Cerebral palsy research news

Monday 22 March 2021

Cerebral Palsy Alliance is delighted to bring you this free weekly bulletin of the latest published research into cerebral palsy. Our organisation is committed to supporting cerebral palsy research worldwide - through information, education, collaboration and funding. Find out more at cerebralpalsy.org.au/our-research

Professor Nadia Badawi AM
Macquarie Group Foundation Chair of Cerebral Palsy

Subscribe to CP Research News

Interventions and Management

1. Bimanual motor performance in everyday life activities of children with hemiplegic cerebral palsy
Tien-Ni Wang, Tsu-Hsin Howe, Kai-Jie Liang, Ting-Wei Chang, Jeng-Yi Shieh, Hao-Ling Chen

Eur J Phys Rehabil Med. 2021 Mar 18. doi: 10.23736/S1973-9087.21.06504-7. Online ahead of print.

Background: Motor impairments in children with cerebral palsy significantly reduce their ability to learn and adapt bimanual actions into their life roles. The current evidence on bimanual coordination performance in children with hemiplegic cerebral palsy were mostly drawn from kinematic studies. Whether these kinematic findings on bimanual motor performance can be observed when performing daily life activities in a natural environment is not clear. Further, there is no evidence what and how the verbal prompting influences bilateral motor performance. We intend to explore its role on bimanual motor performance as well. Aim: This study aimed to investigate the bimanual motor performance in everyday life activities of children with hemiplegic cerebral palsy and the role of verbal prompts in facilitating affected hand use. Design: Observational study. Setting: Local medical center and community. Population: Twenty-five children with hemiplegic cerebral palsy and 25 age-matched typically developing children. Methods: The Observation-based Test of Capacity, Performance, and Developmental Disregard and Melbourne Assessment 2 were used to assess the quantitative and qualitative use of hands in everyday activities. Results: Children with hemiplegic cerebral palsy, demonstrated different motor coordination patterns in daily bimanual activities compared with their counterparts. With verbal prompts, children with hemiplegic cerebral palsy significantly increased the use of their affected hands in bimanual activities. However, the increases were observed only in basic motor components, such as reaching and grasping, and not in complex motor components such as manipulation. Conclusions: These findings will assist researchers and clinicians to develop and refine intervention programs that maximize rehabilitation benefits in improving bimanual hand coordination performance for children with hemiplegic cerebral palsy. Clinical rehabilitation impact: This study increased our understanding of bimanual motor performance of children with hemiplegic cerebral palsy in everyday life activities. The results demonstrated children with cerebral palsy rely more on their less-affected hand to perform bimanual activities with or without verbal prompts. Incorporating bimanual activities and verbal prompts during intervention may only be effective on facilitating basic hand movements but not on improving complex movements of affected hands. Further research is needed to explore other intervention strategies to facilitate complex bilateral hand movements.

PMID: 33733719

2. Tyneside Pegboard Test for unimanual and bimanual dexterity in unilateral cerebral palsy: association with sensorimotor impairment
Lisa Decraene, Hilde Feys, Katrijn Klingels, Anna Basu, Els Ortibus, Cristina Simon-Martinez, Lisa Mailleux

Dev Med Child Neurol. 2021 Mar 15. doi: 10.1111/dmcn.14858. Online ahead of print.

Aim: We explored the psychometric properties of the recently developed Tyneside Pegboard Test (TPT) for unimanual and bimanual dexterity in children with unilateral cerebral palsy (CP) and investigated the impact of sensorimotor impairments on manual dexterity. Method: In this cross-sectional study, the TPT was assessed in 49 children with unilateral CP (mean age 9y 8mo, SD 1y 11mo, range 6-15y; 30 males, 19 females; 23 with right unilateral CP). All participants additionally underwent a standardized upper limb evaluation at body function and activity level. We investigated: (1) known-group, concurrent, and construct validity and (2) impact of sensorimotor impairments including spasticity, grip force, stereognosis, and mirror movements using analysis of covariance, Spearman's rank correlation (r), and multiple linear regression (R2) respectively. Results: TPT outcomes significantly differed according to the Manual Ability Classification System ($p<0.001$, known-group validity). Relationships were found between the unimanual TPT tasks and the Jebsen-Taylor Hand Function Test (r=0.86-0.88, concurrent validity). Bimanual TPT tasks were negatively correlated with the Assisting Hand Assessment, ABILHAND-Kids, and Children's Hand-use Experience Questionnaire (r=-0.38 to -0.78, construct validity). Stereognosis was the main determinant influencing all tasks ($p<0.001$, R2 =37-50%). Unimanual dexterity was additionally determined by grip strength ($p<0.05$, R2 =8-9%) and mirror movements in the more impaired hand ($p<0.05$, R2 =4-8%). Bimanual dexterity was also explained by mirror movements in the more impaired hand ($p<0.01$, R2 =10-16%) and spasticity ($p=0.04$, R2 =5%). Interpretation: The TPT is a valid test to measure unimanual and bimanual dexterity in unilateral CP. The results further emphasize the importance of somatosensory impairments in children with unilateral CP.

PMID: 33720409

3. Somatosensory discrimination impairment in children with hemiplegic cerebral palsy as measured by the sense_assess© kids
Belinda McLean, Susan Taylor, Jane Valentine, Leeanne Carey, Ashleigh Thornton, Catherine Elliott

Aust Occup Ther J. 2021 Mar 18. doi: 10.1111/1440-1630.12729. Online ahead of print.

Introduction: To characterise somatosensory discrimination impairment of the upper-limb across domains of tactile discrimination, limb position sense and haptic object recognition using the sense_assess© kids and examine associations with upper-limb motor performance in children with hemiplegic cerebral palsy (CP). Methods: The sense_assess© kids was administered at one timepoint to 28 children, aged 6-15.5 years (M = 10.1, SD = 2.4), with hemiplegic CP (right hemiplegia n = 15) and Manual Ability Classification System Levels I (n = 11) and II (n = 17). Unimanual motor performance was quantified using the Box and Block Test. Results: Tactile discrimination was impaired in 18, limb position sense in 20, and haptic object recognition was impaired in 21 of 28 children. Over 80% (23/28) of children had impaired somatosensory discrimination in one or more domains. Low to moderate correlations were observed between each measure of somatosensory discrimination and motor performance. Manual ability classification was associated with limb position sense and haptic object recognition. A moderate inverse correlation ($r = -.57$, $p < .01$) exists between the number of somatosensory domains impaired and motor performance. Conclusion: The frequency of somatosensory impairment in the upper limb of children in our sample was high and associated with manual ability, suggesting a need for routine assessment of somatosensation in this population.

PMID: 33738799

4. Microstructural changes in the spinal cord of adults with cerebral palsy
Michael P Trevarrow, Sarah E Baker, Tony W Wilson, Max J Kurz

Dev Med Child Neurol. 2021 Mar 14. doi: 10.1111/dmcn.14860. Online ahead of print.

Aim: To quantify the microstructural differences in the cervical-thoracic spinal cord of adults with cerebral palsy (CP). Method: Magnetic resonance imaging of the proximal spinal cord (C6-T3) was conducted on a cohort of adults with CP (n=13; mean age=31y 11mo, standard deviation [SD] 8y 7mo; range=20y 8mo-47y 6mo; eight females, five males) and population norm adult controls (n=16; mean age=31y 4mo, SD 9y 9mo; range=19y 4mo-49y 5mo; seven females, nine males). The cross-sectional area (CSA) of the spinal cord, gray and white matter, magnetization transfer ratio (MTR), and fractional anisotropy of the cuneatus and corticospinal tracts were calculated. Results: The total spinal cord CSA and proportion of the spinal cord gray matter CSA were significantly decreased in the adults with CP. The corticospinal tracts' MTR was lower in the adults with CP. Individuals that had reduced gray matter also tended to have reduced MTR in their corticospinal tracts (r=0.42, p=0.029) and worse hand dexterity clinical scores (r=0.53, p=0.004). Interpretation: These results show that there are changes in the spinal cord microstructure of adults with CP. Ultimately, these microstructural changes play a role in the extent of the hand sensorimotor deficits seen in adults with CP.

PMID: 33719037

5. Effect of clinician's experience and expertise on the inter- and intra-observer reliability of hip migration index in children with cerebral palsy: A STROBE-compliant retrospective study
Necdet Demir, Mehmet Demirel, Önder Turna, Derya Yildizlar, Önder Demirbaş, Yavuz Sağlam

Medicine (Baltimore). 2021 Mar 12;100(10):e24538. doi: 10.1097/MD.0000000000024538.

Few studies have investigated the reliability of Reimers' hip migration percentage (RMP) in children with cerebral palsy (CP). Most studies on the topic reflected rating results of physician with a similar level of experience from the same expertise. This study aimed to determine the effect of clinician's experience and expertise on the intra-and inter-observer reliability of RMP.In this retrospective observational study, hip radiographs of children with CP were identified. 5 observers with different degrees of working experience from 3 different clinical fields, including orthopedics, radiology, and physical medicine and rehabilitation, performed all RMP measurements. All measurements were repeated 6 weeks later by the same observers. Inter- and intra-observer reliability for RMP measurements were assessed using Intraclass Correlation Coeficient (ICC), calculated from 2 sets of repeated measurements on a subset of 50 hips, with a 6 week apart for each observer.Fifty hip radiographs of 25 children with CP (10 females and 15 males; mean age: 6 years; age range: 2-8 years) were examined in the current study. No significant differences existed in intra-and inter-observer measurements. Excellent intra-observer reliability was observed between the 2 separate measurements for each observer, with a mean ICC of 0.976 (range: 0.956-0.989; P < .001). Among 5 observers, inter-observer reliability was excellent for the 2 separate RMP measurements, with the mean ICC minimally increasing between the 2 measurement periods (mean ICC: 0.928, range: 0.838-0.979 and mean ICC: 0.936, range: 0.861-0.983, respectively) (P < .001).Clinician's experience and expertise may not affect inter-and intra-observer reliability of RMP measurements.

PMID: 33725822

6. Personalized balance games for children with cerebral palsy: A pilot study
Oleh Kachmar, Anna Kushnir, Bohdana Fedchyshyn, Julián Cristiano, John O'Flaherty, Kjetil Helland, Gordon Johnson, Domenec Puig

J Pediatr Rehabil Med. 2021 Mar 5. doi: 10.3233/PRM-190666. Online ahead of print.

Purpose: To assess the changes in balance function in children with cerebral palsy (CP) after two weeks of daily training with personalized balance games. Methods: Twenty-five children with CP, aged 5 to 18 years were randomly selected for experimental or control groups. Over a period of two weeks, all participants received 8-9 game sessions for 15-20 minutes, totaling 150-160 minutes. The experimental group used personalized balance games available from the GAmification for Better LifE (GABLE) online serious gaming platform. Children from the control group played Nintendo Wii games using a handheld Wii Remote. Both groups received the same background treatment. Recorded outcome measures were from a Trunk Control Measurement Scale (TCMS), Timed Up & Go Test (TUG), Center of Pressure Path Length (COP-PL), and Dynamic Balance Test (DBT). Results: After two weeks of training in the experimental group TCMS scores increased by 4.5 points (SD = 3.5, $p< 0.05$) and DBT results increased by 0.88 points (IQR = 1.03, $p< 0.05$) while these scores did not change significantly in the control group. Overall, TUG and COP-PL scores were not affected in either group. Conclusion: This study demonstrates improvement of balancing function in children with CP after a two-week course of training with personalized rehabilitation computer games.

PMID: 33720857

7. A Retrospective Longitudinal Study in a Cohort of Children With Dyskinetic Cerebral Palsy Treated With Tetrabenazine
Roberta Scalise, Giuseppina Sgandurra, Valentina Menici, Nicola Capodagli, Roberta Di Pietro, Domenico M Romeo, Francesca Sini, Emanuela Pagliano, Maria Foscan, Giovanni Cioni, Roberta Battini

Front Neurol. 2021 Feb 26;12:612429. doi: 10.3389/fneur.2021.612429. eCollection 2021.

Tetrabenazine has been studied with a variety of hyperkinetic movement disorders, but there is limited and empirical literature on the potential efficacy of tetrabenazine in children with dyskinetic cerebral palsy (DCP). The purpose of this study was to evaluate the efficacy of tetrabenazine in a sample of children with DCP using the Movement Disorders-Childhood Rating Scale 4-18 Revised (MD-CRS 4-18 R). The study is a multicenter retrospective longitudinal study in which the participants were selected from the databases of each Center involved, according to detailed inclusion criteria. The study was performed on 23 children and adolescents (19 male and 4 females; mean age 8.28 years, SD 3.59) with DCP having been evaluated before starting the treatment (baseline), after 6 and 12 months of treatment and in a sub-cohort after >2 years follow-up. A linear mixed model was used to evaluate the effects of the different timings on each MD-CRS 4-18 R Index (Index I, Index II, and Global Index) adding age and type of movement disorder as random effect. A significant clinical improvement related to a reduction of MD-CRS 4-18 R Indexes was detected between the baseline and after 6 and 12 months of treatment. Findings support the efficacy of tetrabenazine in children with DCP through a standardized outcome measure (MD-CRS 4-18 R) and confirm the use of this scale as a suitable tool to detect changes in further randomized clinical trials.

PMID: 33716922

8. Muscle Tone Assessment under General Anesthesia for Sjögren-Larsson Syndrome and Spasticity
George Georgoulis, Argyrios Dinopoulos, Emmanouil Gkliatis

Case Reports Pediatr Neurosurg. 2021 Mar 16;1-3. doi: 10.1159/000514329. Online ahead of print.

Introduction: Study of muscle tone in individuals with severe spasticity (Modified Asworth Scale - MAS:3) under general anesthesia can confirm or rule out the eventual necessity of the impending spasticity relieving ablative neurosurgery by observing the hypertonia reduction and passive range of motion expansion. Therefore, what we measure under muscle relaxants is practically a fixed deformity. Case presentation: The study was performed on a girl with Sjögren-Larsson syndrome, presenting with icthyosis and spastic diplegia. Proposed intervention was Dorsal Rhizotomy. Under general anesthesia, with and without muscle relaxants, hypertonia was significantly reduced (MAS:1), but the angle of motion did not increase much. Conclusion: We decided not to perform such a neurosurgical procedure. In ambiguous situations, the proposed study can help in decision-making for spasticity treatment.

PMID: 33725695

9. Outcomes of Patellar Tendon Imbrication With Distal Femoral Extension Osteotomy for Treatment of Crouch Gait
Lauren C Hyer, Ashley M Carpenter, Prabhav Saraswat, Jon R Davids, David E Westberry

J Pediatr Orthop. 2021 Mar 17. doi: 10.1097/BPO.0000000000001793. Online ahead of print.

Background: Crouch gait is a frequent gait abnormality observed in children with cerebral palsy. Distal femoral extension osteotomy (DFEO) with the tightening of the extensor mechanism is a common treatment strategy to address the pathologic knee flexion contracture and patella alta. The goal of this study was to review the results of a patellar tendon imbrication (PTI) strategy to address quadriceps insufficiency in the setting of children undergoing DFEO. Methods: After institutional review board approval, all patients with crouch gait treated at a single institution with DFEO and PTI were identified. Clinical, radiographic, and instrumented gait analysis data were analyzed preoperatively and at 1 year following surgery. Results: Twenty-eight patients (54 extremities) with a diagnosis of cerebral palsy and crouch gait were included. Significant improvements were appreciated in the degree of knee flexion contracture, quadriceps strength, knee extensor lag, and popliteal angle ($P<0.01$). Knee flexion at initial contact and during mid-stance improved significantly ($P<0.0001$), and knee moments in late stance were significantly reduced ($P<0.01$). The anterior pelvic tilt, however, significantly increased postoperatively ($P<0.0001$). Radiographic improvements were seen in the knee flexion angle and patellar station as assessed by the Koshino Sugimoto Index ($P<0.0001$). Four patients (14.2%) developed a recurrence of knee flexion contracture requiring further intervention. Conclusions: PTI is a simplified and safe technique to address quadriceps insufficiency when performing DFEO. The short-term results of patients who underwent DFEO with PTI demonstrated improvements in clinical, radiographic, and gait analysis variables of the knee. Investigating long-term outcomes, comparing techniques, and assessing quality of life measures are important next steps in research. Level of evidence: Level IV-case series.

PMID: 33734198

10. Interrater reliability for unilateral and bilateral tests to measure the popliteal angle in children and youth with cerebral palsy
Erika Cloodt, Joanna Krasny, Marek Jozwiak, Elisabet Rodby-Bousquet

BMC Musculoskelet Disord. 2021 Mar 13;22(1):275. doi: 10.1186/s12891-021-04135-6.

Background: Short hamstring muscles can cause several problems for children with cerebral palsy. The results of the clinical measurement of hamstring length are often used in decision-making about treatment of children with cerebral palsy. There are different ways of performing this measurement. The aim of this study was to evaluate the interrater reliability of the unilateral and bilateral measurement of the popliteal angle in children and youth with cerebral palsy. Methods: Two methods for estimating hamstring length using unilateral and bilateral measurements of the popliteal angle were applied in children with cerebral palsy. Both tests were applied bilaterally by two independent examiners on the same day for each child. The intraclass correlation coefficient (ICC) was calculated to evaluate the interrater reliability of both measurements. Seventy young people with cerebral palsy (32 females, 38 males, mean age 10 years 8 months, range 5-22 years) at Gross Motor Function Classification System levels I (n = 17), II (n = 31), III (n = 12) and IV (n = 10) were included. Results: The interrater reliability was good for both measurements. The ICC values were 0.80 on the right and 0.86 on the left for the unilateral popliteal angle, and 0.82 on the right and 0.83 on the left for the bilateral popliteal angle. Conclusions: Both unilateral and bilateral measurement of the popliteal angle is a reliable method for estimating hamstring length in children and youth with cerebral palsy.

PMID: 33714264

11. Calcaneal Sliding Osteotomy Versus Calcaneal Lengthening Osteotomy for Valgus Foot Deformity Correction in Children With Cerebral Palsy
Susan A Rethlefsen, Alison M Hanson, Tishya A L Wren, Robert M Kay, Children's Orthopaedic Center, Children's Hospital Los Angeles

J Pediatr Orthop. 2021 Mar 17. doi: 10.1097/BPO.0000000000001790. Online ahead of print.

Background: Medial calcaneal sliding (CS) osteotomy and lateral column lengthening (LCL) are often performed to relieve pain and improve transverse plane alignment and gait stability for children with cerebral palsy (CP) and valgus foot deformities. The purpose of this study was to examine the effectiveness of these procedures in this population. Methods: Retrospective medical record review (including 3D gait analysis data) of patients with CP who underwent LCL (26 subjects, 46 limbs) or CS (46 subjects, 73 limbs). Data extraction included complications (modified Clavien-Dindo system), change in standing foot position (modified Yoo system), and change in gait kinematics and kinetics preoperatively to postoperatively. Groups were compared using paired t tests, Fisher exact test, and survivorship analysis using Cox proportional hazard models. Results: Subjects were 57% male, average age at surgery 11.1 (SD 2.5) years. Average length of follow-up was 3.2 (SD 2.8) years, and was longer in the LCL group (P=0.0004). Complications were minor with similar rates between groups (P=0.14). Prolonged pain and plantar hypersensitivity occurred only in the CS group. Successful maintenance of deformity correction was achieved in 52/73 limbs (71%) in the CS group and 16/44 limbs (36%) in the LCL group (P<0.001). Recurrent pes valgus and need for repeat foot surgery were more common after LCL (P=0.003 and 0.001, respectively). Recurrent pes valgus never occurred when talonavicular fusion was done concomitantly with CS. After accounting for the between group difference in length of follow-up, there was no difference in the rates of recurrent valgus or repeat foot surgery between LCL and CS. None of the variables predicted development of pes varus (P>0.20). Ankle kinematics and kinetics during gait were unchanged in both groups. Conclusions: CS and LCL have similar effectiveness in providing long-lasting correction of valgus foot deformities. Concomitant talonavicular fusion is key to success of CS for lower functioning patients with severe deformities, and obligate brace wearers. Level of evidence: Level III, retrospective comparative study.

PMID: 33734201

12. Calcaneal lengthening osteotomy in spastic planovalgus feet
Amit Narang, Alok Sud, Dushyant Chouhan

J Clin Orthop Trauma. 2020 Aug 29;13:30-39. doi: 10.1016/j.jcot.2020.08.024. eCollection 2021 Feb.

Purpose of study: Planovalgus deformity in cerebral palsy is disabling for the child in terms of increased energy expenditure during the gait cycle. The lever arm function of the foot is lost due to midfoot break and the achilles tendon is at a disadvantage being unable to lift the body weight during push-off. We evaluated the results of calcaneal lengthening osteotomy in such patients with clinical, radiological and gait parameters. Methods: 17 spastic feet in a sample of 10 children were included in our study. The children were classified according to the GMFCS classification system and clinical parameters such as heel valgus and heel rise tests, radiological angles such as Talo-calcaneal angle and Talo-navicular coverage angle on AP view and Calcaneal pitch angle, calcaneus-5th metatarsal angle and talus-1st metatarsal angle on lateral view were measured. Video gait analysis was performed to observe knee progression angle in mid stance and peak knee flexion angle in mid and terminal stance. Results: Improvement was noted clinically in the heel valgus angle (preop-12.06°, postop-5.12°) and radiological parameters showed an improved coverage of the talus by navicular with simultaneous lifting of the medial longitudinal arch. Gait analysis showed decreased knee flexion trend in mid and terminal stance phase with better restoration of the knee axis. Conclusion: Calcaneal lengthening osteotomy with peroneus brevis lengthening corrects almost all aspects of planovalgus deformity with an improved gait pattern without disturbing joint range of motion. It is a safe procedure for GMFCS grade 1 and 2 patients without much complications.

PMID: 33717872

13. Physical Activity Measurement in Children Who Use Mobility Assistive Devices: Accelerometry and Global Positioning System

Cheryl I Kerfeld, Philip M Hurvitz, Kristie F Bjornson

Pediatr Phys Ther. 2021 Mar 9. doi: 10.1097/PEP.0000000000000786. Online ahead of print.

Purpose: To explore the usefulness of combining accelerometry, global positioning systems, and geographic information systems, to describe the time spent in different locations and physical activity (PA) duration/count levels by location for 4 children with cerebral palsy (CP) who use assistive devices (AD). Methods: A descriptive multiple-case study. Results: Combining the 3 instruments was useful in describing and differentiating duration by location, and amount and location of PA across differing functional levels and AD. For example, the child classified with a Gross Motor Function Classification System (GMFCS) level II exhibited large amounts of PA in community settings. In contrast, the child classified with a GMFCS level V had small amounts of PA and spent most measured time at home. Conclusions: Combined accelerometry, global positioning system, and geographic information system have potential to capture time spent and amount/intensity of PA relative to locations within daily environments for children with CP who use AD.

PMID: 33724239

14. Exploration and Validation of the Behavioural Pain Measures and Physiological Pain Measures Factor Structure Extracted from the Pain Assessment Tool Item Scores for Infants Admitted to Neonatal Intensive Care

Emre Ilhan, Verity Pacey, Laura Brown, Kaye Spence, Claire Galea, Roger Adams, Julia M Hush

Clin J Pain. 2021 Mar 17. doi: 10.1097/AJP.0000000000000931. Online ahead of print.

Objective: To explore then validate the factor structure of the Pain Assessment Tool (PAT). Methods: A retrospective medical record review was performed of all infants who were admitted to a neonatal intensive care unit (NICU) between 2008-2018 and had one PAT assessment (n=2111). Scores on items of the PAT were collected. Infants were randomised to either the Principal Components Analysis (n=1100) to explore the factor structure or Confirmatory Factor Analysis (n=1011). Results: Infants in the two samples were demographically comparable. A two-factor model, consisting of factors Behavioural and Physiological Pain Measures, was extracted, explaining 39.8% of the total variance. There was a low inter-factor correlation (r=0.12), and both Behavioural (r=0.59) and Physiological Pain (r=0.37) Measures factor scores were correlated with nurses' perception of pain scores. When the frequencies in the Gestational age at birth categories were compared between upper and lower quartile score infants, there was more with pain at preterm than at term ($\chi 2(3)=44.9$, $P<0.001$) for the Physiological Pain Measures factor, whereas Behavioural Pain Measures frequency was higher at term than at preterm ($\chi 2(3)=8.1$, $P<0.043$). A similar

pattern was observed for Postmenstrual age at assessment categories: Behavioural Pain Measures ($\chi 2(3)=41.8$, $P<0.001$), Physiological Pain Measures ($\chi 2(3)=46.1$, $P<0.001$). The two-factor correlated model performed better at explaining the observed variances: ($\chi 2(13)=41.6$, $P<0.001$) compared to rival models. Discussion: The PAT assesses both Behavioural Pain and Physiological Pain Measures, and these dimensions need to be considered separately when assessing pain in infants in the NICU. Behavioural item scores may be insufficient for detecting pain in premature infants if used alone.

PMID: 33734145

15. A Systematic Review of Assessments and Interventions for Chronic Pain in Young Children With or at High Risk for Cerebral Palsy
Lisa Letzkus, Darcy Fehlings, Lauren Ayala, Rachel Byrne, Alison Gehred, Nathalie L Maitre, Garey Noritz, Nathan S Rosenberg, Kelly Tanner, Jilda Vargus-Adams, Sarah Winter, Dennis J Lewandowski, Iona Novak

J Child Neurol. 2021 Mar 9;883073821996916. doi: 10.1177/0883073821996916. Online ahead of print.

Background: Pain is common in children with cerebral palsy. The purpose of this systematic review was to evaluate the evidence regarding assessments and interventions for chronic pain in children aged ≤2 years with or at high risk for cerebral palsy. Methods: A comprehensive literature search was performed. Included articles were screened using PRISMA guidelines and quality of evidence was reviewed using best-evidence tools by independent reviewers. Using social media channels, an online survey was conducted to elicit parent preferences. Results: Six articles met criteria. Parent perception was an assessment option. Three pharmacologic interventions (gabapentin, medical cannabis, botulinum toxin type A) and 1 nonpharmacologic intervention were identified. Parent survey report parent-comfort and other nonpharmacologic interventions ranked as most preferable. Conclusion: A conditional GRADE recommendation was in favor of parent report for pain assessment. Clinical trials are sorely needed because of the lack of evidence for safety and efficacy of pharmacologic interventions.

PMID: 33719661

16. The Impact of Oral-Gut Inflammation in Cerebral Palsy
Ana Cristina Fernandes Maria Ferreira, Ryan J Eveloff, Marcelo Freire, Maria Teresa Botti Rodrigues Santos

Front Immunol. 2021 Feb 25;12:619262. doi: 10.3389/fimmu.2021.619262. eCollection 2021.

Background: Oral-gut inflammation has an impact on overall health, placing subjects at risk to acquire chronic conditions and infections. Due to neuromotor disturbances, and medication intake, cerebral palsy (CP) subjects present intestinal constipation, impacting their quality of life (QOL). We aimed to investigate how oral inflammatory levels predicted gut phenotypes and response to therapy. Methods: A total of 93 subjects aging from 5 to 17 years were included in the study, and assigned into one of the 4 groups: CP with constipation (G1, n = 30), CP without constipation (G2, n = 33), and controls without CP with constipation (G3, n = 07) and without CP and without constipation (G4, n = 23). In addition to characterizing subjects' clinical demographics, medication intake, disease severity levels, salivary cytokine levels [TNF-α, interleukin (IL)-1β, IL-6, IL-8, IL-10], and Caregiver Priorities and Child Health Index of Life with Disabilities (CPCHILD). Statistical significance was evaluated by Shapiro-Wilks, Student's T-Test, ANOVA, and ANCOVA analysis. Results: Salivary proinflammatory cytokines were highly correlated with the severe form of gut constipation in G1 ($P < 0.001$), and out of all cytokines IL-1β levels demonstrated highest correlation with all gut constipation ($P < 0.05$). A significant relationship was found between the type of medication, in which subjects taking Gamma-Aminobutyric Acid (GABA) and GABA+ (GABA in association with other medication) were more likely to be constipated than the other groups ($P < 0.01$). Cleary salivary inflammatory levels and gut constipation were correlated, and impacted QOL of CP subjects. G1 presented a lower QOL mean score of CPCHILD (49.0 ± 13.1) compared to G2 (71.5 ± 16.7), when compared to G3 (88.9 ± 7.5), and G4 (95.5 ± 5.0) ($P < 0.01$). We accounted for gingival bleeding as a cofounder of oral inflammation, and here were no differences among groups regarding gender ($P = 0.332$) and age ($P = 0.292$). Conclusions: Collectively, the results suggest that saliva inflammatory levels were linked to gut constipation, and that the clinical impact of medications that controlled gut was reliably monitored via oral cytokine levels, providing reliable and non-invasive information in precision diagnostics.

PMID: 33717115

17. WISC-V motor-free cognitive profile and predictive factors in adolescents with cerebral palsy
Monika Coceski, Darren R Hocking, Hisham M Abu-Rayya, Sarah Sherwell, Susan M Reid, Dinah S Reddihough, Jacquie Wrennall, Robyn Stargatt

Res Dev Disabil. 2021 Mar 16;113:103934. doi: 10.1016/j.ridd.2021.103934. Online ahead of print.

Background: The most commonly used intelligence tests - the Wechsler Scales - do not provide standardised procedures for assessing children with motor impairment, and as a result, may underestimate the intelligence quotient (IQ) of young people with CP. Aims: To characterise a motor-free cognitive profile of adolescents with CP using the Wechsler Intelligence Scale for Children - Fifth edition (WISC-V) and explore the influence of clinical factors on cognitive abilities. Methods and procedure: The WISC-V was used to assess cognitive abilities in 70 adolescents (M = 14 years 6 months, SD = 10 months). Sixty-six adolescents (Gross Motor Function Classification System (GMFCS) Level I, n = 26 ; II, n = 23; III, n = 15; IV, n = 1; V, n = 1) obtained either a Motor-free IQ or index score using the motor-free method. Outcomes and results: MFIQ and index scores fell below the normative data and rates of borderline and impaired cognitive abilities were significantly higher in the CP group. Scores showed an uneven cognitive profile with a relative strength in verbal abilities. Severity of motor impairment and small for gestational age (SGA) were associated with lower IQ scores. A history of seizures was related to lower verbal abilities. Conclusions and implications: Cognitive abilities of adolescents with CP are significantly below expectation compared to normative data. Severity of motor impairment, SGA, and seizures need to be recognised by health professionals as risk factors for cognitive impairment. A substantial proportion of adolescents showed borderline cognitive abilities, constituting a group with CP which are relatively neglected in the literature.

PMID: 33740670

18. Speech Treatment Effects on Narrative Intelligibility in French-Speaking Children with Dysarthria
Gemma Moya-Galé, Bryan Keller, Sergio Escorial, Erika S Levy

J Speech Lang Hear Res. 2021 Mar 9;1-15. doi: 10.1044/2020_JSLHR-20-00258. Online ahead of print.

Purpose This study examined the effects of Speech Intelligibility Treatment (SIT) on intelligibility and naturalness of narrative speech produced by francophone children with dysarthria due to cerebral palsy. Method Ten francophone children with dysarthria were randomized to one of two treatments, SIT or Hand-Arm Bimanual Intensive Therapy Including Lower Extremities, a physical therapy (PT) treatment. Both treatments were conducted in a camp setting and were comparable in dosage. The children were recorded pre- and posttreatment producing a story narrative. Intelligibility was measured by means of 60 blinded listeners' orthographic transcription accuracy (percentage of words transcribed correctly). The listeners also rated the children's naturalness on a visual analogue scale. Results A significant pre- to posttreatment increase in intelligibility was found for the SIT group, but not for the PT group, with great individual variability observed among the children. No significant changes were found for naturalness ratings or sound pressure level in the SIT group or the PT group posttreatment. Articulation rate increased in both treatment groups, although not differentially across treatments. Conclusions Findings from this first treatment study on intelligibility in francophone children with dysarthria suggest that SIT shows promise for increasing narrative intelligibility in this population. Acoustic contributors to the increased intelligibility remain to be explored further. Supplemental Material https://doi.org/10.23641/asha.14161943.

PMID: 33719503

19. Population-based surveillance of children with cerebral palsy enables early diagnosis and intervention
Mahmudul Hassan Al Imam, Israt Jahan, Manik Chandra Das, Mohammad Muhit, Hayley Smithers-Sheedy, Sarah McIntyre, Nadia Badawi, Gulam Khandaker

Dev Med Child Neurol. 2021 Mar 14. doi: 10.1111/dmcn.14861. Online ahead of print.

PMID: 33719074

20. The Singapore Cerebral Palsy Registry: An important new resource for cerebral palsy research
Hayley Smithers-Sheedy

Editorial Ann Acad Med Singap. 2021 Feb;50(2):109-110. doi: 10.47102/annals-acadmedsg.202161.

PMID: 33733252

21. Risk factors for intellectual disability in children with spastic cerebral palsy
David Cummins, Claire Kerr, Karen McConnell, Oliver Perra

Arch Dis Child. 2021 Mar 16;archdischild-2020-320441. doi: 10.1136/archdischild-2020-320441. Online ahead of print.

Background: Cerebral palsy (CP) is a non-progressive disorder of posture and movement caused by prenatal or perinatal lesions of the brain. Children with CP are also at increased risk of other disabilities, for example, intellectual disability. Previous studies suggest the risk of intellectual disability varies in complex ways according to the type of motor impairment and perinatal factors such as gestational age. Objective: To determine the patterns of risk of intellectual disability in children with spastic CP. Design: Cross-sectional, population-based study using the Northern Ireland Cerebral Palsy Register. Participants: Persons born in 1981-2008 with congenital bilateral or unilateral spastic CP (N=1452). Outcome measure: The outcome measure was severe intellectual disability (IQ <50), as reported by clinicians known to the child. Data pertaining to CP subtype, sex, gestational age, birth weight and functional level were included in analyses. Results: Severe intellectual disability was significantly more prevalent in children with bilateral spastic CP (BSCP) compared with children with unilateral spastic CP (χ^2 (2)=162.60, p<0.001). Compared with very preterm infants with BSCP, the risk of intellectual disability increased in moderately preterm (OR=3.97, 95% CI 1.04 to 15.23) and at-term (OR=2.51, 95% CI 1.16 to 5.44) children with BSCP. Conclusions: Children with BSCP are at increased risk of intellectual disability, with those born at term at the highest risk. The findings highlight the importance of early screening, particularly for children with BSCP born at term.

PMID: 33727240

22. Causes, functional outcomes and healthcare utilisation of people with cerebral palsy in Singapore
Zhi Min Ng, Jeremy B Lin, Poh Choo Khoo, Victor Samuel Rajadurai, Derrick W S Chan, Hian Tat Ong, Janice Wong, Chew Thye Choong, Kim Whee Lim, Kevin B L Lim, Tong Hong Yeo

Ann Acad Med Singap. 2021 Feb;50(2):111-118. doi: 10.47102/annals-acadmedsg.2020489.

Introduction: A voluntary cerebral palsy (CP) registry was established in 2017 to describe the clinical characteristics and functional outcomes of CP in Singapore. Methods: People with CP born after 1994 were recruited through KK Women's and Children's Hospital, National University Hospital and Cerebral Palsy Alliance Singapore. Patient-reported basic demographics, service utilisation and quality of life measures were collected with standardised questionnaires. Clinical information was obtained through hospital medical records. Results: Between 1 September 2017 and 31 March 2020, 151 participants were recruited. A majority (n=135, 89%) acquired CP in the pre/perinatal period, where prematurity (n=102, 76%) and the need for emergency caesarean section (n=68, 50%) were leading risk factors. Sixteen (11%) of the total participants had post-neonatally acquired CP. For predominant CP motor types, 109 (72%) had a spastic motor type; 32% with spastic mono/hemiplegia, 41% diplegia, 6% triplegia and 21% quadriplegia. The remaining (42, 27.8%) had dyskinetic CP. Sixty-eight (45.0%) participants suffered significant functional impairment (Gross Motor Functional Classification System levels IV-V). Most participants (n=102, 67.5%) required frequent medical follow-up (≥4 times a year). Conclusion: Optimisation of pre- and perinatal care to prevent and manage prematurity could reduce the burden of CP and their overall healthcare utilisation.

PMID: 33733253

23. [Living with cerebral palsy] [Article in French]
Christèle Kandalaft, Bernard Dan

Rev Prat. 2020 Oct;70(8):873-874.

PMID: 33739692

24. Timecourse of Morbidity Onset Among Adults Living With Cerebral Palsy
Daniel G Whitney, Mary Schmidt, Heidi Haapala, Dayna Ryan, Edward A Hurvitz, Mark D Peterson

Am J Prev Med. 2021 Mar 13;S0749-3797(21)00121-5. doi: 10.1016/j.amepre.2021.01.020. Online ahead of print.

Introduction: Despite the greater risk of an array of morbidities, little is known about when morbidities occur for adults with cerebral palsy. The objective of this study is to determine the timecourse of morbidity risk/development for adults with cerebral palsy and the effect by patient-level factors. Methods: Cross-sectional data from 2016 were used from a random 20% sample from the fee-for-service Medicare database. Diagnosis codes identified adults aged ≥18 years with cerebral palsy and 16 clinically relevant morbidities. Qualitative and quantitative approaches identified the age where each morbidity became exceedingly prevalent. The effect of the timecourse by sex, race, and co-occurring intellectual disabilities and epilepsy was examined. Data were sequestered and analyzed in 2020. Results: Among 16,818 adults with cerebral palsy, the prevalence of most morbidities was already high among those aged 18-30 years, and all morbidities increased with age except liver disease and anxiety. Hypertension and diabetes exhibited a positive linear trend with age. Of the morbidities that did not exhibit a linear trend, the qualitative and quantitative approaches were consistent considering that the cardiorespiratory diseases, osteoarthritis, renal disease, and dementia became exceedingly more prevalent at age >50 years, whereas the threshold was >60 years for depression, cancer, and metastatic cancer. There were interactions with sex, race, and co-occurring intellectual disabilities and epilepsy for some of the morbidities. Conclusions: Morbidity prevalence is already elevated early in adulthood among individuals living with cerebral palsy, with an abrupt increase by age 50 years. Preventive efforts should be adopted early in the lifespan and not later than age 50 years for adults with cerebral palsy.

PMID: 33726991

25. Impact of growing up with somatic long-term health challenges on school completion, NEET status and disability pension: a population-based longitudinal study
Anurajee Rasalingam, Idunn Brekke, Espen Dahl, Sølvi Helseth

BMC Public Health. 2021 Mar 16;21(1):514. doi: 10.1186/s12889-021-10538-w.

Background: Young adulthood is an important transitional life phase that can determine a person's educational and employment trajectories. The aim of this study was to examine the impact of somatic long-term health challenges in adolescence on upper secondary school completion, not in education, employment or training (NEET status) and receiving disability pension in early adulthood. Additional disparities in educational and employment achievements were also investigated in relation to socioeconomic background. Methods: The sample consisted of all young adults born in the period 1990 to 1996, (N = 421,110). Data were obtained from the Norwegian Patient Registry which is linked to the Central Population Register, education and income registries and the Historical Event Database in Statistics Norway. These data sources provide longitudinal population data. Statistical analyses were performed using multiple logistic regression and computed average marginal effects after the multiple logistic regression. Results: The results showed that, compared to young adults without long-term health challenges, young adults with the diagnoses inflammatory bowel disease, epilepsy, diabetes, sensory impairment, spinal muscular atrophy (SMA), spina bifida (SB) and cerebral palsy (CP) had lower odds of completing upper secondary education. Moreover, young adults with long-term health challenges had higher odds of NEET status by age 21 compared to those without a long-term health challenge. As for the odds of NEET status by age 21, the results showed that young adults with epilepsy, SMA, SB and CP in particular had the highest odds of receiving disability pension compared to young adults without long-term health challenges. Conclusions: This longitudinal study revealed that on average young adults with long-term health challenges, compared to those without, struggle to participate in education and employment. The findings highlight the need for preventive measures especially in relation to young adults with neurological conditions such as epilepsy, SMA, SB, and CP.

PMID: 33726730

26. Parent perspective on powered wheelchair standing devices
Jennifer Lyman

Dev Med Child Neurol. 2021 Mar 14. doi: 10.1111/dmcn.14862. Online ahead of print.

PMID: 33719047

27. Early Identification of Cerebral Palsy Using Neonatal MRI and General Movements Assessment in a Cohort of High-Risk Term Neonates
Hannah C Glass, Yi Li, Marisa Gardner, A James Barkovich, Iona Novak, Charles E McCulloch, Elizabeth E Rogers

Pediatr Neurol. 2021 Feb 15;118:20-25. doi: 10.1016/j.pediatrneurol.2021.02.003. Online ahead of print.

Background: Cerebral palsy (CP) is the most common motor disability of childhood. Its early identification is an important priority for parents and is critical for access to early intervention resources, which may optimize function. Methods: A prospective cohort of term neonates at high risk for CP was assessed by neonatal magnetic resonance imaging (MRI) to determine myelination of the posterior limb of the internal capsule, General Movements Assessment to assess typical fidgety movements at age three months, and followed to at least age two years to determine diagnosis of CP based on neurological examination. Results: Seven of 58 children developed CP (12%), two with moderate/severe CP. Sensitivity and specificity for abnormal myelination of the posterior limb of the internal capsule were (PLIC) was 29% and 94%, and for absent fidgety movements, 29% and 98%, respectively. Negative predictive value of both absent myelination of the PLIC and absent fidgety movements was 90% (79% to 96%) for any CP and 98% (90% to 100%) for moderate/severe CP cerebral palsy. None of the children with both normal PLIC and normal fidgety movements had moderate/severe CP. Conclusion: Normal neonatal MRI and General Movements Assessment at age three months are reassuring that a high-risk term-born child is at low risk for moderate/severe CP. These results are important for counseling parents and individualizing therapy resources in the community.

PMID: 33714922

28. COL4A1 mutation in an Indian child presenting as 'Cerebral Palsy' mimic
Siddharth M Shah, Drushi D Patel

Case Reports Indian J Radiol Imaging. Oct-Dec 2020;30(4):500-503. doi: 10.4103/ijri.IJRI_274_20. Epub 2021 Jan 13.

The COL4A1 gene (COL4A1) plays an important role in vascular basement membrane function and pathogenic mutations have been reported in mice and humans. The gene is expressed mainly in the human brain, eyes and kidneys. Pathogenic mutations result in a vast array of manifestations that can present throughout life including the foetal period. We present a case of an 11-year-old girl with right hemiparesis, congenital cataracts, epilepsy and magnetic resonance imaging (MRI) brain findings with a pathogenic COL4A1 mutation. Many of her clinical features are similar to those of a non-genetic cause of cerebral palsy highlighting the difficulties and delays in making this genetic diagnosis.

PMID: 33737780

29. One healthy live birth after preimplantation genetic testing of a cryptic balanced translocation (9;13) in a family with cerebral palsy and glaucoma: a case report
Xiliang Wang, Changsheng Wu, Dongmei Hao, Jinyan Zhang, Chang Tan, De-Hua Cheng, Jia Fei, Yuexin Yu

BMC Med Genomics. 2021 Mar 17;14(1):82. doi: 10.1186/s12920-021-00938-7.

Background: Cryptic balanced translocations often evade detection by conventional cytogenetics. The preimplantation genetic testing (PGT) technique can be used to help carriers of balanced translocations give birth to healthy offspring; however, for

carriers of cryptic balanced translocations, there is only one report about trying assisted reproduction using the PGT technique but with no pregnancy. Case presentation: A couple had 3 births out of 4 pregnancies, and all died very young, with two of them having both cerebral palsy and glaucoma. The husband with oligoasthenospermia was found to be a cryptic balanced translocation carrier for t (9,13) (p24.3, q31.3) with G-banding, FISH (fluorescence in-situ hybridization), and MicroSeq techniques; live birth of a healthy baby girl was achieved with PGT/NGS (next-generation sequencing) for the couple. Conclusion: Here, we report for the first time a successful live birth of a healthy baby through the PGT technique for a family in which the husband is a carrier of the cryptic balanced translocation t (9,13) (p24.3, q31.3), presumably causative for cerebral palsy and glaucoma. Our study showed that the PGT/NGS technique can effectively help families with a cryptic balanced translocation have healthy offspring.

PMID: 33731094

30. Muscle Characteristics in Pediatric Hereditary Spastic Paraplegia vs. Bilateral Spastic Cerebral Palsy: An Exploratory Study

Nathalie De Beukelaer, Lynn Bar-On, Britta Hanssen, Nicky Peeters, Sandra Prinsen, Els Ortibus 5, Kaat Desloovere, Anja Van Campenhout

Front Neurol. 2021 Feb 26;12:635032. doi: 10.3389/fneur.2021.635032. eCollection 2021.

Hereditary spastic paraplegia (HSP) is a neurological, genetic disorder that predominantly presents with lower limb spasticity and muscle weakness. Pediatric pure HSP types with infancy or childhood symptom onset resemble in clinical presentation to children with bilateral spastic cerebral palsy (SCP). Hence, treatment approaches in these patient groups are analogous. Altered muscle characteristics, including reduced medial gastrocnemius (MG) muscle growth and hyperreflexia have been quantified in children with SCP, using 3D-freehand ultrasound (3DfUS) and instrumented assessments of hyperreflexia, respectively. However, these muscle data have not yet been studied in children with HSP. Therefore, we aimed to explore these MG muscle characteristics in HSP and to test the hypothesis that these data differ from those of children with SCP and typically developing (TD) children. A total of 41 children were retrospectively enrolled including (1) nine children with HSP (ages of 9-17 years with gross motor function levels I and II), (2) 17 age-and severity-matched SCP children, and (3) 15 age-matched typically developing children (TD). Clinically, children with HSP showed significantly increased presence and severity of ankle clonus compared with SCP ($p = 0.009$). Compared with TD, both HSP and SCP had significantly smaller MG muscle volume normalized to body mass ($p \leq 0.001$). Hyperreflexia did not significantly differ between the HSP and SCP group. In addition to the observed pathological muscle activity for both the low-velocity and the change in high-velocity and low-velocity stretches in the two groups, children with HSP tended to present higher muscle activity in response to increased stretch velocity compared with those with SCP. This exploratory study is the first to reveal MG muscle volume deficits in children with HSP. Moreover, high-velocity-dependent hyperreflexia and ankle clonus is observed in children with HSP. Instrumented impairment assessments suggested similar altered MG muscle characteristics in pure HSP type with pediatric onset compared to bilateral SCP. This finding needs to be confirmed in larger sample sizes. Hence, the study results might indicate analogous treatment approaches in these two patient groups.

PMID: 33716937

31. Microsomic and macrosomic body structure in children and adolescents affected by syndromes or diseases associated with neurodysfunction

Lidia Perenc, Agnieszka Guzik, Justyna Podgórska-Bednarz, Mariusz Drużbicki

Sci Rep. 2021 Mar 18;11(1):6349. doi: 10.1038/s41598-021-85587-7.

In Poland the issue of microsomic body structure (micro-SBS) and macrosomic body structure (macro-SBS) has so far been overlooked. Up until now only a small amount of data have been published, most often as an overview of the problem. The current study was designed to investigate the co-occurrence of microsomic/macrosomic body structure (micro/macro-SBS) and congenital nervous system disorders or neurological syndromes with symptoms visible from infancy, based on essential data acquired during admission procedures at a neurological rehabilitation ward for children and adolescents. The study applied a retrospective analysis of data collected during hospitalization of 327 children and adolescents, aged 4-18 years who had been affected since infancy by congenital disorders of the nervous system and/or neurological syndromes associated with a minimum of one neurodysfunction. To identify subjects with microsomic or macrosomic body structure in the group of children and adolescents, the adopted criteria took into account z-score values for body height (z-score Ht), body weight (z-

score Wt), head circumference (z-score HC), BMI (z-score BMI) and head circumference index (z-score HCI). The rates of micro/macro-SBS in the study group amounted to 7.3% and 0.6%, respectively. The findings show a more frequent co-occurrence of, as well as statistically significant correlations between, micro/macro-SBS and type of spasticity (cerebral palsy) ($p = 0.024$) as well as hydrocephalus not treated surgically ($p < 0.001$). Macro-SBS was found to more frequently co-occur with hemiplegia and hydrocephalus not treated surgically.

PMID: 33737592

32. Stakeholder Perspectives on Engaging with Cerebral Palsy Research Studies Following Onset of COVID-19 in the United States
Divya Joshi, Nayo Hill, Alexandra Hruby, Shreya Viswanathan, Carson Ingo, Heidi Roth, Theresa Sukal-Moulton

Arch Phys Med Rehabil. 2021 Mar 10;S0003-9993(21)00223-9. doi: 10.1016/j.apmr.2021.02.017. Online ahead of print.

Objective: To investigate the effect of the COVID-19 pandemic on perspectives towards participation in cerebral palsy (CP) research. Design: An online survey with questions relating to the comfort levels of research participation was filled out by people who had CP or had a child with CP. Setting: The online survey was administered through Research Electronic Data Capture (REDCap) platform. Participants: 233 individuals with CP (42.5%) or with a child with CP (57.1%) consented and at least partially completed the online survey (n=210 complete; n=23 partially complete). All participants resided in the United States. Interventions: Not applicable. Main outcome measures: Readiness to participate was analyzed in the context of the timepoint for research participation (TRP) during COVID-19 and whether or not the study offered direct benefits to participants. Results: Participants were consistently willing to participate sooner in studies that offered direct benefit than in those that did not. Adults responding for themselves had sooner timepoints for studies without direct benefit compared to parents answering for a child (p=0.030). GMFCS level, but not age or CP type, impacted the timepoint for studies without direct benefit (p=0.017). Personal values influenced selected timepoint for studies without direct benefit (p=0.007), while environmental factors impacted the timepoint for studies with direct benefit (p=0.002). Local COVID-19 incidence rates were not associated with timepoints for either research type, however respondents expected precautions to be taken if they chose to participate.

PMID: 33713698

Prevention and Cure

33. Sulforaphane (SFA) protects neuronal cells from oxygen & glucose deprivation (OGD)
Zeenat Ladak, Elizabeth Garcia, Jenny Yoon, Takaaki Landry, Edward A Armstrong, Jerome Y Yager, Sujata Persad

PLoS One. 2021 Mar 18;16(3):e0248777. doi: 10.1371/journal.pone.0248777. eCollection 2021.

Background: Perinatal brain injury results in neurodevelopmental disabilities (neuroDDs) that include cerebral palsy, autism, attention deficit disorder, epilepsy, learning disabilities and others. Commonly, injury occurs when placental circulation, that is responsible for transporting nutrients and oxygen to the fetus, is compromised. Placental insufficiency (PI) is a reduced supply of blood and oxygen to the fetus and results in a hypoxic-ischemic (HI) environment. A significant HI state in-utero leads to perinatal compromise, characterized by fetal growth restriction and brain injury. Given that over 80% of perinatal brain injuries that result in neuroDDs occur during gestation, prior to birth, preventive approaches are needed to reduce or eliminate the potential for injury and subsequent neuroDDs. Sulforaphane (SFA) derived from cruciferous vegetables such as broccoli sprouts (BrSps) is a phase-II enzyme inducer that acts via cytoplasmic Nrf2 to enhance the production of anti-oxidants in the brain through the glutathione pathway. We have previously shown a profound in vivo neuro-protective effect of BrSps/SFA as a dietary supplement in pregnant rat models of both PI and fetal inflammation. Strong evidence also points to a role for SFA as treatment for various cancers. Paradoxically, then SFA has the ability to enhance cell survival, and with conditions of cancer, enhance cell death. Given our findings of the benefit of SFA/Broccoli Sprouts as a dietary supplement during pregnancy, with improvement to the fetus, it is important to determine the beneficial and toxic dosing range of SFA. We therefore explored, in vitro, the dosing range of SFA for neuronal and glial protection and toxicity in normal and oxygen/glucose deprived (OGD) cell cultures. Methods: OGD simulates, in vitro, the condition experienced by the fetal brain due to PI. We developed a cell

culture model of primary cortical neuronal, astrocyte and combined brain cell co-cultures from newborn rodent brains. The cultures were exposed to an OGD environment for various durations of time to determine the LD50 (duration of OGD required for 50% cell death). Using the LD50 as the time point, we evaluated the efficacy of varying doses of SFA for neuroprotective and neurotoxicity effects. Control cultures were exposed to normal media without OGD, and cytotoxicity of varying doses of SFA was also evaluated. Immunofluorescence (IF) and Western blot analysis of cell specific markers were used for culture characterization, and quantification of LD50. Efficacy and toxicity effect of SFA was assessed by IF/high content microscopy and by AlamarBlue viability assay, respectively. Results: We determined the LD50 to be 2 hours for neurons, 8 hours for astrocytes, and 10 hours for co-cultures. The protective effect of SFA was noticeable at 2.5 μM and 5 μM for neurons, although it was not significant. There was a significant protective effect of SFA at 2.5 μM ($p<0.05$) for astrocytes and co-cultures. Significant toxicity ranges were also confirmed in OGD cultures as ≥ 100 μM ($p<0.05$) for astrocytes, ≥ 50 μM ($p<0.01$) for co -cultures, but not toxic in neurons; and toxic in control cultures as ≥ 100 μM ($p<0.01$) for neurons, and ≥ 50 μM ($p<0.01$) for astrocytes and co-cultures. One Way ANOVA and Dunnett's Multiple Comparison Test were used for statistical analysis. Conclusions: Our results indicate that cell death shows a trend to reduction in neuronal and astrocyte cultures, and is significantly reduced in co-cultures treated with low doses of SFA exposed to OGD. Doses of SFA that were 10 times higher were toxic, not only under conditions of OGD, but in normal control cultures as well. The findings suggest that: 1. SFA shows promise as a preventative agent for fetal ischemic brain injury, and 2. Because the fetus is a rapidly growing organism with profound cell multiplication, dosing parameters must be established to insure safety within efficacious ranges. This study will influence the development of innovative therapies for the prevention of childhood neuroDD.

PMID: 33735260