutic agent to reduce brain injury induced by intra-amniotic administration of lipopolysaccharide (LPS) in preterm fetal sheep. Pregnant ewes underwent surgery at approximately 110 days of gestation (term is approx. 147 days) for implantation of catheters into the amniotic cavity, fetal trachea, carotid artery and jugular vein. LPS was administered at 117 days; hAECs were labeled with carboxyfluorescein succinimidyl ester and administered at 0, 6 and 12 h, relative to LPS administration, into the fetal jugular vein, trachea or both. Control fetuses received an equivalent volume of saline. Brains were collected 7 days later for histological assessment of brain injury. Microglia (Iba-1-positive cells) were present in the brain of all fetuses and were significantly increased in the cortex, subcortical and periventricular white matter in fetuses that received LPS, indicative of inflammation. Inflammation was reduced in fetuses that received hAECs. In LPS fetuses, the number of TUNEL-positive cells was significantly elevated in the cortex, periventricular white matter, subcortical white matter and hippocampus compared with controls, and reduced in fetuses that received hAECs in the cortex and periventricular white matter. Within the fetal brains studied there was a significant positive correlation between the number of Iba-1-immunoreactive cells and the number of TUNEL-positive cells ($R2 = 0.19$, $p < 0.001$). The administration of hAECs protects the developing brain when administered concurrently with the initiation of intrauterine inflammation.

PMID: 23571644 [PubMed - as supplied by publisher]

20. Future Neurol. 2013 Mar 1;8(2):193-203.

Advances in the Cell-based Treatment of Neonatal Hypoxic-ischemic Brain Injury.

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Stem cell therapy for adult stroke has reached limited clinical trials. Here, we provide translational research guidance on stem cell therapy for neonatal hypoxic-ischemic brain injury requiring a careful consideration of clinically relevant animal models, feasible stem cell sources, and validated safety and efficacy endpoint assays, as well as a general understanding of modes of action of this cellular therapy. To this end, we refer to existing translational guidelines, in particular the recommendations outlined in the consortium of academicians, industry partners and regulators called Stem cell Therapeutics as an Emerging Paradigm for Stroke or STEPS. Although the STEPS guidelines are directed at enhancing the successful outcome of cell therapy in adult stroke, we highlight overlapping pathologies between adult stroke and neonatal hypoxic-ischemic brain injury. We are, however, cognizant that the neonatal hypoxic-ischemic brain injury displays disease symptoms distinct from adult stroke in need of an innovative translational approach that facilitates the entry of cell therapy in the clinic. Finally, insights into combination therapy are provided with the vision that stem cell therapy may benefit from available treatments, such as hypothermia, already being tested in children diagnosed with hypoxic-ischemic brain injury.

PMID: 23565051 [PubMed] PMCID: PMC3615569

21. J Matern Fetal Neonatal Med. 2013 Apr 8. [Epub ahead of print]

Neurodevelopmental Outcome of Extremely Premature Infants Exposed to Incomplete, No or Complete Antenatal Steroids.

Chawla S, Bapat R, Pappas A, Bara R, Zidan M, Natarajan G.

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Objective: To compare the neurodevelopmental outcomes at 18-22 months' corrected age of extremely premature infants exposed to a complete course, an incomplete course or no dose of antenatal steroids (ANS). Methods: Retrospective chart review of extremely premature (< 28 weeks gestational age) neonates over a 3 year period. Neurodevelopmental assessment at 18-22 months' corrected age included a standardized neurologic examination and the Bayley Scales of Infant and Toddler development II or III. Intact survival was defined as survival without cerebral palsy, blindness or deafness and mental developmental index (MDI) /cognitive score > 85. Neurodevelopmental impairment (NDI) was defined as any of: moderate or severe cerebral palsy (CP), MDI/ cognitive score < 70, deafness or blindness. Patients were categorized into 3 groups: A) No ANS; B) Incomplete course; and C) Complete course of ANS. Results: Outcome data were available for 134 (88%) patients of our cohort (n=153). Severe intraventricular hemorrhage (IVH) was significantly lower and intact survival higher in the complete ANS group (p<0.01). On logistic regression, with gestational age, gender, maternal insurance and ANS exposure as covariates, an incomplete (vs. complete) course of ANS (p=0.006) and gestational age were significantly associated with lower intact survival at 18-22 months. Conclusions: A complete course of ANS was associated with an increased likelihood of intact survival at a corrected age of 18-22 months among extremely premature infants, compared with an incomplete course. Follow-up studies should account for the differential benefit of complete versus incomplete course of ANS administration.

PMID: 23565886 [PubMed - as supplied by publisher]

22. Transl Stroke Res. 2013 Apr 1;4(2):158-170.

Vascular endothelial growth factors A and C are induced in the SVZ following neonatal hypoxia-ischemia and exert different effects on neonatal glial progenitors.

Bain JM, Moore L, Ren Z, Simonishvili S, Levison SW.

UMDNJ - New Jersey Medical School, Department of Neurology & Neurosciences, University Hospital Cancer Center, Newark, NJ 07103 ; UMDNJ - Graduate School Biomedical Sciences, University Hospital Cancer Center, Newark, NJ 07103 ; New Jersey Medical School University Hospital Cancer Center, Newark, NJ 07103.

Episodes of neonatal hypoxia-ischemia (H-I) are strongly associated with cerebral palsy and a wide spectrum of other neurological deficits in children. Two key processes required to repair damaged organs are to amplify the number of precursors capable of regenerating damaged cells and to direct their differentiation towards the cell types that need to be replaced. Since hypoxia induces vascular endothelial growth factor (VEGF) production, it is logical to predict that VEGFs are key mediators of tissue repair after H-I injury. The goal of this study was to test the hypothesis that certain VEGF isoforms increase during recovery from neonatal H-I and that they would differentially affect the proliferation and differentiation of subventricular zone (SVZ) progenitors. During the acute recovery period from H-I both VEGF-A and VEGF-C were transiently induced in the SVZ, which correlated with an increase in SVZ blood vessel diameter. These growth factors were produced by glial progenitors, astrocytes and to a lesser extent, microglia. VEGF-A promoted the production of astrocytes from SVZ glial progenitors while VEGF-C stimulated the proliferation of both early and late oligodendrocyte progenitors, which was abolished by blocking the VEGFR-3. Altogether, these results provide new insights into the signals that coordinate the reactive responses of the progenitors in the SVZ to neonatal H-I. Our studies further suggest that therapeutics that extend VEGF-C production and/or agonists that stimulate the VEGFR-3 will promote oligodendrocyte progenitor cell development to enhance myelination after perinatal brain injury.

PMID: 23565129 [PubMed] PMCID: PMC3613784 [Available on 2014/4/1]

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