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NEWS
Cerebral Palsy Research

Monday 1 June 2015

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Interventions and Management

1. Eur J Paediatr Neurol. 2015 Mar 24. pii: S1090-3798(15)00067-7. doi: 10.1016/j.ejpn.2015.03.007. [Epub ahead of print]

Mirror movements in unilateral spastic cerebral palsy: Specific negative impact on bimanual activities of daily living.

Adler C, Berweck S, Lidzba K, Becher T, Staudt M.

AIM: Mirror movements are involuntary movements of the other hand during voluntary unimanual movements. Some, but not all children with unilateral spastic cerebral palsy (USCP) show this phenomenon. In this observational study, we investigated whether these mirror movements have a specific negative impact on bimanual activities of daily living. METHODS: Eighteen children (six girls; age range, 6-16 years; mean age, 12 years 1 month; SD, 3 years 3 month) with USCP, nine with and nine without mirror movements, underwent the Jebsen Taylor Hand Function Test (unimanual capacity) and the Assisting Hand Assessment (bimanual performance). In addition, we measured the time the participants needed for the completion of five activities we had identified as particularly difficult for children with mirror movements. RESULTS: Multivariate analysis demonstrated that mirror movements indeed have a specific negative impact on bimanual performance (Assisting Hand Assessment) and on the time needed for the completion of these five particularly difficult activities. This effect was independent from unimanual capacity. CONCLUSION: Functional therapies in children with USCP and mirror movements should address this phenomenon.

PMID: 26004994 [PubMed - as supplied by publisher]

2. Pediatr Phys Ther. 2015 May 27. [Epub ahead of print]

The Manual Ability Classification System: A Scoping Review.

Jeevanantham D, Dyszuk E, Bartlett D.

PURPOSE: To examine the use of the Manual Ability Classification System (MACS) and to identify gaps in the literature by conducting a thorough search of existing publications from 2006 to March 2013. METHODS: An extensive literature search included 15 databases, using the search terms "Manual Ability Classification System" or "MACS" to retrieve relevant abstracts. RESULTS: A total of 161 articles were identified for final inclusion. The review identified literature that supports the reliability, validity, and stability of the MACS. CONCLUSIONS: The MACS could be considered as a standard classification for children with cerebral palsy on the basis of manual abilities.

The MACS can be reliably used for children between 4 and 18 years and adults between 18 and 24 years. The use of the MACS is expected to increase; further work is required to explore the use of the MACS in clinical practice.

PMID: 26020598 [PubMed - as supplied by publisher]

3. Neuropediatrics. 2015 May 26. [Epub ahead of print]

Practical Recommendations for Robot-Assisted Treadmill Therapy (Lokomat) in Children with Cerebral Palsy: Indications, Goal Setting, and Clinical Implementation within the WHO-ICF Framework.

Tabea Aurich (-Schuler), Warken B, Graser JV, Ulrich T, Borggraefe I, Heinen F, Meyer-Heim A, van Hedel HJ, Schroeder AS.

Active participation and the highest level of independence during daily living are primary goals in neurorehabilitation. Therefore, standing and walking are key factors in many rehabilitation programs. Despite inconclusive evidence considering the best application and efficacy of robotic tools in the field of pediatric neurorehabilitation, robotic technologies have been implemented to complement conventional therapies in recent years. A group of experienced therapists and physicians joined in an "expert panel." They compared their clinical application protocols, discussed recurring open questions, and developed experience-based recommendations for robot-assisted treadmill therapy (exemplified by the Lokomat, Hocoma, Volketswil, Switzerland) with a focus on children with cerebral palsy. Specific indications and therapeutic goals were defined considering the severity of motor impairments and the International Classification of Functioning, Disability and Health framework (ICF). After five meetings, consensus was found and recommendations for the implementation of robot-assisted treadmill therapy including postsurgery rehabilitation were proposed. This article aims to provide a comprehensive overview on therapeutical applications in a fast developing field of medicine, where scientific evidence is still scarce. These recommendations can help physicians and therapists to plan the child's individual therapy protocol of robot-assisted treadmill therapy.

PMID: 26011438 [PubMed - as supplied by publisher]

4. Phys Ther. 2015 May 28. [Epub ahead of print]

Comparison of Patterns of Physical Activity and Sedentary Behavior Between Children With Cerebral Palsy and Children With Typical Development.

Ryan JM, Forde C, Hussey JM, Gormley J.

BACKGROUND:Reduced participation in physical activity and increased time in sedentary behavior is associated with overweight, chronic disease and disability. In order to optimize recommendations and interventions to increase physical activity and reduce sedentary behavior in children with cerebral palsy (CP) knowledge of their physical activity and sedentary behavior is required. OBJECTIVES: The aim of this study was to describe light, moderate, and vigorous physical activity and sedentary behaviour in pre-adolescent children with and without CP, and to compare physical activity and sedentary behavior between the two groups. STUDY DESIGN: This was a cross-sectional study of 33 children, aged 6 to 10 years, with CP [Gross Motor Function Classification System (GMFCS) levels I-III] and 33 age- and sex-matched children with typical development. METHODS: Physical activity was measured using the RT3 accelerometer over 7 days. RESULTS: Children with CP spent more time in sedentary behavior ($p<0.001$) and accumulated less total activity ($p<0.01$), moderate activity ($p<0.05$), vigorous activity ($p<0.05$) and sustained bouts of moderate-to-vigorous activity (MVPA) ($p<0.01$). They also accumulated a fewer number of bouts of MVPA and vigorous activity ($p<0.05$ and $p<0.01$, respectively), despite spending a similar amount of time in each bout. LIMITATIONS: The small number of children in GMFCS levels II and III did not allow us to adjust for GMFCS level when comparing physical activity between children with and without CP. CONCLUSIONS: Pre-adolescent children with CP spent less time in moderate and vigorous activity, and more time in sedentary behaviour than children with typical development. Children with CP also accumulated less continuous MVPA and vigorous activity as a result of achieving fewer sustained bouts of MVPA and vigorous activity throughout the day. © 2015 American Physical Therapy Association.

PMID: 26023216 [PubMed - as supplied by publisher]

5. Pediatr Phys Ther. 2015 May 27. [Epub ahead of print]

Standing Programs to Promote Hip Flexibility in Children With Spastic Diplegic Cerebral Palsy.

Macias-Merlo L, Bagur-Calafat C, Girabent-Farrés M, Stuberg WA.

PURPOSE: To investigate the effects of a standing program on the range of motion (ROM) of hip abduction in children with spastic diplegic cerebral palsy.
METHODS: The participants were 13 children, Gross Motor Functional Classification System level III, who received physical therapy and a daily standing program using a custom-fabricated stander from 12 to 14 months of age to the age of 5 years. Hip abduction ROM was goniometrically assessed at baseline and at 5 years. RESULTS: Baseline hip abduction was 42° at baseline and 43° at 5 years. CONCLUSIONS: This small difference was not clinically significant, but did demonstrate that it was possible to maintain hip abduction ROM in the spastic adductor muscles of children with cerebral palsy with a daily standing program during the children's first 5 years of development.

PMID: 26020594 [PubMed - as supplied by publisher]

6. Pediatr Phys Ther. 2015 May 27. [Epub ahead of print]

Commentary on: "Standing Programs to Promote Hip Flexibility in Children With Spastic Diplegic Cerebral Palsy".

Bishop N, Smith BA, Prieto N.

PMID: 26020595 [PubMed - as supplied by publisher]

7. Phys Ther. 2015 May 28. [Epub ahead of print]

Predictive Value of General Movement Assessment for Cerebral Palsy When Used in Routine Clinical Practice.

Øberg GK, Jacobsen BK, Jørgensen L.

BACKGROUND: Early identification of children at high risk of future neurodevelopmental disability is important for initiation of appropriate therapy. In research settings, the assessment of fidgety movements (FMs) at 3 months supports General Movement Assessment (GMA) as a strong predictor for subsequent motor development, but there are few studies from clinical routine settings. OBJECTIVE: To examine the relationship between FMs and neurodevelopmental outcome by 2 years in high-risk infants in a routine clinical hospital setting. DESIGN: A prospective study. METHODS: GMA was performed in 87 high-risk infants at 3 months post-term age. The infants were clinically assessed for cerebral palsy (CP) at 2 years. Sensitivity, specificity, likelihood ratios, positive and negative predictive value was computed. The relative risk of motor problems at age 2 according to the GMA was estimated. RESULTS: In infants with FMs present, 93%(50/54) had normal development and none were diagnosed with CP, whereas 75%(12/16) with abnormal or sporadic FMs had normal development. In contrast, 53%(9/17) of those without FMs had CP. Considering GMA as a test for CP and absent FMs as test positive; the sensitivity was 90%, specificity 90%. The likelihood ratio for positive and negative test results were 8.7 and 0.1, respectively. The negative predictive value was 99%, the positive predictive value 53%. The risk of having motor problems by the age of 2 increased linearly with the extent of pathological GMA and was 10 times higher if FMs were absent by 3 months compared to infants with normal FMs. LIMITATIONS: Relatively small study sample CONCLUSIONS: Our study shows that GMA when applied in a routine clinical setting strongly predicts neurodevelopmental impairments at 2 years in high-risk infants.

PMID: 26023214 [PubMed - as supplied by publisher]

8. Dev Med Child Neurol. 2015 May 26. doi: 10.1111/dmcn.12815. [Epub ahead of print]

Tailoring neuromotor interventions for children with cerebral palsy.

Bassan H.

This commentary is on the original article by **Rackauskaite et al. Impact of child and family characteristics on cerebral palsy treatment.**

PMID: 26011227 [PubMed - as supplied by publisher]

9. J Child Neurol. 2015 May 26. pii: 0883073815587028. [Epub ahead of print]

School Performance and Neurodevelopment of Very Low Birth Weight Preterm Infants: First Report From Turkey.

Koç Ö, Kavuncuoğlu S, Ramoğlu M, Aldemir E, Aktalay A, Eras Z.

Very low birth weight preterm infants are under significant risk of neurologic, developmental, and somatic problems. In this study, 90 infants born with a birth weight <1500 g and/or with a gestational age <32 weeks were evaluated after the first year of elementary school to assess neurodevelopment. The Wechsler Intelligence Scale for Children-Revised (WISC-R) test, Pediatric Symptom Checklist, and Parent Evaluation of Developmental Status were performed. Mental retardation, cerebral palsy, blindness, epilepsy, and posthemorrhagic hydrocephaly incidences were 14%, 7%, 2%, 5%, and 2%, respectively. The WISC-R score of 32 patients (35.5%) were below 85.
Perinatal asphyxia, abnormal neurologic examination, and delayed or impaired speech correlated significantly with low WISC-R scores. Education and income of the father had positive impact on WISC-R scores (P = .042 and P = .026). Parents' concern and presence of cognitive problems were correlated (P = .026). Environmental factors, as well as the prevention of morbidity, affected school performance positively.

PMID: 26012506 [PubMed - as supplied by publisher]

10. Zhongguo Ying Yong Sheng Li Xue Za Zhi. 2014 Nov;30(6):511-5.

[How to deal with cerebral palsy in 21st century-a new epoch in clinic treatment].
[Article in Chinese]

Tian CY, Leng LG, Tian ZM.

The aims of this paper were to define (1) criteria of cerebral palsy; (2) classification of cerebral palsy; (3) etiology, neuroimaging, and epidemiology of cerebral palsy; (4) different kinds of treatments of cerebral palsy. Data were drawn from an international survey of PUBMED (1994-2014) and CNKI (1994-2014). An expert panel used a consensus building technique. The10-point Jadad scale was used to assess the quality of the trials based on the following items, including allocation sequence generation, randomization concealment, methods of blinding, and descriptions of withdrawals and dropouts. Our clinical experience was also summarized. Below is a summary. (1) Further work is warranted to reach agreement for the classification of cerebral palsy. (2) A worldwide prevalence of 1.5-4.0 per 1 000 live births, with an average lifetime cost of 1 million dollars per person in the United States, while it is 1.8-6.0 per 1000 live births in China. (3) Comparison of clinical efficacy of different treatments. In this review, the current advances in different kind of treatments of brain injury are discussed with specific relevance to cerebral palsy.

PMID: 26016360 [PubMed - in process]

11. Dev Med Child Neurol. 2015 May 22. doi: 10.1111/dmcn.12808. [Epub ahead of print]

Variation in cerebral palsy profile by socio-economic status.

Oskoui M, Messerlian C, Blair A, Gamache P, Shevell M.

AIM: Socio-economic differences in maternal and child health are well recognized, but the role of individual-level and area-level determinants in cerebral palsy (CP) phenotypes is debated. We set out to examine (1) the association between area-level and individual-level measures of socio-economic deprivation and CP phenotype among children, including subtype, severity, and comorbidities; and (2) the direct effect of area-level deprivation not mediated through individual-level deprivation. METHOD: Regional data from a provincial CP register were analyzed. The outcome of interest was CP phenotype. The area-level exposure was measured using the Pampalon Deprivation Index. Individual-level socio-economic status (SES) was determined using maternal education. We conducted multiple regression models, stratified by preterm birth, controlling for key covariates, and a mediation analysis of area-level deprivation on the association between individual SES and CP phenotype. RESULTS: A socio-economic gradient in mobility was seen in our cohort, above and beyond differences in maternal and perinatal factors. The added direct effect of area-level deprivation was seen only in children whose mothers were educated to a higher level, suggesting no additional contribution of area-level deprivation in children of mothers with a lower level of education. INTERPRETATION: Contextual socio-economic factors can impact the severity of CP. These findings indicate important areas for potential community-level or area-level public health intervention (i.e. neighborhood reinvestment, preventive measures), and suggest that neighborhood-level research in maternal and perinatal health should continue to be pursued.

PMID: 26010819 [PubMed - as supplied by publisher]

Prevention and Cure

12. Am J Obstet Gynecol. 2015 May 20. pii: S0002-9378(15)00510-4. doi: 10.1016/j.ajog.2015.05.034. [Epub ahead of print]

Cerebral Palsy - Causes, pathways, and the role of genetic variants.

MacLennan AH, Thompson SC, Gecz J.

Cerebral palsy (CP) is heterogeneous with different clinical types, co-morbidities, brain imaging patterns, causes and now also heterogeneous underlying genetic variants. Few are solely due to severe hypoxia or ischemia at birth. This common myth has held back research in causation. The cost of litigation has devastating effects on maternity services with unnecessarily high cesarean delivery rates and subsequent maternal morbidity and mortality. CP rates have remained the same for 50 years despite a sixfold increase in cesarean birth. Epidemiological studies have shown that the origins of most CP are prior to labor. Increased risk is associated with preterm delivery, congenital malformations, intrauterine infection, fetal growth restriction, multiple pregnancy and placental abnormalities. Hypoxia at birth may be primary or secondary to pre-existing pathology and international criteria help to separate the few cases of CP due to acute intrapartum hypoxia. Until recently 1-2% of CP (mostly familial) had been linked to causative mutations. Recent genetic studies of sporadic CP cases using new generation exome sequencing show that 14% of cases have likely causative single gene mutations and up to 31% have clinically relevant copy number variations. The genetic variants are heterogeneous and require function investigations to prove causation. Whole genome sequencing, fine scale copy number variant investigations and gene expression studies may extend the percentage of cases with a genetic pathway. Clinical risk factors could act as triggers for CP where there is genetic susceptibility. These new findings should refocus research about the causes of these complex and varied neurodevelopmental disorders.

PMID: 26003063 [PubMed - as supplied by publisher]

13. Am J Perinatol. 2015 May 29. [Epub ahead of print]

Differential Morbidity in Preterm Small versus Appropriate for Gestational Age: Perhaps Unverifiable.

Marrs CC, Mendez-Figueroa H, Hammad IA, Chauhan SP.

Objective The objective of this study was to determine the morbidity of preterm small for gestational age (SGA) infants compared with appropriate for GA (AGA). Study Design This is a secondary analysis of the randomized trial evaluating magnesium sulfate for the prevention of cerebral palsy (CP). We compared outcomes of preterm (< 37 weeks) nonanomalous infants who were SGA (birth weight < 10% for GA) versus AGA (birth weight 10-89% for GA). We compared (1) the parent trial primary outcome, a composite of stillbirth, infant death by 1 year of age, or moderate to severe CP at 2 years of age and (2) composite neonatal morbidity (CNM). Results Of the 1,948 infants who met inclusion criteria, 95% were AGA and 5% were SGA. The primary outcome was similar (10 and 15%, p = 0.08), as was the CNM (24 and 25%, p = 0.89). Sample size calculations indicate that detection of a one-third higher rate of CNM among SGA compared with AGA infants requires more than 93,900 preterm births; for a one-third difference in moderate to severe CP, more than 1.4 million infants. Conclusion Owing to the prohibitive sample size required, ascertaining a difference in sequela between preterm SGA and AGA infants is possibly unverifiable.

PMID: 26023905 [PubMed - as supplied by publisher]

14. Behav Brain Res. 2015 May 23. pii: S0166-4328(15)00362-9. doi: 10.1016/j.bbr.2015.05.033. [Epub ahead of print]

Broccoli sprout supplementation during pregnancy prevents brain injury in the newborn rat following placental insufficiency.

Black AM, Armstrong EA, Scott O, Juurlink BJ, Yager JY.

Chronic placental insufficiency and subsequent intrauterine growth restriction (IUGR) increase the risk of hypoxic-ischemic encephalopathy in the newborn by 40 fold. The latter, in turn, increases the risk of cerebral palsy and developmental disabilities. This study seeks to determine the effectiveness of broccoli sprouts (BrSp), a rich source of the isothiocyanate sulforaphane, as a neuroprotectant in a rat model of chronic placental insufficiency and IUGR. Placental insufficiency and IUGR was induced by bilateral uterine artery ligation (BUAL) on day E20 of gestation. Dams were fed standard chow or chow supplemented with 200mg of dried BrSp from E15 - postnatal day 14 (PD14). Controls received Sham surgery and the same dietary regime. Pups underwent neurologic reflex testing and open field testing, following which they were euthanized and their brains frozen for neuropathologic assessment. Compared to Sham, IUGR pups were delayed in attaining early reflexes and performed worse in the open field, both of which were significantly improved by maternal supplementation of BrSp ($p<0.05$). Neuropathology revealed diminished white matter, ventricular dilation, astrogliosis and reduction in hippocampal neurons in IUGR animals compared to Sham, whereas broccoli sprout supplementation improved outcome in all histological assessments ($p<0.05$). Maternal dietary supplementation with BrSp prevented the detrimental neurocognitive and neuropathologic effects of chronic intrauterine ischemia. These findings suggest a novel approach for prevention of cerebral palsy and/or developmental disabilities associated with placental insufficiency.

PMID: 26014855 [PubMed - as supplied by publisher]

15. BMC Pregnancy Childbirth. 2015 May 27;15(1):124. doi: 10.1186/s12884-015-0553-9.

Severe fetal acidemia in cases of clinical chorioamnionitis in which the infant later developed cerebral palsy.

Matsuda Y, Ogawa M, Nakai A, Tagawa M, Ohwada M, Ikenoue T.

BACKGROUND: The umbilical arterial pH (UApH) in cases of clinically apparent chorioamnionitis (CAM) in which the infant later develop severe cerebral palsy (CP) has not yet been fully investigated. The objective of this study was to determine the UApH in CAM cases in which the infant later develop severe CP. METHODS: A review was conducted unti1 April 2014 among 324 infants with CP diagnosed to be caused by antenatal and/or intrapartum conditions, as determined by the Japan Council for Quality Health Care. Eighty-six infants born at over 34 weeks of gestation with an abnormal FHR pattern during labor were selected. The subjects were divided into the following two groups: cases with (Group I, n = 19) and those without (Group II, n = 67) clinical CAM. Severe fetal acidemia was defined as a pH of less than 7.0. RESULTS: The frequency of severe acidemia in Groups 1 and II was 26.3 and 74.6 %, respectively. In addition, the frequency of severe acidemia was significantly less in Group I (odds ratio (OR) 0.12, 95 % confidence interval (CI) 0.03-0.53) than in Group II, while the frequency of fetal tachycardia was greater in Group I (OR 7.61, 95 % CI 1.82-31.7) than in Group II, after adjusting for confounding effects. CONCLUSIONS: The frequency of severe acidemia was lower in the cases of clinical CAM in which the infant later developed severe cerebral palsy than in the cases without clinical CAM. The relation of fetal tachycardia to CP with clinical CAM, but not to acidemia, should be reevaluated in such cases.

PMID: 26013539 [PubMed - in process] PMCID: PMC4445276 Free PMC Article

16. PLoS One. 2015 May 28;10(5):e0128007. doi: 10.1371/journal.pone.0128007. eCollection 2015.

Abbreviated exposure to hypoxia is sufficient to induce CNS dysmyelination, modulate spinal motor neuron composition, and impair motor development in neonatal mice.

Watzlawik JO, Kahoud RJ, O'Toole RJ, White KA, Ogden AR, Painter MM, Wootla B, Papke LM, Denic A, Weimer JM, Carey WA, Rodriguez M.

Neonatal white matter injury (nWMI) is an increasingly common cause of cerebral palsy that results predominantly from hypoxic injury to progenitor cells including those of the oligodendrocyte lineage. Existing mouse models of nWMI utilize prolonged periods of hypoxia during the neonatal period, require complex cross-fostering and exhibit poor growth and high mortality rates. Abnormal CNS myelin composition serves as the major explanation for persistent neuro-motor deficits. Here we developed a simplified model of nWMI with low mortality rates and improved growth without cross-fostering. Neonatal mice are exposed to low oxygen from postnatal day (P) 3 to P7, which roughly corresponds to the period of human brain development between gestational weeks 32 and 36. CNS hypomyelination is detectable for 2-3 weeks post injury and strongly correlates with levels of body and brain weight loss. Immediately following hypoxia treatment, cell death was evident in multiple brain regions, most notably in superficial and deep cortical layers as well as the subventricular zone progenitor compartment. PDGFαR, Nkx2.2, and Olig2 positive oligodendrocyte progenitor cell were significantly reduced until postnatal day 27. In addition to CNS dysmyelination we identified a novel pathological marker for adult hypoxic animals that strongly correlates with life-long neuro-motor deficits. Mice reared under hypoxia reveal an abnormal spinal neuron composition with increased small and medium diameter axons and decreased large diameter axons in thoracic lateral and anterior funiculi. Differences were particularly pronounced in white matter motor tracts left and right of the anterior median fissure. Our findings suggest that 4 days of exposure to hypoxia are sufficient to induce experimental nWMI in CD1 mice, thus providing a model to test new therapeutics. Pathological hallmarks of this model include early cell death, decreased OPCs and hypomyelination in early postnatal life, followed by dysmyelination, abnormal spinal neuron composition, and neuro-motor deficits in adulthood.

PMID: 26020269 [PubMed - in process] Free full text