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Interventions and Management

1. Construct and discriminative validity and reliability of the Selective Control of the Upper Extremity Scale (SCUES) in children with unilateral cerebral palsy
Ayse Yildiz, Ramazan Yildiz, Halil Ibrahim Celik, Omer Faruk Manzak, Bulent Elbasan

Aims: One of the impairments evaluated in children with cerebral palsy (CP), which perhaps has been least investigated, is reduced selective motor control. The aim of the present study was to determine construct validity, discriminative validity, and intra- and interrater reliability of the Selective Control of the Upper Extremity Scale (SCUES). Methods: Thirty-three children with unilateral CP, with a mean age of 11.5 ± 3.3 years, at level I to IV according to the Manual Ability Classification System (MACS), participated. The children were video-recorded and scored using the SCUES. The videos were scored twice to determine the intra- and interrater reliability. Reliability was assessed using the intraclass correlation coefficient, the standard error of the measurement (SEM), and the smallest real difference (SRD). Differences in the SCUES scores were determined between the less- and more-affected arm and across all MACS levels for discriminative validity. Construct validity of the SCUES was established by the MACS, and the Jebsen Taylor Hand Function Test (JTT). Results: SCUES scores were significantly different between the less- and more-affected arm ($p < .001$) and between the arm joints. SCUES scores were also significantly different among MACS levels ($p < .001$). The SCUES was strongly correlated with the JTT (Spearman's rho $= -0.80$, $p < .001$) and MACS (rho $= -0.78$, $p < .001$). Intra- and interrater reliability were excellent (intraclass correlation coefficient [ICC] > 0.75) for all joints of the more-affected extremity. The SRDs at the 95% confidence level for intra- and interrater reliability were 2.11 and 1.16, respectively. Conclusions: The SCUES is a valid and reliable tool to assess selective motor control of the upper extremity in children with unilateral CP.

PMID: 32787483

2. Caregiver perception of hand function in infants with cerebral palsy: psychometric properties of the Infant Motor Activity Log
Helen Carey, Krystal Hay, Mary Ann Nelin, Brianna Sowers, Dennis J Lewandowski, Melissa Moore-Clingenpeel, Nathalie L Maitre

Aim: To evaluate the properties of the Infant Motor Activity Log (IMAL), a caregiver-report for frequency and quality of use of more affected upper extremity in infants with neurological and functional impairments. Method: This was a prospective cohort study of 66 children (34 females, 32 males) aged 6 to 24 months (mean age [SD] 13.7mo [5.3]) with neurological and functional impairments and a confirmed cerebral palsy diagnoses after 2 years, and 51 age-matched typically developing children. The IMAL was administered at baseline and 4 weeks later. Typically developing infants were tested with randomly

assigned 'more affected' upper extremity. Psychometric properties were evaluated using Spearman's correlation coefficient, Cronbach's alpha, and Jonckheere-Terpstra tests. Results: In the children with impairments, the IMAL showed internal consistency (alpha≥0.88) for the How Well Scale (HWS) and How Often Scale (HOS). Test-retest reliability was 0.64 (HOS) and 0.70 (HWS), demonstrating stability over time. Correlation with Bayley Scales of Infant and Toddler Development, Third Edition more affected arm raw scores were 0.70 (HOS) and 0.72 (HWS) (p<0.001) demonstrating construct validity. Both scale scores decreased with increasing Gross Motor Function Classification System and Mini-Manual Ability Classification System (p<0.001) levels, supporting discriminative validity. Discrimination between typically developing infants and infants with impairments was high (HWS: area under the receiver operating characteristic curve [AUC] 0.96, 95% confidence interval [CI] 0.94-0.99 and HOS AUC=0.95, CI 0.92-0.99). Interpretation: The IMAL is a valid and reliable discriminative caregiver measure of upper limb performance and may complement measures of capacity in infants with neurological and functional impairments.

PMID: 32779197

3. Selective dorsal rhizotomy; evidence on cost-effectiveness from England
Mark Pennington, Jennifer Summers, Bola Coker, Saskia Eddy, Muralikrishnan R Kartha, Karen Edwards, Robert Freeman, John Goodden, Helen Powell, Christopher Verity, Janet L Peacock

PLoS One. 2020 Aug 10;15(8):e0236783. doi: 10.1371/journal.pone.0236783. eCollection 2020.

Objectives: Selective dorsal rhizotomy (SDR) has gained interest as an intervention to reduce spasticity and pain, and improve quality of life and mobility in children with cerebral palsy mainly affecting the legs (diplegia). We evaluated the cost-effectiveness of SDR in England. Methods: Cost-effectiveness was quantified with respect to Gross Motor Function Measure (GMFM-66) and the pain dimension of the Cerebral Palsy Quality of Life questionnaire for Children (CPQOL-Child). Data on outcomes following SDR over two years were drawn from a national evaluation in England which included 137 children, mean age 6.6 years at surgery. The incremental impact of SDR on GMFM-66 was determined through comparison with data from a historic Canadian cohort not undergoing SDR. Another single centre provided data on hospital care over ten years for 15 children undergoing SDR at a mean age of 7.0 years, and a comparable cohort managed without SDR. The incremental impact of SDR on pain was determined using a before and after comparison using data from the national evaluation. Missing data were imputed using multiple imputation. Incremental costs of SDR were determined as the difference in costs over 5 years for the patients undergoing SDR and those managed without SDR. Uncertainty was quantified using bootstrapping and reported as the cost-effectiveness acceptability curve. Results: In the base case, the incremental cost-effectiveness ratios (ICERs) for SDR are £1,382 and £903 with respect to a unit improvement in GMFM-66 and the pain dimension of CPQOL-Child, respectively. Inclusion of data to 10 years indicates SDR is cheaper than management without SDR. Incremental costs and ICERs for SDR rose in sensitivity analysis applying an alternative regression model to cost data. Conclusions: Data on outcomes from a large observational study of SDR and long-term cost data on children who did and did not receive SDR indicates SDR is cost-effective.

PMID: 32776949

4. Walking Speed of Children and Adolescents With Cerebral Palsy: Laboratory Versus Daily Life
Lena Carcreff, Corinna N Gerber, Anisoara Paraschiv-Ionescu, Geraldo De Coulon, Kamiar Aminian, Christopher J Newman, Stéphane Armand

Front Bioeng Biotechnol. 2020 Jul 14;8:812. doi: 10.3389/fbioe.2020.00812. eCollection 2020.

The purpose of this pilot study was to compare walking speed, an important component of gait, in the laboratory and daily life, in young individuals with cerebral palsy (CP) and with typical development (TD), and to quantify to what extent gait observed in clinical settings compares to gait in real life. Fifteen children, adolescents and young adults with CP (6 GMFCS I, 2 GMFCS II, and 7 GMFCS III) and 14 with TD were included. They wore 4 synchronized inertial sensors on their shanks and thighs while walking at their spontaneous self-selected speed in the laboratory, and then during 2 week-days and 1 weekend day in their daily environment. Walking speed was computed from shank angular velocity signals using a validated algorithm. The median of the speed distributions in the laboratory and daily life were compared at the group and individual levels using Wilcoxon tests and Spearman's correlation coefficients. The corresponding percentile of daily life speed equivalent to the speed in the laboratory was computed and observed at the group level. Daily-life walking speed was significantly lower compared to the laboratory for the CP group (0.91 [0.58-1.23] m/s vs 1.07 [0.73-1.28] m/s, p = 0.015), but not for TD (1.29 [1.24-1.40] m/s vs 1.29 [1.20-1.40] m/s, p = 0.715). Median speeds correlated highly in CP (p < 0.001, rho = 0.89), but not in TD. In children

with CP, 60% of the daily life walking activity was at a slower speed than in-laboratory (corresponding percentile = 60). On the contrary, almost 60% of the daily life activity of TD was at a faster speed than in-laboratory (corresponding percentile = 42.5). Nevertheless, highly heterogeneous behaviors were observed within both populations and within subgroups of GMFCS level. At the group level, children with CP tend to under-perform during natural walking as compared to walking in a clinical environment. The heterogeneous behaviors at the individual level indicate that real-life gait performance cannot be directly inferred from in-laboratory capacity. This emphasizes the importance of completing clinical gait analysis with data from daily life, to better understand the overall function of children with CP.

PMID: 32766230

5. The benefits of strength training in cerebral palsy
Jakob Lorentzen, Jens Bo Nielsen

Dev Med Child Neurol. 2020 Aug 8. doi: 10.1111/dmcn.14625. Online ahead of print.

PMID: 32770743

6. Effects of High-Velocity Strength Training on Movement Velocity and Strength Endurance in Experienced Powerlifters with Cerebral Palsy
Rafał Szafraniec, Aleksandra Kisilewicz, Martyna Kumorek, Mathias Kristiansen, Pascal Madeleine, Dariusz Mroczek

J Hum Kinet. 2020 Jul 21;73:235-243. doi: 10.2478/hukin-2020-0009. eCollection 2020 Jul.

The present study aimed to evaluate the effects of a 6-week high-velocity strength training (HVST) intervention on movement velocity and strength endurance in experienced powerlifters with cerebral palsy (CP). Eleven experienced powerlifters with CP and seven from a control group (CON), were subjected to 6-week HVST. An assessment of movement velocity and strength endurance was conducted one week before (T1) and one week after (T2) the 6-week training intervention. During testing, athletes performed a maximum number of bench press repetitions possible within 5 sets of 15 s each, with 1-min passive rest intervals in-between. The indicator of movement velocity was the weight pressed in the first 5 s (5sW) in all performed sets. Strength endurance was described by the total weight (TW) pressed during the test. 5sW in T2 was significantly higher as compared with T1 in the CP group only (T1 928.9 ± 342.9 kg vs. T2 1007.3 ± 324.6 kg; p = 0.016). TW in T2 was significantly higher as compared with T1, both in the CP group (T1 2550.5 ± 843.9 kg vs. T2 2809.8 ± 981.3 kg; p < 0.001) and in the CON group (T1 2300.7 ± 845.1 kg vs. T2 2468.9 ± 890.1 kg; p = 0.049). A 6-week program of HVST increased movement velocity in resistance trained CP athletes. The gains of strength endurance were observed in both groups.

PMID: 32774555

7. Sedentary Behavior in Children With Cerebral Palsy Between 1.5 and 12 Years: A Longitudinal Study
Sarah E Reedman, Emily Johnson, Leanne Sakzewski, Sjaan Gomersall, Stewart G Trost, Roslyn N Boyd

Pediatr Phys Ther. 2020 Aug 7. doi: 10.1097/PEP.0000000000000740. Online ahead of print.

Purpose: To determine longitudinal change in sedentary behavior in children with cerebral palsy (CP) from 1.5 to 12 years. Methods: Ninety-one children, Gross Motor Function Classification System (GMFCS) levels I to III, who participated in a large longitudinal cohort study were participants. Longitudinal change was analyzed in objectively measured sedentary behavior and associations with sex, body mass index Z score, and socioeconomic status. Moderate-vigorous intensity physical activity (MVPA) was estimated at 8 to 12 years. Results: Average sedentary minutes/day peaked at 4 years in children at GMFCS I and 5 years in children at GMFCS II to III, then plateaued. Male sex was associated with increased sedentary behavior. At 8 to 12 years, children at GMFCS I, II, and III accumulated on average 54, 47, and 14 minutes/day, respectively, of MVPA. Conclusions: When measured to 12 years, sedentary behavior peaks by 5 years for children with CP who are walking with differences in trajectory according to GMFCS.

PMID: 32773523

8. Development and testing of the eye-pointing classification scale for children with cerebral palsy

Michael T Clarke, Jenefer Sargent, Rosemary Cooper, Gabriella Aberbach, Laura McLaughlin, Gurveen Panesar, Amie Woghiren, Tom Griffiths, Katie Price, Caroline Rose, John Swettenham

Purpose: The aim of this study was to develop and test a new classification scale to describe looking behaviours (gaze fixations and gaze shifts) in relation to eye-pointing. Methods: The Eye-pointing Classification Scale (EpCS) was developed and tested following established procedures for the construction and evaluation of equivalent scales, and involved 2 phases: Drawing on research literature, Phase 1 involved initial drafting of the scale through a series of multi-disciplinary group discussions; evaluation of the scale through a survey procedure, and subsequent expert group evaluation. Phase 2, was an examination of scale reliability and relationships between child characteristics and level of EpCS classification. Results: In Phase 1, an initial draft of the scale was developed and then evaluated by 52 participants in 10 countries, leading to its refinement. Subsequent expert evaluation of content, style and structure indicated that no further refinement was required. In Phase 2, the scale achieved excellent levels of reliability in clinical testing. A significant relationship was identified between level of child motor ability and EpCS classification, and level of child language understanding and EpCS classification. Implications for rehabilitation Non-speaking children with severe bilateral cerebral palsy who have limited upper limb movement may communicate by using controlled looking behaviours to point to objects and people, referred to as eye-pointing. However, there is little consensus as to which looking behaviours represent eye-pointing and which do not. The Eye-pointing Classification Scale (EpCS) was developed to describe looking behaviours related to eye-pointing in this population of children The EpCS provides a new robust tool for clinical management and research with children with cerebral palsy.

PMID: 32783539

9. Longitudinal Growth in Intelligibility of Connected Speech From 2 to 8 Years in Children With Cerebral Palsy: A Novel Bayesian Approach

Tristan J Mahr, Paul J Rathouz, Katherine C Hustad

Aim The aim of the study was to examine longitudinal growth in intelligibility in connected speech from 2 to 8 years of age in children with cerebral palsy. Method Sixty-five children with cerebral palsy participated in the longitudinal study. Children were classified into speech-language profile groups using age-4 data: no speech motor impairment (SMI), SMI with typical language comprehension, and SMI with impaired language comprehension. We fit a Bayesian nonlinear mixed-effects model of intelligibility growth at the child and group levels. We compared groups by age of steepest growth, maximum growth rate, and predicted intelligibility at 8 years of age. Results The no SMI group showed earlier and steeper intelligibility growth and higher average outcomes compared to the SMI groups. The SMI groups had more variable growth trajectories, but the SMI with typical language comprehension group had higher age-8 outcomes and steeper rates of maximum growth than the SMI with impaired language comprehension group. Language comprehension impairment at age of 4 years predicted lower intelligibility outcomes at age of 8 years, compared to typical language at age of 4 years. Interpretation Children with SMI at age of 4 years show highly variable intelligibility growth trajectories, and comorbid language comprehension impairment predicts lower intelligibility outcomes. Supplemental Material https://doi.org/10.23641/asha.12777659.

PMID: 32783783

10. [Botulinum toxin type A (Incobotulinum toxin A) in spastic forms of cerebral palsy: a retrospective analysis of clinical experience][Article in Russian]

A L Kurenkov, L M Kuzenkova, B I Bursagova, O A Klochkova, V V Chernikov, M A Kuznetsova, U S Ashrafova, O S Kuprianova

Objective: A retrospective analysis of the experience of using Incobotulinum toxin A injections for the treatment of spasticity in children with cerebral palsy (CP). Material and methods: One hundred and eighty-five children with spastic forms of CP, including 114 boys (61,6%), were studied. The average age of the patients was 3,8±2,5 years; the average weight was 14,2±6,9. The patients received injections of Incobotulinum toxin A according to registered indications or recommendations of a consultation of specialists and voluntary informed consent of the patient's representative. At least 1 point decrease of muscle tone according to the modified Ashworth scale was used as a criterion of the antispastic effect of Incobotulinum toxin A. Results: The total dose of Incobotulinum toxin A for the whole group of patients with CP was 154,5±67,7 U and 11,6±4,7 U per kg/body weight. The gracilis muscle (65,4% of cases, 95%CI 58,1-72,2) and the gastrocnemius muscle (49,4% of cases, 95%CI 41,8-56,6) were the most frequently injected targets in the lower extremities, and the pronator teres muscle (58,9% of cases, 95%CI 51,5-66,1) - in the upper extremities. Adverse events were observed in 13 patients (7,0%). They were mild in 9 patients and moderate in 4 patients. Conclusion: Our data confirmed the effectiveness and safety of Incobotulinum toxin A injections in spastic CP. The calculated average doses of Incobotulinum toxin A for target muscles and the frequency of different spasticity patterns could serve as a reference for the botulinum therapy planning.

PMID: 32790979

11. Effect of "Tonifying Kidney and Invigorating Brain" acupuncture in children with spastic cerebral palsy analyzed by multi-modality MRI combined with dynamic electroencephalogram

Dong Chen, Chao Bao, Yan-Xia Geng, Ming Yang, Elsie Sin May Teo, Jan-Bing Li, Yan-Cai Li, Nan Wang, Meng-Qian Yuan, Qin Zou, Ping-Ping Tang, Li-Li Zhu, Bin Xu

Introduction: Cerebral palsy is the most common motor disability of childhood. Spastic cerebral palsy accounts for 60% to 70% of cases. Research has shown that acupuncture can improve the quality of life of children with cerebral palsy, but the mechanism of action remains unclear. This study aims to determine the effectiveness of acupuncture for treatment of children with spastic cerebral palsy and to assess the value of multimodal magnetic resonance imaging (MRI) and ambulatory electroencephalogram (EEG) for evaluation of treatment effect. Methods and analysis: This randomized controlled trial will enroll a total of 72 children with CP from 2 hospitals-Jiangsu Province Hospital of Chinese Medicine and Nanjing State Hospital of Pediatric-with 36 participants from each hospital. Patients will be randomly assigned (1:1 ratio) to receive "Tonifying Kidney and Invigorating Brain" acupuncture treatment plus standardized physical rehabilitation treatment (treatment group) or only standardized physical rehabilitation (control group). All participants will receive 3 treatment sessions per week for 3 consecutive months; they will then be followed up for another 3 months. The primary outcome measures will include multimodal magnetic resonance imaging (MRI), ambulatory electroencephalogram (EEG), and Gesell Developmental Diagnostic Schedules. The secondary outcome measures will include Gross Motor Function Classification System (GMFCS), Gross Motor Function Measure (GMFM), Functional Independence Measure (WeeFIM), and Modified Ashworth Scale score. Outcome measures (including primary and secondary outcome measures) were collected at the baseline, 3 months and 6 months prior to the intervention.Ethics and dissemination PATIENTS CONSENT:: Obtained. Ethics approval: The central independent ethics committee of Jiangsu Province Hospital of Traditional Chinese Medicine approved the protocol (2017NL-115-02). Safety considerations: Routine blood tests and liver and kidney function tests will be conducted to exclude patients with severe heart, liver, or kidney diseases. The same examinations will be performed again at the end of the study to detect any possible side effects. Possible acupuncture-related adverse events (e.g., fainting, needle stick injury, local infection, subcutaneous hematoma, and low-grade fever) will be documented. Serious adverse events will be reported to the principal investigator immediately. All unexpected and unintended responses, even those not necessarily related to the acupuncture intervention, will be documented as adverse events. Case dropout management: Participants have a right to withdraw from the study at any time if they feel uncomfortable upon receiving the treatments or being diagnosed with serious complications or diseases. They will then be referred to the preferred department for further treatment and management. If cases of dropout, the researcher need to contact the participant to reason the problem out, collect and record all the necessary assessments on the last visit as well as the date of last visit. All data available until the date of withdrawal will be stored for further statistical analysis. Discussion: This research is being conducted to assess the value of acupuncture as an intervention for rehabilitation of children with spastic cerebral palsy and also to evaluate the usefulness of multimodal MRI and ambulatory EEG for identifying changes in brain function. Trial registration: This trial is registered with Chinese Clinical Trials Register, ChiCTR 1900024546 (registered 15 July 2019; retrospective registration, http://www.chictr.org.cn/showproj.aspx?proj=35763).

PMID: 32791681

12. A survey-based report on the occurrence of cerebral palsy in Urban areas of Karachi

Ammara Rafique, Hajra Naz

Cerebral Palsy (CP), a non-progressive motor disorder, which arises due to lesions of the brain during pregnancy, labour or shortly after birth effects 1-1.5/1000 live births. Altogether 658 CP cases were acquitted from 14 health organizations that permitted access to the data. Data was assembled with respect to topography, muscle tone, severity level and Gross Motor Function Classification System (GMFCS) is accompanied by the comorbidities and co-mitigating factors from 2010-2016. Data represented topographically showed a greater percentage of quadriplegic cases i.e.186 (39.9%). Spastic tone was the most commonly presented muscle tone i.e. 352 (53.4%) and 235 (57.7%) cases were in the mild severity zone. Level II was the most prevalent GMFCS i.e. 189 (34.4%). The most prevalent comorbidity was epilepsy i.e. 96 (14.58%) and co-mitigating factor was Attention Deficit/Hyperactivity Disorder i.e. 18 (2.73%). A dominant male to female ratio was seen as 1.4:1. The prevalence of males was exhibiting an increase of 80.3% in contrast to females.

PMID: 32794503

13. Associations between antenatal and perinatal risk factors and cerebral palsy: a Swedish cohort study

Anna Jöud, Andréa Sehlstedt, Karin Källén, Lena Westbom, Lars Rylander

Objectives: To investigate known and suggested risk factors associated with cerebral palsy in a Swedish birth cohort, stratified by gestational age. Setting: Information on all births between 1995 and 2014 in Skåne, the southernmost region in Sweden, was extracted from the national birth register. Participants: The cohort comprised a total of 215 217 children. Information on confirmed cerebral palsy and subtype was collected from the national quality register for cerebral palsy (Cerebral Palsy Follow-up Surveillance Programme). Primary and secondary outcome measures: We calculated the prevalence of risk factors suggested to be associated with cerebral palsy and used logistic regression models to investigate the associations between potential risk factors and cerebral palsy. All analyses were stratified by gestational age; term ($\geq$37 weeks), moderately or late preterm (32-36 weeks) and very preterm (<32 weeks). Results: In all, 381 (0.2 %) children were assigned a cerebral palsy diagnosis. Among term children, maternal preobesity/obesity, small for gestational age, malformations, induction, elective and emergency caesarian section, Apgar <7 at 5 min and admission to neonatal care were significantly associated with cerebral palsy (all p values<0.05). Among children born moderately or late preterm, small for gestational age, malformations, elective and emergency caesarian section and admission to neonatal care were all associated with cerebral palsy (all p values <0.05), whereas among children born very preterm no factors were significantly associated with the outcome (all p values>0.05). Conclusion: Our results support and strengthen previous findings on factors associated with cerebral palsy. The complete lack of significant associations among children born very preterm probably depends on to the small number of children with cerebral palsy in this group.

PMID: 32771990

14. Physical workload during caregiving activities and related factors among the caregivers of children with cerebral palsy

Asuman Gokcin Eminel, Turhan Kahraman, Arzu Genc

Background: Caregiving demands contribute to both psychological and physical health of caregivers. Physical workload (PW) can be an important cause of musculoskeletal disorders in caregivers of children with cerebral palsy (CP). Aims: To investigate PW during caregiving activities and related factors among caregivers of children with CP. Methods: Children with CP (n = 291) and their caregivers (n = 291) were recruited for this cross-sectional study. Caregivers were categorized as their child has presence of intellectual disability (ID) and independent walking ability. Gross motor function was assessed using the Gross Motor Function Classification System (GMFCS) in children. PW; presence and distribution of musculoskeletal pain sites; levels of disability of neck, low back, arm, and leg; levels of depressive symptoms; and health-related quality of life (HRQOL)

were assessed in caregivers. Results: Significant differences were observed in PW, low back pain-related disability, depressive symptoms, and HRQOL between caregivers of children with and without an ID (p < 0.05). All study variables were significantly different between caregivers of children who can and cannot independently walk (p < 0.05). PW was correlated with caregiver's age, body mass index, lower extremity dysfunction, depressive symptoms, and child's GMFCS level (p < 0.05). Conclusions: Caregivers of a child having an ID and walking disability had higher PW. These caregivers had more problems related to musculoskeletal disorders, higher depressive symptoms, and lower HRQOL. Higher PW was associated with lower level of gross motor function of child and older age, higher body mass index, higher level of lower extremity disfunction and low back pain disability, and lower HRQOL of caregivers.

PMID: 32789552

15. Did previous involvement in research affect recruitment of young people with cerebral palsy to a longitudinal study of transitional health care?

Elena Guiomar Garcia Jalón, Hanna Merrick, Allan Colver, Mark Linden, Transition Collaborative Group; Transition Collaborative Group

Objective: To assess whether being contacted about or participating in previous research and method of approaching potential participants affected recruitment to a transition study from child to adult healthcare services of young people with cerebral palsy (CP). Design and methods: Young people with CP aged 14-18 years without severe intellectual impairment were identified from regional registers of CP in Northern Ireland and the North of England. χ2 and Mann-Whitney U tests were used to assess differences in CP and sociodemographic characteristics between those recruited and those who refused. Logistic regression was used to assess contact about and recruitment to previous research and method of approach as predictors of recruitment, controlling for demographic and CP characteristics. Results: Of the 410 young people who were approached; 162 did not respond and of the 248 who responded, 96 (23%) were recruited. There were significant differences between those recruited and those who refused in age and number of previous studies they had participated in. Those who were older or who had previously been approached about research were more likely to be recruited to our study. However, those who had been recruited to previous studies were more likely to refuse to join our study. Conclusions: The method of approach to potential participants did not affect recruitment. Older adolescents and those who had been approached about previous research were more likely to take part in our study, although there was evidence of research fatigue because if they had actually been recruited to the previous studies they were less likely to join our study. Recruitment of adolescents to studies remains challenging.

PMID: 32788185

16. Early detection of general movements trajectories in very low birth weight infants

Matteo Porro, Camilla Fontana, Maria Lorella Giannì, Nicola Pesenti, Tiziana Boggini, Agnese De Carli, Giovanna De Bon, Giovanna Lucco, Fabio Mosca, Monica Fumagalli, Odoardo Picciolini

The aim of the study was to investigate General Movements'(GMs) neonatal trajectories and their association with neurodevelopment at three months corrected age (CA) in preterm infants. We conducted an observational, longitudinal study in 216 very low birth weight infants. GMs were recorded at 31 ± 1, 35 ± 1, 40 ± 1 weeks of postmenstrual age and at three months of corrected age (CA). More than 90% of infants showing neonatal trajectories with persistent Normal (N-N) or initial Poor Repertoire to Normal (PR-N) movements presented fidgety pattern at three months CA. On the contrary, fidgety movements were not detected in any infant with a trajectory of persistent Cramped-Synchronized (CS-CS) or an initial Poor-Repertoire to Cramped-Synchronized (PR-CS) movements. Trajectories with initial Normal to Poor-Repertoire (N-PR) or persistent Poor-Repertoire (PR-PR) movements showed an increased risk of having a non-normal Fidgety pattern compared with the N-N group (OR = 8.43, 95% CI: 2.26-31.45 and OR = 15.02, 95% CI: 6.40-35.26, respectively). These results highlight the importance to evaluate neonatal GMs' trajectory to predict infants' neurodevelopment. N-N or PR-N trajectories suggest normal short-term neurodevelopment, especially a lower risk of Cerebral Palsy; whereas findings of N-PR and PR-PR trajectories indicate the need for closer follow up to avoid delay in programming intervention strategies.

PMID: 32764577

17. Sensitivity and specificity of general movements assessment for detecting cerebral palsy in an Australian context: 2-year outcomes

Traci-Anne Goyen, Catherine Morgan, Cathryn Crowle, Caroline Hardman, Rosemary Day, Iona Novak, Nadia Badawi

Aim: We previously reported sensitivity and specificity levels of the general movements assessment (GMA) to detect cerebral palsy (CP) at 1 year within a clinical setting and with the assistance of the New South Wales (NSW) Rater Network. The aim of this study was to determine whether similarly high levels of validity could be maintained in the same group at 2 years. Methods: A prospective longitudinal cross-sectional study was conducted. GMA was blind-rated from conventional video by two independent certified raters, blinded to medical history. A third rater resolved disagreements. High-risk population screening for CP using the GMA during the fidgety period (12-20 weeks) was carried out in four neonatal intensive care units and one CP service over a 30-month period. Participants were 259 high-risk infants for the initial study. Multidisciplinary follow-up at 2-3 years included Bayley Scales of Infant Development and confirmed diagnosis of CP. Sensitivity and specificity values were calculated with true positives defined as a confirmed diagnosis of CP. Results: At 2-3 years, 184 (71%) completed the follow-up assessment. GMA was normal for 134 (73%, low risk for CP), absent fidgety for 48 (26%, high risk for CP) and abnormal fidgety for 2 (1%, high risk for abnormal neurological disorder). Sensitivity for detecting CP was 97.6% (40/41) and specificity 95.7% (133/139). Sensitivity for detecting any abnormal outcome with absent/abnormal fidgety general movements (GMs) was 57.9% (44/76) and specificity 94.4% (101/107). Conclusion: Excellent levels of sensitivity and specificity of the GMA for detecting CP in the clinical setting were maintained at 2 years and were similar to our previously reported findings.

PMID: 32767642

18. Use of consensus methods to determine the early clinical signs of cerebral palsy

Zachary Boychuck, John Andersen, André Bussières, Darcy Fehlings, Adam Kirton, Patricia Li, Maryam Oskoui, Charo Rodriguez, Michael Shevell, Laurie Snider, Annette Majnemer, PROMPT Group

Objectives: To develop expert-informed content regarding the early motor attributes of cerebral palsy (CP) that should prompt physician referral for diagnostic assessment of CP, as well as concurrent referral recommendations. This content will be used in the creation of knowledge translation (KT) tools for primary care practitioners and parents. Methods: Two nominal group processes were conducted with relevant stakeholders, representing Canadian 'content experts' and 'knowledge-users', using an integrated KT approach. Results: Six attributes were identified that should prompt referral for diagnosis. If the child demonstrates: Early handedness <12 months; stiffness or tightness in the legs between 6 and 12 months; persistent fisting of the hands >4 months; persistent head-lag >4 months; inability to sit without support >9 months; any asymmetry in posture or movement. Five referral recommendations were agreed upon: Motor intervention specialist (physical therapy and/or occupational therapy) for ALL; speech-language pathology IF there is a communication delay; audiology IF there is parental or healthcare professional concern regarding a communication delay; functional vision specialist (e.g., optometrist or occupational therapist) IF there is a vision concern (e.g., not fixating, following, or tracking); feeding specialist (e.g., occupational therapist, speech-language pathologist) IF there are feeding difficulties (e.g., poor sucking, poor swallowing, choking, and/or not gaining weight). Conclusion: Rigorous consensus methods provided the initial evidence necessary to inform the content of tools to assist primary care providers in the early detection of CP. Results will be validated through a Delphi process with international experts, and user-friendly formats of this KT tool will be developed collaboratively with stakeholders.

PMID: 32765166

19. Birth Asphyxia Is Associated With Increased Risk of Cerebral Palsy: A Meta-Analysis

Shan Zhang, Bingbing Li, Xiaoli Zhang, Changlian Zhu, Xiaoyang Wang

Objective: To assess the association between birth asphyxia-as defined by the pH of umbilical cord blood-and cerebral palsy in asphyxiated neonates ≥35 weeks' gestation. Methods: Two reviewers independently selected English-language studies that included data on the incidence of cerebral palsy in asphyxiated neonates ≥35 weeks' gestation. Studies were searched from the Embase, Google Scholar, PubMed, and Cochrane Library databases up to 31 December 2019, and the references in the retrieved articles were screened. Results: We identified 10 studies that met the inclusion criteria for our meta-analysis, including 8 randomized controlled trials and 2 observational studies. According to a random effects model, the pooled rate of cerebral palsy in the randomized controlled trials was 20.3% (95% CI: 16.0-24.5) and the incidence of cerebral palsy in the observational studies was 22.2% (95% CI: 8.5-35.8). Subgroup analysis by treatment for hypoxic ischemic encephalopathy in asphyxiated neonates showed that the pooled rates of cerebral palsy were 17.3% (95% CI: 13.3-21.2) and 23.9% (95% CI: 18.1 -29.7) for the intervention group and non-intervention group, respectively. Conclusion: Our findings suggest that the incidence of cerebral palsy in neonates (≥35 weeks' gestation) with perinatal asphyxia is significantly higher compared to that in the healthy neonate population. With the growing emphasis on improving neonatal neurodevelopment and reducing neurological sequelae, we conclude that the prevention and treatment of perinatal asphyxia is essential for preventing the development of cerebral palsy.

PMID: 32765409

20. Neurodevelopmental outcomes of very preterm and very-low-birthweight infants in a population-based clinical cohort with a definite perinatal treatment policy

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Background: With constant changes in neonatal care practices, recent information is valuable for healthcare providers and for parental counselling. The aim of the study was to describe the neurodevelopmental outcome in a cohort of very preterm (VPT)/ very-low-birthweight (VLBW) infants at 2 years corrected age (CA). Material and methods: This is a population-based cohort study of all infants born with a GA <31 weeks and/or BW < 1500 g between 2014 and 2016 admitted to the Flemish (Belgium) neonatal intensive care units. Infants had routine clinical follow-up around 2 years CA. The diagnosis of cerebral palsy (CP), visual and hearing impairments were recorded. Motor, cognitive and language outcomes were assessed using the Bayley-III. Neurodevelopmental impairment (NDI) was classified as mild (<1 standard deviation [SD]) or moderate-severe (<2SD) based on the defined categories of motor, cognitive, hearing, and vision impairments. Results: Of the 1941 admissions, 92% survived to discharge and follow-up data were available for 1089 infants (61.1%). Overall, 19.3%, 18.9% and 41.8% of infants had a motor, cognitive and language delay, respectively. CP was diagnosed in 4.3% of the infants. Mild and moderate-to-severe NDI was observed in 25.2% and 10.9% of the infants, respectively. The number of infants with a normal outcome increased from nearly 40% in the category of GA<26 weeks to 70% for infants in the category of 30─31 weeks GA. Conclusion: At 2 years CA, 64% were free from NDI and 90% were free from moderate-to-severe NDI. However, a lower GA and BW are associated with higher rates of adverse neurodevelopmental outcomes at 2 years CA.

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21. Effects of Liberal vs Restrictive Transfusion Thresholds on Survival and Neurocognitive Outcomes in Extremely Low-Birth-Weight Infants: The ETTNO Randomized Clinical Trial

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Importance: Red blood cell transfusions are commonly administered to infants weighing less than 1000 g at birth. Evidence-based transfusion thresholds have not been established. Previous studies have suggested higher rates of cognitive impairment

with restrictive transfusion thresholds. Objective: To compare the effect of liberal vs restrictive red blood cell transfusion strategies on death or disability. Design, setting, and participants: Randomized clinical trial conducted in 36 level III/IV neonatal intensive care units in Europe among 1013 infants with birth weights of 400 g to 999 g at less than 72 hours after birth; enrollment took place between July 14, 2011, and November 14, 2014, and follow-up was completed by January 15, 2018. Interventions: Infants were randomly assigned to liberal (n = 492) or restrictive (n = 521) red blood cell transfusion thresholds based on infants' postnatal age and current health state. Main outcome and measures: The primary outcome, measured at 24 months of corrected age, was death or disability, defined as any of cognitive deficit, cerebral palsy, or severe visual or hearing impairment. Secondary outcome measures included individual components of the primary outcome, complications of prematurity, and growth. Results: Among 1013 patients randomized (median gestational age at birth, 26.3 [interquartile range {IQR}, 24.9-27.6] weeks; 509 [50.2%] females), 928 (91.6%) completed the trial. Among infants in the liberal vs restrictive transfusion thresholds groups, respectively, incidence of any transfusion was 400/492 (81.3%) vs 315/521 (60.5%); median volume transfused was 40 mL (IQR, 16-73 mL) vs 19 mL (IQR, 0-46 mL); and weekly mean hematocrit was 3 percentage points higher with liberal thresholds. Among infants in the liberal vs restrictive thresholds groups, the primary outcome occurred in 200/450 (44.4%) vs 205/478 (42.9%), respectively, for a difference of 1.6% (95% CI, -4.8% to 7.9%; P = .72). Death by 24 months occurred in 38/460 (8.3%) vs 44/491 (9.0%), for a difference of -0.7% (95% CI, -4.3% to 2.9%; P = .70), cognitive deficit was observed in 154/410 (37.6%) vs 148/430 (34.4%), for a difference of 3.2% (95% CI, -3.3% to 9.6%; P = .47), and cerebral palsy occurred in 18/419 (4.3%) vs 25/443 (5.6%), for a difference of -1.3% (95% CI, -4.2% to 1.5%; P = .37), in the liberal vs the restrictive thresholds groups, respectively. In the liberal vs restrictive thresholds groups, necrotizing enterocolitis requiring surgical intervention occurred in 20/492 (4.1%) vs 28/518 (5.4%); bronchopulmonary dysplasia occurred in 130/458 (28.4%) vs 126/485 (26.0%); and treatment for retinopathy of prematurity was required in 41/472 (8.7%) vs 38/492 (7.7%). Growth at follow-up was also not significantly different between groups. Conclusions and relevance: Among infants with birth weights of less than 1000 g, a strategy of liberal blood transfusions compared with restrictive transfusions did not reduce the likelihood of death or disability at 24 months of corrected age. Trial registration: ClinicalTrials.gov Identifier: NCT01393496.

PMID: 32780138

22. Pilot study to establish a prospective neonatal cohort: Study of Preterm Infants and Neurodevelopmental Genes (SPRING)

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Background: Genetic risk variants and preterm birth are early and potent risk factors for later neuropsychiatric disorders. To understand the interrelationships between these factors, a large-scale genetic study of very preterm (VPT, <32 weeks gestation) infants with prospective follow-up is required. In this paper, we describe a streamlined study approach, using efficient processes for biological and clinical data collection, to feasibly establish such a cohort. Methods: We sought to recruit 500 VPT families within a 1 year period from neonatal units. Treating clinical teams recruited eligible participants, obtained parent consent, collected blood samples and posted specimens to the research laboratory. We extracted all clinical data from the National Neonatal Research Database, an existing UK resource that captures daily patient-level data on all VPT infants. Results: Between May 2017 and June 2018, we established a cohort of 848 VPT infants and their parents from 60 English neonatal units. The study population (median (IQR), gestation: 28.9 (26-30) weeks; birth weight: 1120 (886-1420) g) represented 18.9% of eligible infants born at the study sites during the recruitment period (n=4491). From the subset of 521 complete family trios, we successfully completed genotyping for 510 (97.9%) trios. Of the original 883 infants whose parents consented to participate, the parents of 796 (90.1%) infants agreed to future data linkage and 794 (89.9%) agreed to be recalled. Conclusion: We demonstrate the feasibility and acceptability of streamlined strategies for genetic, neonatal and longitudinal data collection and provide a template for future cost-effective and efficient cohort development.

PMID: 32789195

23. Definitions and classification of malformations of cortical development: practical guidelines

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Malformations of cortical development are a group of rare disorders commonly manifesting with developmental delay, cerebral palsy or seizures. The neurological outcome is extremely variable depending on the type, extent and severity of the malformation and the involved genetic pathways of brain development. Neuroimaging plays an essential role in the diagnosis of these malformations, but several issues regarding malformations of cortical development definitions and classification remain unclear. The purpose of this consensus statement is to provide standardized malformations of cortical development terminology and classification for neuroradiological pattern interpretation. A committee of international experts in paediatric neuroradiology prepared systematic literature reviews and formulated neuroimaging recommendations in collaboration with geneticists, paediatric neurologists and pathologists during consensus meetings in the context of the European Network Neuro-MIG initiative on Brain Malformations (https://www.neuro-mig.org/). Malformations of cortical development neuroimaging features and practical recommendations are provided to aid both expert and non-expert radiologists and neurologists who may encounter patients with malformations of cortical development in their practice, with the aim of improving malformations of cortical development diagnosis and imaging interpretation worldwide.

PMID: 32779696

24. Postnatal corticosteroids to prevent or treat bronchopulmonary dysplasia in preterm infants [Article in En, French]
Brigitte Lemyre, Michael Dunn, Bernard Thebaud

Review Paediatr Child Health. 2020 Aug;25(5):322-331. doi: 10.1093/pch/pxaa073. Epub 2020 Aug 1.

Historically, postnatal corticosteroids have been used to prevent and treat bronchopulmonary dysplasia (BPD), a significant cause of morbidity and mortality in preterm infants. Administering dexamethasone to prevent BPD in the first 7 days post-birth has been associated with increasing risk for cerebral palsy, while early inhaled corticosteroids appear to be associated with an increased risk of mortality. Neither medication is presently recommended to prevent BPD. New evidence suggests that prophylactic hydrocortisone, when initiated in the first 48 hours post-birth, at a physiological dose, and in the absence of indomethacin, improves survival without BPD, with no adverse neurodevelopmental effects at 2 years. This therapy may be considered by clinicians for infants at highest risk for BPD. Routine dexamethasone therapy for all ventilator-dependent infants is not recommended, but after the first week post-birth, clinicians may consider a short course of low-dose dexamethasone (0.15 mg/kg/day to 0.2 mg/kg/day) for individual infants at high risk for, or with evolving, BPD. There is no evidence that hydrocortisone is an effective or safe alternative to dexamethasone for treating evolving or established BPD. Current evidence does not support inhaled corticosteroids for the treatment of BPD.

PMID: 32765169

25. Impact of tocolysis-intent magnesium sulfate and beta-adrenergic agonists on perinatal brain damage in infants born between 28-36 weeks' gestation
Emi Kino, Masanao Ohhashi, Yasuyuki Kawagoe, Hiroshi Sameshima, Masato Kamitomo, Sachie Suga, Ichiro Yasuhi, Toru Funakoshi

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Aims: Magnesium sulfate has neuroprotective effects in preterm infants. Whether other antepartum treatments interfere with the neuroprotective actions is not well known. This study aims to explore the impacts of antenatal administration of Magnesium sulfate or beta-2 adrenergic agonists as tocolytic agents on the developing brain in premature infants. Methods: This is a retrospective cohort study in four tertiary perinatal centers in Japan. We collected data of pregnant women and infants born between 28 and 36 weeks for tocolytic agents, gestational age, sex, antenatal corticosteroid, fetal growth restriction, pathological chorioamnionitis, low umbilical arterial pH values (<7.1), multiple pregnancy, mode of delivery and institutions after excluding clinical chorioamnionitis, non-reassuring fetal status or major anomalies. Tocolytic agents were categorized into four groups: no-tocolysis, magnesium sulfate, beta-2 adrenergic agonists and the combination of them. We conducted multiple comparisons with multivariate analyses using generalized linear regression models to compare the prevalence of a poor perinatal outcome defined as infant's death, brain damage, particularly cerebral palsy and developmental delay. Results: Among 1083 infants, 39% were no-tocolysis, 47% were magnesium sulfate, 41% were beta-2 adrenergic agonists and 27% were combination group, including the duplication. The incidence of poor perinatal outcome was decreased by magnesium sulfate (OR 0.27, 95% CI 0.10-0.72), but not changed significantly by beta-2 adrenergic agonists (OR 1.28, 95% CI 0.63-2.59) or the combination group (OR 2.24, 95% CI 0.67-7.54), compared with the no-tocolysis. Conclusion: The combination therapy for tocolysis with beta-2 adrenergic agonists diminished the magnesium sulfate neuroprotective action after adjusting for

covariables.

PMID: 32779268

26. [Twin pregnancy and polymalformative syndrome by Enterovirus][Article in French]
N Cortisse, G Bruck, S Kreitz, F Chantraine, R Viellevoye, J M Senterre, J Pierart

Rev Med Liege. 2020 Jul;75(7-8):489-493.

Prenatal diagnosed congenital infection by Enterovirus is rarely described in the literature. A few casereports describe severe abnormalities observed by ultrasound that have led to spontaneous intrauterine demise or early death of the newborn. We report the case of a dichorionic diamniotic twin pregnancy. At 24 weeks of gestation, the second trimester ultrasound examination shows cardiac, brain and abdominal abnormalities in one of the fetuses. The other fetus has a normal appearance. "Standard" serological tests conducted on the mother are negative and amniocentesis reveals no genetic abnormality. After birth, Reverse Transcription Polymerase Chain Reaction (PCR) on samples of blood, ascites and stool reveals to be positive for Enterovirus in both newborns. Both are viable and exhibit severe brain abnormalities with severe neurological sequelae such as cerebral palsy, visual and hearing impairment. This case report illustrates the difficulty of prenatal diagnosis of congenital Enterovirus infection and informs about its possible neurological sequelae.

PMID: 32779895

Prevention and Cure

27. Therapeutic Evidence of Human Mesenchymal Stem Cell Transplantation for Cerebral Palsy: A Meta-Analysis of Randomized Controlled Trials
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Review Stem Cells Int. 2020 Jul 20;2020:5701920. doi: 10.1155/2020/5701920. eCollection 2020.

Cerebral palsy (CP) is a kind of movement and posture disorder syndrome in early childhood. In recent years, human mesenchymal stem cell (hMSC) transplantation has become a promising therapeutic strategy for CP. However, clinical evidence is still limited and controversial about clinical efficacy of hMSC therapy for CP. Our aim is to evaluate the efficacy and safety of hMSC transplantation for children with CP using a meta-analysis of randomized controlled trials (RCTs). We conducted a systematic literature search including Embase, PubMed, ClinicalTrials.gov, Cochrane Controlled Trials Register databases, Chinese Clinical Trial Registry, and Web of Science from building database to February 2020. We used Cochrane bias risk assessment for the included studies. The result of pooled analysis showed that hMSC therapy significantly increased gross motor function measure (GMFM) scores (standardized mean difference (SMD) = 1.10, 95%CI = 0.66-1.53, P < 0.00001, high-quality evidence) and comprehensive function assessment (CFA) (SMD = 1.30, 95%CI = 0.71-1.90, P < 0.0001, high-quality evidence) in children with CP, compared with the control group. In the subgroup analysis, the results showed that hMSC therapy significantly increased GMFM scores of 3, 6, and 12 months and CFA of 3, 6, and 12 months. Adverse event (AE) of upper respiratory infection, diarrhea, and constipation was not statistically significant between the two groups. This meta-analysis synthesized the primary outcomes and suggested that hMSC therapy is beneficial, effective, and safe in improving GMFM scores and CFA scores in children with CP. In addition, subgroup analysis showed that hMSC therapy has a lasting positive benefit for CP in 3, 6, and 12 months.

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