Cerebral Palsy ALLIANCE

NEWS
Cerebral Palsy Research

Monday 5 May 2014

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Interventions and Management

1. Dev Med Child Neurol. 2014 Apr 26. doi: 10.1111/dmcn.12471. [Epub ahead of print]

Mastery motivation as a predictor of occupational performance following upper limb intervention for school-aged children with congenital hemiplegia.

Miller L1, Ziviani J, Ware RS, Boyd RN.

AIM: To determine the extent to which children's mastery motivation predicts occupational performance outcomes following upper limb intervention (ULI). METHOD: In this cohort study, participants received 45 hours of ULI, either in an intensive group-based or distributed individualized model. The Dimensions of Mastery Questionnaire (DMQ) measured mastery motivation at baseline. Occupational performance outcomes were assessed at baseline and 13 weeks' post-intervention using the Canadian Occupational Performance Measure (COPM). Multivariable models determined the contribution of mastery motivation to COPM outcome irrespective of group membership. RESULTS: Forty-two children with congenital hemiplegia (29 males, 13 females; mean age 7y 8mo [SD 2y 2mo]; range 5y 1mo-12y 8mo; Manual Ability Classification System [MACS] I=20 and II=22; predominant motor type unilateral spastic n=41) participated in the study. Significant gains were seen in COPM performance and satisfaction scores ($p<0.001$) post-intervention with no between group differences. Children who had greater persistence with object-oriented tasks ($p=0.02$) and better manual ability ($p=0.03$) achieved higher COPM performance scores at 13 weeks. Children's persistence on object-oriented tasks was the strongest predictor of COPM satisfaction ($p=0.01$). INTERPRETATION: Children's persistence with object-oriented tasks as well as manual abilities needs to be considered when undertaking ULI. Predetermining children's motivational predispositions can assist clinicians to tailor therapy sessions individually based on children's strengths, contributing to effective engagement in ULI.

PMID: 24766637 [PubMed - as supplied by publisher]

2. Front Neurol. 2014 Apr 9;5:48. doi: 10.3389/fneur.2014.00048. eCollection 2014.

Hand functioning in children with cerebral palsy.

Arnould C1, Bleyenheuft Y2, Thonnard JL3.

Brain lesions may disturb hand functioning in children with cerebral palsy (CP), making it difficult or even impossible for them to perform several manual activities. Most conventional treatments for hand dysfunction in CP assume that reducing the hand dysfunctions will improve the capacity to manage activities (i.e., manual ability, MA). The aim of this study was to investigate the directional relationships (direct and indirect pathways) through which hand skills influence MA in children with CP. A total of 136 children with CP (mean age: 10 years; range: 6-16 years; 35 quadriplegics, 24 diplegics, 77 hemiplegics) were assessed. Six hand skills were measured on both hands: touch-pressure detection (Semmes-Weinstein esthesiometer), stereognosis (Manual Form Perception Test), proprioception (passive mobilization of the metacarpophalangeal joints), grip strength (GS) (Jamar dynamometer), gross manual dexterity (GMD) (Box and Block Test), and fine finger dexterity (Purdue Pegboard Test). MA was measured with the ABILHAND-Kids questionnaire. Correlation coefficients were used to determine the linear associations between observed variables. A path analysis of structural equation modeling was applied to test different models of causal relationships among the observed variables. Purely sensory impairments did seem not to play a significant role in the capacity to perform manual activities. According to path analysis, GMD in both hands and stereognosis in the dominant hand were directly related to MA, whereas GS was indirectly related to MA through its relationship with GMD. However, one-third of the variance in MA measures could not be explained by hand skills. It can be concluded that MA is not simply the integration of hand skills in daily activities and should be treated per se, supporting activity-based interventions.

PMID: 24782821 [PubMed] Free full text

3. Gait Posture. 2014 Apr 5. pii: S0966-6362(14) 00285-9. doi: 10.1016/j.gaitpost.2014.03.187. [Epub ahead of print]

Energy cost of walking in children with spastic cerebral palsy: Relationship with age, body composition and mobility capacity.

Kamp FA1, Lennon N2, Holmes L3, Dallmeijer AJ1, Henley J3, Miller F3.

The energy cost (EC) of walking is different for typically developing (TD) and children with cerebral palsy (CP). The associated factors of EC are not fully understood in children with CP. We assessed the relationship between EC and age, body surface area (BSA), and gross motor function measure (GMFM). We retrospectively examined data collected between 2003 and 2011 on 276 children aged 4-18 years who were classified as Gross Motor Function Classification System level I, n=79; II, n=123; and III, n=74. Energy cost was assessed while children walked 6-8min at a comfortable, self-selected speed using their typical walking aids and/or orthoses as part of a clinical gait analysis. During the test, participants wore a breath-by-breath portable gas analysis system, measuring oxygen consumption. To calculate EC (J/kg/m), oxygen consumption was converted to J/kg/min and divided by walking speed. Data were analyzed using linear regression model. Energy cost correlated inversely with age (ß=-0.16, R2=0.02, P=0.01), BSA (ß=-3.35, R2=0.11, P<0.0001), and GMFM (ß=-0.12, R2=0.42, P<0.0001). In the multiple linear regression model, GMFM was the most potent correlate of EC, BSA explained another 10% of the variance (R2=0.53), and age was a marginally significant correlate of EC (P=0.08). In summary, in children with CP in our study, EC decreased as GMFM and BSA increased, and GMFM was the most potent correlate of EC.

PMID: 24768085 [PubMed - as supplied by publisher]

4. Phys Ther. 2014 May 1. [Epub ahead of print]

Measurement Properties of Gait-Related Outcomes in Youth With Neuromuscular Diagnoses: A Systematic Review.

Ammann-Reiffer C1, Bastiaenen CH, de Bie RA, van Hedel HJ.

Background: Sound measurement properties of outcome tools are essential when evaluating outcomes of an intervention, in clinical practice and in research.PurposeTo review the evidence on reliability, measurement error and responsiveness of measures of gait function in children with neuromuscular diagnoses. Data Sources: The databases MEDLINE, CINAHL, EMBASE and PsycINFO were searched up to June 15 2012.Study Selection: Studies evaluating reliability, measurement error or responsiveness of measures of gait function in 1-18 years old

children with neuromuscular diagnoses were included. Data Extraction: Quality of the studies was independently rated by 2 raters using a modified COSMIN checklist. Studies with a fair quality rating or better were considered for best evidence synthesis. Data Synthesis: Regarding the methodological quality, 32 out of 35 reliability studies, all of the 13 measurement error studies and 5 out of 10 responsiveness studies were of fair or good quality. Best evidence synthesis revealed moderate to strong evidence for reliability for several measures in children with cerebral palsy (CP), but was limited or unknown in other diagnoses. The Functional Mobility Scale (FMS) and the Gross Motor Function Measure (GMFM) dimension E showed limited positive evidence for responsiveness in children with CP, but it was unknown or controversial in other diagnoses. No information was reported on the minimal important change, thus evidence on measurement error remained undetermined.ConclusionsThere is moderate to strong evidence on reliability for several measures of gait function in children with CP, while evidence on responsiveness only exists for the FMS and the GMFM dimension E.

PMID: 24786947 [PubMed - as supplied by publisher]

5. Maedica (Buchar). 2013 Sep;8(4):388-393.

Cerebral Palsy Gait, Clinical Importance.

Tugui RD1, Antonescu D2.

Cerebral palsy refers to a lesion on an immature brain, that determines permanent neurological disorders. Knowing the exact cause of the disease does not alter the treatment management. The etiology is 2-2.5/1000 births and the rate is constant in the last 40-50 years because advances in medical technologies have permitted the survival of smaller and premature new born children. Gait analysis has four directions: kinematics (represents body movements analysis without calculating the forces), kinetics (represents body moments and forces), energy consumption (measured by oximetry), and neuromuscular activity (measured by EMG). Gait analysis can observe specific deviations in a patient, allowing us to be more accurate in motor diagnoses and treatment solutions: surgery intervention, botulinum toxin injection, use of orthosis, physical kinetic therapy, oral medications, baclofen pump.

PMID: 24790675 [PubMed - as supplied by publisher]

6. Bone Joint J. 2014 May 1;96-B(5):701-706.

Proximal femoral resection without post-operative traction for the painful dislocated hip in young patients with cerebral palsy: a review of 79 cases.

Dartnell J1, Gough M, Paterson JM, Norman-Taylor F.

Proximal femoral resection (PFR) is a proven pain-relieving procedure for the management of patients with severe cerebral palsy and a painful displaced hip. Previous authors have recommended post-operative traction or immobilisation to prevent a recurrence of pain due to proximal migration of the femoral stump. We present a series of 79 PFRs in 63 patients, age 14.7 years (10 to 26; 35 male, 28 female), none of whom had post-operative traction or immobilisation. A total of 71 hips (89.6%) were reported to be pain free or to have mild pain following surgery. Four children underwent further resection for persistent pain; of these, three had successful resolution of pain and one had no benefit. A total of 16 hips (20.2%) showed radiographic evidence of heterotopic ossification, all of which had formed within one year of surgery. Four patients had a wound infection, one of which needed debridement; all recovered fully. A total of 59 patients (94%) reported improvements in seating and hygiene. The results are as good as or better than the historical results of using traction or immobilisation. We recommend that following PFR, children can be managed without traction or immobilisation, and can be discharged earlier and with fewer complications. However, care should be taken with severely dystonic patients, in whom more extensive femoral resection should be considered in combination with management of the increased tone. Cite this article: Bone Joint J 2014; 96-B:701-6.

PMID: 24788508 [PubMed - as supplied by publisher]

7. Bone Joint J. 2014 May 1;96-B(5):567-568.

Salvage hip surgery in severe cerebral palsy: some answers, more questions?

K Graham H1, Narayanan UG.

PMID: 24788487 [PubMed - as supplied by publisher]

8. J Pediatr. 2014 Apr 27. pii: S0022-3476(14) 00295-9. doi: 10.1016/j.jpeds.2014.03.041. [Epub ahead of print]

Further Evidence for Botulinum Toxin A in Cerebral Palsy.

Chau V1, Fehlings D2, Miller SP3.

PMID: 24787538 [PubMed - as supplied by publisher]

9. J Infect Public Health. 2014 Apr 26. pii: S1876-0341(14)00042-2. doi: 10.1016/j.jiph.2014.03.001. [Epub ahead of print]

Infection in long term care facility in the kingdom of Bahrain.

Al Salman J1, Al Agha RA2, Mussayab YA3, Hassan AF4.

Infections in long term care facilities (LTCF) are common and are considered a major cause of mortality and morbidity. Endemic infections and outbreaks are observed in LTCF. Of particular concern is the growth of multi-drug resistant organisms. A study was conducted in the Kingdom of Bahrain concerning infections among the residents in a LTCF. The aim was to define the rate, type and outcomes of institutional infections. The different treatment modalities and antimicrobials used were evaluated. Our facility cares for the elderly and a heterogeneous group of patients from different populations (e.g., mentally retarded, bedbound due to various disabilities and other forms of consciousness impairment such as post stroke disability, cerebral palsy and anoxic brain damage). The initial span of six months was changed to seven months to increase the sample size and improve the data analysis. This was a prospective study conducted in Muharaq Geriatric Hospital in the Kingdom of Bahrain. The study was conducted over seven months from January 2013 to July 2013 on 104 patients. During that period, patients with new positive cultures from different sites were included. The clinical features, microbiological features and outcomes of the bacteremic episodes were included. The information was collected by a questionnaire created by the research team. From a total of 104 patients staying in the LTFC, 19 had positive cultures from different sites at different times. The study showed that infections are common, especially urinary tract infections.

PMID: 24780187 [PubMed - as supplied by publisher]

10. Clin Exp Optom. 2014 May;97(3):196-208. doi: 10.1111/cxo.12155.

Identifying and characterising cerebral visual impairment in children: a review.

Philip SS1, Dutton GN.

Cerebral visual impairment (CVI) comprises visual malfunction due to retro-chiasmal visual and visual association pathway pathology. This can be isolated or accompany anterior visual pathway dysfunction. It is a major cause of low vision in children in the developed and developing world due to increasing survival in paediatric and neonatal care. CVI can present in many combinations and degrees. There are multiple causes and it is common in children with cerebral palsy. CVI can be identified easily, if a structured approach to history-taking is employed. This review describes the features of CVI and describes practical management strategies aimed at helping affected children. A literature review was undertaken using 'Medline' and 'Pubmed'. Search terms included cerebral visual impairment,

cortical visual impairment, dorsal stream dysfunction and visual function in cerebral palsy.

PMID: 24766507 [PubMed - in process]

11. Res Dev Disabil. 2014 Apr 24;35(7):1551-1561. doi: 10.1016/j.ridd.2014.03.035. [Epub ahead of print]

Validity and reliability of the Mastication Observation and Evaluation (MOE) instrument.

Remijn L1, Speyer R2, Groen BE3, van Limbeek J4, Nijhuis-van der Sanden MW5.

The Mastication Observation and Evaluation (MOE) instrument was developed to allow objective assessment of a child's mastication process. It contains 14 items and was developed over three Delphi rounds. The present study concerns the further development of the MOE using the COSMIN (Consensus based Standard for the Selection of Measurement Instruments) and investigated the instrument's internal consistency, inter-observer reliability, construct validity and floor and ceiling effects. Consumption of three bites of bread and biscuit was evaluated using the MOE. Data of 59 healthy children (6-48 mths) and 38 children (bread) and 37 children (biscuit) with cerebral palsy (24-72 mths) were used. Four items were excluded before analysis due to zero variance. Principal Components Analysis showed one factor with 8 items. Internal consistency was >0.70 (Chronbach's alpha) for both food consistencies and for both groups of children. Inter-observer reliability varied from 0.51 to 0.98 (weighted Gwet's agreement coefficient). The total MOE scores for both groups showed normal distribution for the population. There were no floor or ceiling effects. The revised MOE now contains 8 items that (a) have a consistent concept for mastication and can be scored on a 4-point scale with sufficient reliability and (b) are sensitive to stages of chewing development in young children. The removed items are retained as part of a criterion referenced list within the MOE.

PMID: 24770467 [PubMed - as supplied by publisher]

12. Dev Med Child Neurol. 2014 Apr 29. doi: 10.1111/dmcn.12473. [Epub ahead of print]

Developmental trajectories of receptive and expressive communication in children and young adults with cerebral palsy.

Vos RC1, Dallmeijer AJ, Verhoef M, Van Schie PE, Voorman JM, Wiegerink DJ, Geytenbeek JJ, Roebroeck ME, Becher JG; the PERRIN+ Study Group.

AIM: The aim of this study was to determine the developmental trajectories of expressive (speech) and receptive (spoken and written language) communication by type of motor disorder and intellectual disability in individuals with cerebral palsy (CP). METHOD: The development of 418 participants (261 males, 157 females; mean age 9y 6mo [SD 6y 2mo], range 1-24y; Gross Motor Function Classification System (GMFCS) level I [n=206], II [n=57], III [n=59], IV [n=54], V [n=42]) was followed for 2 to 4 years in a longitudinal study. Communication performance was measured using the Vineland Adaptive Behavior Scales. The type of motor disorder was differentiated by type of CP as unilateral spastic (USCP, n=161), bilateral spastic (BSCP, n=202), and non-spastic (NSCP, n=55), while intellectual disability was determined by IQ or school type (regular or special). A multilevel analysis was then used to model the developmental trajectories. RESULTS: The most favourable development of expressive communication was seen in USCP (vs BSCP ß [SE]-2.74 [1.06], NSCP ß [SE]-2.67 [1.44]). The difference between the development trajectory levels of children with and without intellectual disability was smaller for children with USCP than for those with BSCP and NSCP. For receptive communication, the most favourable development was found for all children with USCP and for BSCP or NSCP without intellectual disability (vs intellectual disability ß [SE] -4.00 [1.16]). Development of written language was most favourable for children without intellectual disability (vs intellectual disability ß [SE]-23.11 [2.85]). INTERPRETATION: The development of expressive communication was found to be most closely related to type of motor disorder, whereas the development of receptive communication was found to be most closely related to intellectual disability.

PMID: 24773274 [PubMed - as supplied by publisher]

13. Philos Trans R Soc Lond B Biol Sci. 2014 Apr 28;369(1644):20130185. doi: 10.1098/rstb.2013.0185. Print 2014.

Action observation treatment: a novel tool in neurorehabilitation.

Buccino G.

This review focuses on a novel rehabilitation approach known as action observation treatment (AOT). It is now a well-accepted notion in neurophysiology that the observation of actions performed by others activates in the perceiver the same neural structures responsible for the actual execution of those same actions. Areas endowed with this action observation-action execution matching mechanism are defined as the mirror neuron system. AOT exploits this neurophysiological mechanism for the recovery of motor impairment. During one typical session, patients observe a daily action and afterwards execute it in context. So far, this approach has been successfully applied in the rehabilitation of upper limb motor functions in chronic stroke patients, in motor recovery of Parkinson's disease patients, including those presenting with freezing of gait, and in children with cerebral palsy. Interestingly, this approach also improved lower limb motor functions in post-surgical orthopaedic patients. AOT is well grounded in basic neuroscience, thus representing a valid model of translational medicine in the field of neurorehabilitation. Moreover, the results concerning its effectiveness have been collected in randomized controlled studies, thus being an example of evidence-based clinical practice.

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14. Disabil Rehabil. 2014 Apr 30. [Epub ahead ofprint]

"It's fun, but?…" Children with cerebral palsy and their experiences of participation in physical activities.

Lauruschkus K1, Nordmark E, Hallström I.

Purpose: To explore the experiences of children with cerebral palsy (CP) regarding participation in physical activities, and to describe facilitators and barriers. Methods: Sixteen children with CP 8-11 years old who varied in gross motor, cognitive and communicative function participated in either an individual interview or a focus group. Results: Two categories and 10 sub-categories emerged from the content analysis. The category "Being physically active, because?…" describes facilitators for being physically active divided into the sub-categories "Enjoying the feeling", "Being capable", "Feeling of togetherness", "Being aware it is good for me", and "Using available opportunities". The second category "Being physically active, but?…" describes barriers to being physically active, divided into the sub-categories "Getting tired and experiencing pain", "Something being wrong with my body", "Being dependent on others", "Not being good enough" and "Missing available opportunities". Conclusions: Asking children with CP about the physical activities they enjoy, and giving them the opportunity of trying self-selected activities with the right support is important for facilitating an increased participation in physical activities. Having fun with family and friends when being physically active, and enjoying the sensation of speed should be taken into consideration when designing interventions. When supporting children to become and remain physically active, attention should be paid to pain, fatigue and the accessibility of activities and locations. Implications for Rehabilitation: Children want to be physically active together with friends or others. Children want to have fun and enjoy the sensation of speed when being physically active. Self-selected physical activities and the opportunity of trying new activities with the right support is essential for facilitating an increased participation in physical activities. Service planning and design may be facilitated by asking children about the physical activities they enjoy.

PMID: 24786968 [PubMed - as supplied by publisher]

15. Dev Med Child Neurol. 2014 Apr 29. doi: 10.1111/dmcn.12472. [Epub ahead of print]

'He does not see himself as being different': the perspectives of children and caregivers on relevant areas of functioning in cerebral palsy.

Schiariti V1, Sauve K, Klassen AF, O'Donnell M, Cieza A, Mâsse LC.

AIMS: In the context of the development of the International Classification of Functioning, Disability and Health (ICF) Core Sets for children and adolescents with cerebral palsy (CP), we investigated the strengths and limitations in functioning important to children with CP, through either child self-reports or caregiver proxy reports, using components of the International Classification of Functioning, Disability and Health for Children and Youth (ICF-CY). METHOD: We conducted semi-structured interviews with 10 children with CP (children self-reporting), 10 caregivers of children self-reporting (10 child-caregiver dyads), and 12 caregivers of children not self-reporting. Mean age 10y 6mo, range 4-16y. A convenience sample was recruited representing Gross Motor Function Classification System (GMFCS) levels I to V. Interviews were audio-taped and the content covered all of the relevant ICF-CY components. The interviews were then transcribed verbatim and coded in N-Vivo 10 using the ICF-CY coding system. RESULTS: We identified 1956 themes that linked to 175 ICF-CY categories. Most of the themes were represented by the ICF-CY components activities and participation and environmental factors. The children interviewed discussed issues related to mobility, self-care, and recreation and leisure, whereas the caregivers focused more on physical limitations and on the environmental factors associated with everyday activities. INTERPRETATION: The children and their caregivers described many of the same areas of functioning but provided unique perspectives. Children talked more frequently about their abilities with CP, whereas the caregivers interviewed talked more about their concern over the limitations and broader issues facing their child. The findings highlight the need to explore the perspectives of both the child and the caregiver when characterizing the functional profile of children with CP.

PMID: 24773255 [PubMed - as supplied by publisher]

16. Disabil Rehabil. 2014 Apr 30. [Epub ahead of print]

Self-reported mental health in youth with cerebral palsy and associations to recurrent musculoskeletal pain.

Ramstad K1, Loge JH, Jahnsen R, Diseth TH.

Purpose: To explore self-reports on emotional, conduct, hyperactivity and peer problems and on prosocial behaviour in youth with cerebral palsy (CP), compare the reports to normative data and to mothers' reports and to analyse if recurrent CP-related musculoskeletal pain (RMP) influence the self-reports. Methods: Eighty-one youth with CP (mean age 14.2 years, 40 boys) were assessed by clinical examination, interview and the questionnaire Strengths and Difficulties Questionnaire (SDQ) filled in by the youths and their mothers. Gross motor function (GMFCS) was: level I 43%, level II 41%, level III 12% and level IV-V 4%. Results: Compared to normative data, youth with CP reported similar levels of peer problems, less conduct problems ($p<0.01$), less hyperactivity problems ($p<0.01$) and more prosocial behaviour ($p<0.01$). Compared to the mothers' reports, youth with CP reported lower levels of peer problems ($p<0.01$). Twenty-six boys (65%) and 28 girls (68%) had RMP. Girls, but not boys with RMP reported a higher level of peer problems ($p=0.02$) than youth without RMP. Conclusion: Self-report on mental health in addition to parental proxy-report is important because it yields additional information. Peer acceptance and the impact of pain on peer problems and participation are candidate topics for further research. Implications for Rehabilitation In children and adolescents with CP, self-report on mental health and peer problems is warranted because they provide different information than proxy-report. Self-reported behaviour may be a starting point for counselling and interventions to improve peer acceptance in children and adolescents with CP. When exploring how pain related to CP influences the daily activities of the individual child or adolescent; health care providers should pay special attention to peer problems and female gender.

PMID: 24786760 [PubMed - as supplied by publisher]

Prevention and Cure

17. Ann Neurol. 2014 Apr 26. doi: 10.1002/ana.24164. [Epub ahead of print]

UBQLN2 Mutation Causing Heterogeneous X-linked Dominant Neurodegeneration.

Fahed AC1, McDonough B, Gouvion CM, Newell KL, Dure LS, Bebin M, Bick AG, Seidman JG, Harter DH, Seidman CE.

We report a five-generation family with phenotypically diverse neurodegenerative disease including relentlessly progressive choreoathetoid movements, dysarthria, dysphagia, spastic paralysis, and behavioral dementia in descendants of a 67-year-old woman with amyotrophic lateral sclerosis. Disease onset varied with gender, occurring in male children and adult women. Exome sequence analyses revealed a novel mutation (c.1490C>T, p.P497L) in the ubiquilin-2 gene (UBQLN2) with X-linked inheritance in all studied affected individuals. As ubiquilin-2 positive inclusions were identified in brain we suggest that mutant peptide predisposes to protein misfolding and accumulation. Our findings expand the spectrum of neurodegenerative phenotypes caused by UBQLN2 mutations. ANN NEUROL 2014. © 2014 American Neurological Association.

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18. Aust N Z J Obstet Gynaecol. 2014 Apr 29. doi: 10.1111/ajo.12216. [Epub ahead of print]

Are 1st-trimester ß-human chorionic gonadotrophin and pregnancy-associated plasma protein A levels predictive of intrapartum fetal compromise in a selected normal population?

Prior T1, Mullins E, Bennett P, Kumar S.

BACKGROUND: The incidence of cerebral palsy in term infants has not changed over the last 30 years. Current intrapartum monitoring techniques are limited by their inherent poor specificity. Changes in fetal haemodynamics in the term fetus, similar to those seen in fetal growth restriction, have been associated with an increased risk of subsequent intrapartum fetal compromise. Alterations in first-trimester ß-hCG and PAPP-A levels are predictive of fetal growth restriction. AIMS: In this study, we aimed to establish whether first-trimester ß-hCG and PAPP-A levels were predictive of fetal compromise in labour and whether these first-trimester markers could be correlated with fetal haemodynamics at term in a low-risk population. MATERIALS AND METHODS: Over a two-year period, 427 women with low risk, uncomplicated pregnancies were recruited to this study. All participants underwent a prelabour ultrasound examination during which fetal biometry and haemodynamics were assessed. First-trimester ß-hCG and PAPP-A levels were recorded from the case notes. All cases were followed up within 48 hours of delivery, and first-trimester ß-hCG and PAPP-A levels correlated with intrapartum outcomes and fetal haemodynamics. RESULTS: No significant relationship between first-trimester ß-hCG and PAPP-A levels and subsequent intrapartum fetal compromise was observed. Weak but significant correlations were observed between ß-hCG levels and umbilical venous flow rate, as well as PAPP-A levels and uterine artery pulsatility index. CONCLUSIONS: ß-hCG and PAPP-A levels measured during the first trimester are not predictive of subsequent intrapartum fetal compromise within a low-risk population.

PMID: 24773613 [PubMed - as supplied by publisher]

19. Cell. 2014 Apr 24;157(3):636-50. doi: 10.1016/j.cell.2014.02.058.

Human CLP1 Mutations Alter tRNA Biogenesis, Affecting Both Peripheral and Central Nervous System Function.

Karaca E1, Weitzer S2, Pehlivan D1, Shiraishi H2, Gogakos T3, Hanada T4, Jhangiani SN5, Wiszniewski W1,

Withers M1, Campbell IM1, Erdin S6, Isikay S7, Franco LM8, Gonzaga-Jauregui C1, Gambin T1, Gelowani V1, Hunter JV9, Yesil G10, Koparir E11, Yilmaz S12, Brown M3, Briskin D3, Hafner M3, Morozov P3, Farazi TA3, Bernreuther C13, Glatzel M13, Trattnig S14, Friske J14, Kronnerwetter C14, Bainbridge MN5, Gezdirici A11, Seven M11, Muzny DM5, Boerwinkle E15, Ozen M11; Baylor Hopkins Center for Mendelian Genomics, Clausen T16, Tuschl T3, Yuksel A11, Hess A17, Gibbs RA18, Martinez J19, Penninger JM20, Lupski JR21.

CLP1 is a RNA kinase involved in tRNA splicing. Recently, CLP1 kinase-dead mice were shown to display a neuromuscular disorder with loss of motor neurons and muscle paralysis. Human genome analyses now identified a CLP1 homozygous missense mutation (p.R140H) in five unrelated families, leading to a loss of CLP1 interaction with the tRNA splicing endonuclease (TSEN) complex, largely reduced pre-tRNA cleavage activity, and accumulation of linear tRNA introns. The affected individuals develop severe motor-sensory defects, cortical dysgenesis, and microcephaly. Mice carrying kinase-dead CLP1 also displayed microcephaly and reduced cortical brain volume due to the enhanced cell death of neuronal progenitors that is associated with reduced numbers of cortical neurons. Our data elucidate a neurological syndrome defined by CLP1 mutations that impair tRNA splicing. Reduction of a founder mutation to homozygosity illustrates the importance of rare variations in disease and supports the clan genomics hypothesis.

PMID: 24766809 [PubMed - in process]

20. Eur J Paediatr Neurol. 2014 Apr 18. pii: S1090-3798(14)00055-5. doi: 10.1016/j.ejpn.2014.04.003. [Epub ahead of print]

Gene sequences regulating the production of apoE and cerebral palsy of variable severity.

Lien E1, Andersen GL2, Bao Y3, Gordish-Dressman H4, Skranes J5, Blackman JA6, Vik T5.

BACKGROUND: The apoE protein is the most important lipid transporter in the brain and has also been shown to have several regulatory functions in the central nervous system. The production of apoE is regulated by a number of genes and increases under certain conditions such as cerebral injury in adults. AIMS: Our aim was to study whether variations in genes regulating the expression of the APOE gene were associated with severity of cerebral palsy (CP). METHODS: Children enrolled in the Cerebral Palsy Register of Norway (CPRN) were invited to participate in this cross-sectional study; 281 of the invited 703 children (40%) returned swabs with buccal cells collected by parents. Six genetic variations thought to affect the production of apoE were genotyped and correlated with clinical data recorded in the CPRN. RESULTS: Compared with children carrying the GG allele, children with genotype GT or TT in a specific genetic variation (rs59007384 located in the nearby TOMM40 gene) had excess risk for worse fine motor function (Odds ratio (OR): 1.82; 95% Confidence interval (CI): 1.10-2.99; p = 0.019) and epilepsy (OR: 2.32; CI: 1.17-4.61; p = 0.016). There was no association between severity of CP and any of the other five genetic variations analyzed. CONCLUSION: Our findings suggest that genetic variations in one of the sequences regulating the expression of APOE, may be associated with worse clinical outcome in children with cerebral palsy.

PMID: 24786335 [PubMed - as supplied by publisher]

21. Korean J Pediatr. 2014 Mar;57(3):101-109. Epub 2014 Mar 31.

Evidence for adverse effect of perinatal glucocorticoid use on the developing brain.

Chang YP.

The use of glucocorticoids (GCs) in the perinatal period is suspected of being associated with adverse effects on long-term neurodevelopmental outcomes for preterm infants. Repeated administration of antenatal GCs to mothers at risk of preterm birth may adversely affect fetal growth and head circumference. Fetal exposure to excess GCs during critical periods of brain development may profoundly modify the limbic system (primarily the hippocampus), resulting in long-term effects on cognition, behavior, memory, co-ordination of the autonomic nervous system, and

regulation of the endocrine system later in adult life. Postnatal GC treatment for chronic lung disease in premature infants, particularly involving the use of dexamethasone, has been shown to induce neurodevelopmental impairment and increases the risk of cerebral palsy. In contrast to studies involving postnatal dexamethasone, long-term follow-up studies for hydrocortisone therapy have not revealed adverse effects on neurodevelopmental outcomes. In experimental studies on animals, GCs has been shown to impair neurogenesis, and induce neuronal apoptosis in the immature brains of newborn animals. A recent study has demonstrated that dexamethasone-induced hypomyelination may result from the apoptotic degeneration of oligodendrocyte progenitors in the immature brain. Thus, based on clinical and experimental studies, there is enough evidence to advice caution regarding the use of GCs in the perinatal period; and moreover, the potential long-term effects of GCs on brain development need to be determined.

PMID: 24778691 [PubMed - as supplied by publisher] Free PMC Article

22. Obstet Gynecol. 2014 May;123 Suppl 1:152S-3S. doi: 10.1097/01.AOG.0000447144.44382.5a.

Optimal timing of delivery in obese women: a decision analysis.

Lee VR1, Niu B, Kaimal A, Little S, Nicholson J, Caughey AB.

INTRODUCTION: Maternal obesity complicates over 20% of pregnancies in the United States and increases the risk of many adverse perinatal outcomes. However, limited data exist on the timing of delivery in such cases. The purpose of this study was to determine the optimal gestational age of delivery in an obese patient. METHODS: A decision-analytic model was created using TreeAge software to determine the optimal timing of delivery in a theoretical cohort of 100,000 singleton pregnancies in obese women. Model options ranged from delivery at 37 weeks to 41 weeks of gestation. Strategies involving expectant management until a later gestational age accounted for the probabilities of spontaneous delivery and intrauterine fetal demise at each successive week. Neonatal complications included permanent brachial plexus injury, cerebral palsy, and neonate death. All probability estimates were derived from the literature, and total quality-adjusted life-years were calculated. RESULTS: The lowest rates of neonate death and cerebral palsy were associated with delivery at 39 weeks of gestation, whereas rates of intrauterine fetal demise and brachial plexus injuries were lowest at earlier gestational ages (). Balancing these outcomes, the optimal strategy was delivery at 38 weeks of gestation, which maximized quality-adjusted life-years. Delivery at 38 weeks of gestation would prevent 203 intrauterine fetal demises compared with expectant management until 41 weeks of gestation. Sensitivity analysis found that 38 weeks of gestation remained the optimal strategy until the risks of neonate death and intrauterine fetal demise were 5.57-fold and 1.25-fold, respectively, our baseline assumptions. (Table is included in full-text article.) CONCLUSIONS: Weighing the risks of intrauterine fetal demise against the risks of neonate death and significant neonatal morbidities, the ideal gestational age to deliver obese women is 38 weeks.

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23. Obstet Gynecol. 2014 May;123 Suppl 1:148S-9S. doi: 10.1097/01.AOG.0000447135.85178.77.

Timing delivery of vasa previa: a decision analysis.

Hoover MA1, Allen A, La Rochelle F, Baig-Lewis S, Pilliod R, Caughey AB.

INTRODUCTION: The objective of this study was to determine the optimal gestational age for delivery in cases of vasa previa. METHODS: A decision-analytic model was designed to compare gestational age of delivery in vasa previa for gestational ages between 32 and 37 weeks using maternal and fetal quality-adjusted life-years in a theoretical cohort of 1,000 women with vasa previa. At each week of gestational age, we allowed for different delivery strategies: 1) premature labor with emergent delivery or 2) planned delivery by cesarean at a predetermined gestational age. Quality-adjusted life-years were calculated based on the probability of fetal bleed or no fetal bleed, with or without development of cerebral palsy, stillbirth, or uncomplicated fetal delivery. RESULTS: Delivery at 33 weeks of gestation for women with vasa previa optimizes maternal and neonatal outcomes, resulting in 6.98 stillbirths per 1,000 and 12.2 cases of cerebral palsy per 1,000. Delivery at 33 weeks of gestation maximizes total quality-adjusted life-years at 56.4. CONCLUSION: Delivery at 33 weeks of gestation for women with vasa previa optimizes maternal and fetal outcomes.(Figure is included in full-text article.)

PMID: 24770031 [PubMed - in process]

24. Res Dev Disabil. 2014 Apr 22;35(7):1544-1550. doi: 10.1016/j.ridd.2014.03.048. [Epub ahead of print]

Association between mechanical ventilation and neurodevelopmental disorders in a nationwide cohort of extremely low birth weight infants.

Tsai WH1, Hwang YS2, Hung TY3, Weng SF4, Lin SJ3, Chang WT5.

Mechanical ventilation for preterm infants independently contributes to poor neurodevelopmental performance. However, few studies have investigated the association between the duration of mechanical ventilation and the risk for various developmental disorders in extremely low birth weight (ELBW) (<1000g) infants. Using a large nationwide database, we did a 10-year retrospective follow-up study to explore the effect of mechanical ventilation on the incidence of cerebral palsy (CP), autism spectrum disorder (ASD), intellectual disability (ID), and attention-deficit/hyperactivity disorder (ADHD) in ELBW infants born between 1998 and 2001. Seven hundred twenty-eight ELBW infants without diagnoses of brain insults or focal brain lesions in the initial hospital stay were identified and divided into three groups (days on ventilator: 2, 3-14, 15 days). After adjusting for demographic and medical factors, the infants in the 15 days group had higher risks for CP (adjusted hazard ratio: 2.66; 95% confidence interval: 1.50-4.59; p<0.001) and ADHD (adjusted hazard ratio: 1.95; 95% confidence interval: 1.02-3.76; p<0.05), than did infants in the 2 days group. The risk for ASD or ID was not significantly different between the three groups. We conclude that mechanical ventilation for 15 days increased the risk for CP and ADHD in ELBW infants even without significant neonatal brain damage. Developing a brain-protective respiratory support strategy in response to real-time cerebral hemodynamic and oxygenation changes has the potential to improve neurodevelopmental outcomes in ELBW infants.

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25. Masui. 2014 Apr;63(4):459-61.

Anesthetic management of a patient with 8 trisomy mosaic combined with cerebral palsy].
[Article in Japanese]

Matsuda K, Yakushiji T, Ryo J, Higashimoto S, Sasaki K.

We administered general anesthesia for a patient with 8 trisomy mosaic and cerebral palsy. Constitutional 8 trisomy mosaic has been associated with syndromic dysmorphology, corneal opacities, leukemia and trophoblastic disease. In Japan only 4 reports of general anesthesia related with 8 trisomy were found. This patient was a 24-year-old woman (140 cm, 35 kg), with mental retardation, poor body development and severe scoliosis. Since she suffered from repeated serious asthma and pneumonia since childhood, tracheotomy was performed at the age of 9. Epileptic seizures were also seen and antiepileptics were prescribed. This time, general anesthesia was scheduled for the extraction of a maxillary cyst. Anesthesia was induced slowly with sevoflurane from the tracheotomy, followed by rocuronium 25 mg i.v., and maintained with sevoflurane 1.5-2 % and remifentanil 0.05-0.2 microg x kg(-1) x min(-1) Throughout the operation, BIS score fluctuated between 40-60, and stable anesthesia was maintained. We reversed the rocuronium with sugammadex 140 mg promptly. The 8 trisomy mosaic patient is known to have various complications related to circulation and respiration. Careful management is necessary in anesthesia for an 8 trisomy patient.

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