NEWS
Cerebral Palsy Research

Monday DD Month YYYY

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Interventions and Management

1. Influence of Spinal Manipulation on Muscle Spasticity and Manual Dexterity in Participants With Cerebral Palsy: Randomized Controlled Trial.
Kachmar O, Kushnir A, Matiushenko O, Hasiuk M.

J Chiropr Med. 2018 Sep;17(3):141-150. doi: 10.1016/j.jcm.2018.03.004. Epub 2018 Aug 28.

OBJECTIVES: The aim of this study was to investigate the short-term effects of spinal manipulation (SM) on wrist muscle spasticity and manual dexterity in participants with cerebral palsy (CP). METHODS: After baseline examination, 78 participants with spastic CP (7-18 years) without contractures or hyperkinetic syndrome were randomly allocated into 2 groups. The experimental group underwent SM to the cervical, thoracic, and lumbar spine, and the control group received sham SM. A second evaluation was performed 5 minutes postintervention. Wrist muscle spasticity was measured quantitatively with NeuroFlexor (Aggero MedTech AB, Solna, Sweden), a device assessing resistance to passive movements of different velocities. Between-group difference was calculated using the Mann-Whitney U test. Manual dexterity was evaluated by the Box and Block test. RESULTS: In the experimental group, muscle spasticity was reduced by 2.18 newton from median 5.53 with interquartile range 8.66 to median 3.35 newton with interquartile range 7.19; the difference was statistically significant (P = .002). In the control group, reduction in spasticity was negligible. The between-group difference in change of muscle spasticity was statistically significant (P = .034). Improvement of manual dexterity was not statistically significant (P = .28). CONCLUSIONS: These findings suggest that SM may, in the short term, help to reduce spasticity in participants with CP. Long-term effects of SM on muscle spasticity have yet to be studied.

PMID: 30228805

2. Standing frames for children with cerebral palsy: a mixed-methods feasibility study.
Goodwin J, Lecouturier J, Basu A, Colver A, Crombie S, Smith J, Howel D, McColl E, Parr JR, Kolehmainen N, Roberts A, Miller K, Cadwgan J.

Health Technol Assess. 2018 Sep;22(50):1-232. doi: 10.3310/hta22500.

BACKGROUND: Standing frames are recommended as part of postural management for young people with cerebral palsy (CP) Gross Motor Function Classification System (GMFCS) level IV or V. They may have a variety of benefits, including improving bone mineral density, gastrointestinal function and social participation. The NHS needs to know if these benefits are real, given the cost implications of use and the reported negative effects (e.g. pain). The lack of evidence for the clinical effectiveness of standing frames demonstrates the need for evaluative research. OBJECTIVE(S): The aim of the study was to explore the acceptability of a future trial to determine the clinical effectiveness of standing frames. DESIGN: A sequential mixed-methods design was used. The findings of each stage informed the next stage. We conducted surveys, focus groups and in-depth interviews. PARTICIPANTS: Professionals who work with young people who use standing frames and parents who

have a child who uses a standing frame took part in a survey of current standing frame practice (n = 551), a series of focus groups (seven focus groups, 49 participants in total) and a survey of research trial acceptability and feasibility (n = 585). Twelve young people who use a standing frame were interviewed. RESULTS: Standing frames were widely used as part of postural management for young people with CP both in school and at home but more frequently in school, and particularly by young people in primary school. Achieving the prescribed use was not always possible owing to resources, environment and family factors. Participation and activity engagement were important to young people. The majority of participants believed that standing frames research is necessary. Some reported concern that stopping standing frame use for a trial would cause irreversible damage. The maximum amount of time most health professionals and parents would agree to suspend standing frame use would be 12 weeks. LIMITATIONS: Owing to the nature of recruitment, we could not calculate response rates or determine non-response bias. Therefore, participants may not be representative of all standing frame users. CONCLUSIONS: Although parents and professionals who engaged in the qualitative aspect of this research and stakeholders who took part in the design workshops appreciated the lack of clinical evidence, our surveys, qualitative information and PPI demonstrated that most people had strong beliefs regarding the clinical effectiveness of standing frames. However, with key stakeholder engagement and careful planning, a trial would be acceptable. FUTURE WORK: We recommend a carefully planned trial that includes a pilot phase. The trial should evaluate the following question: 'does using a standing frame in school improve patient-reported outcomes of participation (primary outcome), quality of life, subjective well-being, body function and body structure (secondary outcomes) in young children (aged 4-11 years) with CP GMFCS III-V?'. FUNDING: The National Institute for Health Research Health Technology Assessment programme.

PMID: 30234480

3. The lethal twist - a story of unspoken pain: small intestinal volvulus in cerebral palsy.
Krishnamurthy K, El Hussein S, Omarzai Y.

Autops Case Rep. 2018 Sep 14;8(3):e2018037. doi: 10.4322/acr.2018.037. eCollection 2018 Jul-Sep.

Small intestinal volvulus (SBV) is the abnormal twisting of bowel around the axis of its mesentery, leading to obstruction and vascular compromise, resulting in bowel ischemia and necrosis which are life-threatening. Risk factors include malformation, malrotation, and adhesions. Its rare incidence and vague clinical presentation make it a difficult diagnosis, more so in a nonverbal patient who cannot express his pain, which is the first and most prominent symptom. Studies suggest an increased frequency of intestinal obstruction in cerebral palsy patients. There are no reported cases of small intestinal volvulus in association with cerebral palsy. We present a case of a 21-year-old man with severe cerebral palsy and kyphoscoliosis. The patient presented to the emergency room with respiratory distress and abdominal distension. An acute abdomen was noted. Abdominal X-rays revealed gas patterns suggestive of small intestinal obstruction. The patient rapidly deteriorated, and resuscitation attempts were unsuccessful. Autopsy revealed peritoneal cavity filled with extensively dilated and thin-walled loops of small intestine. Twisting of the small intestine, showing 360° rotation around the mesenteric root in a clockwise manner at two separate sites, was noted. On bowel dissection, mucosal folds were absent, and mucosa was green with patchy areas of hemorrhage consistent with ischemic necrosis. There was no evidence of any malformation, malrotation or adhesions. Small intestinal volvulus is a rare entity with a nonspecific clinical presentation that poses a diagnostic challenge. This autopsy highlights the need to maintain a high index of suspicion for small intestinal volvulus in cases of bowel obstruction in cerebral palsy patients to expedite surgery and prevent mortality. The primary caregivers of non-verbal cerebral palsy patients living outside of healthcare facilities need to be trained in recognition of life-threatening medical emergencies such as gastrointestinal obstruction and seek emergent attention at the earliest to prevent treatment delays.

PMID: 30237988

4. Adjuvant treatments associated with botulinum toxin injection for managing spasticity: An overview of the literature.
Picelli A, Santamato A, Chemello E, Cinone N, Cisari C, Gandolfi M, Ranieri M, Smania N, Baricich A.

Ann Phys Rehabil Med. 2018 Sep 13. pii: S1877-0657(18)31445-3. doi: 10.1016/j.rehab.2018.08.004. [Epub ahead of print]

BACKGROUND AND OBJECTIVE: A wide range of adjunct therapies after botulinum toxin administration have been proposed. The aim of the present paper is to provide an overview of major writings dealing with adjuvant (non-pharmacological) treatments associated with botulinum toxin for managing spasticity in order to provide some up-to-date information about the usefulness of the most commonly used procedures. METHODS: The literature in PubMed was searched with the MeSH terms botulinum toxins, muscle spasticity, physical therapy modalities, and rehabilitation. The results were limited to studies focusing on adjuvant treatments associated with botulinum toxin for managing spasticity. We excluded papers on the use of non-drug treatments for spasticity not associated with botulinum toxin serotype A (BoNT-A) injection. Relevant literature known to the authors along with this complementary search represented the basis for this overview of the

literature. RESULTS: Adhesive taping and casting effectively improved the botulinum toxin effect in patients with upper- and lower-limb spasticity. There is level 1 evidence that casting is better than taping for outcomes including spasticity, range of motion and gait. However, consensus about their most appropriate timing, duration, target and material is lacking. In terms of physical modalities combined with botulinum toxin injection, we found level 1 evidence that extracorporeal shock wave therapy is better than electrical stimulation for some post-injection outcomes including spasticity and pain. Furthermore, electrical stimulation of injected muscles might be useful to boost the toxin effect. However, the best stimulation protocol has not been defined. In addition, we found level 2b evidence that whole-body vibration therapy might reduce spasticity with cerebral palsy. CONCLUSION: Future research in this field should focus on investigating the most appropriate post-injection treatment protocol for each goal to achieve.

PMID: 30219307

5. An untethered ankle exoskeleton improves walking economy in a pilot study of individuals with cerebral palsy.
Lerner ZF, Gasparri GM, Bair MO, Lawson JL, Luque J, Harvey TA, Lerner AT.

IEEE Trans Neural Syst Rehabil Eng. 2018 Sep 17. doi: 10.1109/TNSRE.2018.2870756. [Epub ahead of print]

The high energy cost of walking in individuals with cerebral palsy (CP) contributes significantly to reduced mobility and quality of life. The purpose of this study was to develop and clinically evaluate an untethered ankle exoskeleton with the ability to reduce the metabolic cost of walking in children and young adults with gait pathology from CP. We designed a battery-powered device consisting of an actuator-and-control module worn above the waist with a Bowden cable transmission used to provide torque to pulleys aligned with the ankle. Special consideration was made to minimize adding mass to the body, particularly distal portions of the lower-extremity. The exoskeleton provided plantar-flexor assistance during the mid-to-late stance phase, controlled using a real-time control algorithm and embedded sensors. We conducted a device feasibility and a pilot clinical evaluation study with five individuals with CP ages five through thirty years old. Participants completed an average of 130 minutes of exoskeleton-assisted walking practice. We observed a 19 ± 5% improvement in the metabolic cost of transport ($p = 0.011$) during walking with untethered exoskeleton assistance compared to how participants walked normally. These preliminary findings support the future investigation of powered ankle assistance for improving mobility in this patient population.

PMID: 30235140

6. Children With Cerebral Palsy Have Greater Stride-to-Stride Variability of Muscle Synergies During Gait Than Typically Developing Children: Implications for Motor Control Complexity.
Kim Y, Bulea TC, Damiano DL.

Neurorehabil Neural Repair. 2018 Sep;32(9):834-844. doi: 10.1177/1545968318796333.

BACKGROUND: There is mounting evidence that the central nervous system utilizes a modular approach for neuromuscular control of walking by activating groups of muscles in units termed muscle synergies. Examination of muscle synergies in clinical populations may provide insights into alteration of neuromuscular control underlying pathological gait patterns. Previous studies utilizing synergy analysis have reported reduced motor control complexity during walking in those with neurological deficits, revealing the potential clinical utility of this approach. METHODS: We extracted muscle synergies on a stride-to-stride basis from 20 children with cerebral palsy (CP; Gross Motor Function Classification System levels I-II) and 8 children without CP, allowing the number of synergies to vary for each stride. Similar muscle synergies across all participants and strides were grouped using a k-means clustering and discriminant analysis. RESULTS: In total, 10 clusters representing 10 distinct synergies were found across the 28 individuals. Relative to their total number of synergies deployed during walking, synergies from children with CP were present in a higher number of clusters than in children with typical development (TD), indicating significantly greater stride-to-stride variability. This increased variability was present despite reduced complexity, as measured by the mean number of synergies in each stride. Whereas children with CP demonstrate some novel synergies, they also deploy some of the same muscle synergies as those with TD, although less frequently and with more variability. CONCLUSION: A stride-by-stride approach to muscle synergy analysis expands its clinical utility and may provide a method to tailor rehabilitation strategies by revealing inconsistent but functional synergies in each child with CP.

PMID: 30223739

7. The paediatric version of Wisconsin gait scale, adaptation for children with hemiplegic cerebral palsy: a prospective observational study.
Guzik A, Drużbicki M, Kwolek A, Przysada G, Bazarnik-Mucha K, Szczepanik M, Wolan-Nieroda A, Sobolewski M.

BMC Pediatr. 2018 Sep 15;18(1):301. doi: 10.1186/s12887-018-1273-x.

BACKGROUND: In clinical practice there is a need for a specific scale enabling detailed and multifactorial assessment of gait in children with spastic hemiplegic cerebral palsy. The practical value of the present study is linked with the attempts to find a new, affordable, easy-to-use tool for gait assessment in children with spastic hemiplegic cerebral palsy. The objective of the study is to evaluate the Wisconsin Gait Scale (WGS) in terms of its inter- and intra-rater reliability in observational assessment of walking in children with hemiplegic cerebral palsy. METHODS: The study was conducted in a group of 34 patients with hemiplegic cerebral palsy. At the first stage, the original version of the ordinal WGS was used. The WGS, consisting of four subscales, evaluates fourteen gait parameters which can be observed during consecutive gait phases. At the second stage, a modification was introduced in the kinematics description of the knee and weight shift, in relation to the original scale. The same video recordings were rescored using the new, paediatric version of the WGS. Three independent examiners performed the assessment twice. Inter and intra-observer reliability of the modified WGS were determined. RESULTS: The findings show very high inter- and intra-observer reliability of the modified WGS. This was reflected by a lack of systematically oriented differences between the repeated measurements, very high value of Spearman's rank correlation coefficient $0.9 \leq |R| < 1$, very high value of ICC > 0.9, and low value of CV < 2.5% for the specific physical therapists. CONCLUSIONS: The new, ordinal, paediatric version of WGS, proposed by the authors, seems to be useful as an additional tool that can be used in qualitative observational gait assessment of children with spastic hemiplegic cerebral palsy. Practical dimension of the study lies in the fact that it proposes a simple, easy-to-use tool for a global gait assessment in children with spastic hemiplegic cerebral palsy. However, further research is needed to validate the modified WGS by comparing it to other observational scales and objective 3-dimensional spatiotemporal and kinematic gait parameters. TRIAL REGISTRATION: anzctr.org.au , ID: ACTRN12617000436370 . Registered 24 March 2017.

PMID: 30219044

8. An investigation of the quality of pretend play ability in children with cerebral palsy.
Dos Santos DM, Lucisano RV, Pfeifer LI.

Aust Occup Ther J. 2018 Sep 21. doi: 10.1111/1440-1630.12539. [Epub ahead of print]

BACKGROUND: Cerebral palsy (CP) describes a group of permanent disorders in the development of movement and posture due to non-progressive disturbances during foetal or infant brain development that can result in activity limitations, including engagement in pretend play. METHODS: Twenty children aged four to seven years with spastic CP participated in this descriptive qualitative study. The Child-Initiated Pretend Play Assessment (ChIPPA) clinical observations were analysed from five categories: Time, Interaction with the examiner, Imitation, Theme and Story. RESULTS: Seventy per cent (70%) of the children completed the assessment (Time), and 90% of children interacted socially with the examiner during the play (Interaction with the examiner). All children initiated their pretend play without requiring examiner demonstration (Imitation). Sixty per cent (60%) of the children were appropriate to their stage of development for Theme. Finally, 60% of the children set up a scenario, but did not develop a narrative (Story). CONCLUSION: Qualitative aspects of the children's pretend play performance were satisfactory, showing typical play indicators in all the categories, except for 'Story'. 'Story' represents more complexity in a child's pretend play ability. Therefore, a play intervention is suggested to stimulate and expand the pretend play ability of preschool children with CP.

PMID: 30238695

9. Family impact of childhood neurodevelopmental disability: considering adaptive and maladaptive behaviour.
Gardiner E, Miller AR, Lach LM.

J Intellect Disabil Res. 2018 Oct;62(10):888-899. doi: 10.1111/jir.12547.

BACKGROUND: The aim of the current study was to identify functional predictors of perceived impact of childhood disability among families of children with neurodevelopmental disorders and disabilities. We first examined the relationship between sub-domains of adaptive and problematic behaviour and perceived family impact. Second, we examined whether the same sub-domains would emerge as significant after controlling for the impact of child diagnosis, including autism spectrum

disorder, cerebral palsy and intellectual disability. METHOD: Caregivers of 216 children and adolescents (M = 8.17 years) with neurodevelopmental disorder and disability completed measures of children's practical, conceptual and social skills (i.e. adaptive behaviour), behaviour problems and positive and negative family impact. RESULTS: Indices of child adaptive and problematic behaviour were only significantly associated with perceived negative family impact. Children's practical and social skills, as well as emotional symptoms, emerged as significant predictors of perceived negative family impact, with emotional symptoms accounting for greatest variance. Including diagnosis in our statistical models did not explain additional variance above and beyond these particular sub-domains of child functioning. CONCLUSIONS: The study findings suggest that it is not children's most impaired domains of functioning that are perceived as significantly impactful by the family. The findings highlight the importance of devoting consideration to the ways in which the functional limitations experienced by children with chronic developmental health conditions similarly impact family life and well-being, regardless of disorder designation.

PMID: 30230656

10. The psychometric properties of the Childhood Health Assessment Questionnaire (CHAQ) in children with cerebral palsy.
Chae S, Park EY, Choi YI.

BMC Neurol. 2018 Sep 20;18(1):151. doi: 10.1186/s12883-018-1154-9.

BACKGROUND: The evaluation of children with cerebral palsy (CP) focuses on activity level measurement to examine the effect of health-care interventions on their physical functioning in the home, school, and community settings. This study aimed to identify the psychometric properties of the Korean version of the Childhood Health Assessment Questionnaire (CHAQ) by applying the Rasch model. The use of the Rasch model has an advantage in that item characteristic curve estimation is not affected by the characteristics of subject groups. METHODS: Data were collected from 65 children with CP aged 75-190 months using the Korean version of the CHAQ. Response data were analyzed according to the Rasch model, and item fitness and difficulty and the appropriateness and reliability of the rating scale were evaluated. RESULTS: Among the 30 items of the Korean version of the CHAQ, two items (nail-cutting and opening a bottle cap that was already opened) were shown to be misfit items with low fitness. The analysis results for item difficulty indicated the requirement for modification of item difficulty, pointing out the need for the addition of question items with both higher and lower difficulty. The use of 4-point rating scale in the evaluation questionnaire was shown to be appropriate. With respect to analysis outcomes, the subjects' separation reliability value and separation index were 0.97 and 5.92, respectively. In contrast, the separation reliability value and separation index for the question items were 0.95 and 4.51, respectively. CONCLUSIONS: The results of this study suggest the need for the modification of item fitness and difficulty. The psychometric properties of the Korean version of the CHAQ were identified using the item response theory-based Rasch analysis.

PMID: 30236077

11. Cardiovascular disease and related risk factors in adults with cerebral palsy: a systematic review.
Mcphee PG, Claridge EA, Noorduyn SG, Gorter JW.

Dev Med Child Neurol. 2018 Sep 17. doi: 10.1111/dmcn.14028. [Epub ahead of print]

AIM: To summarize the literature on the prevalence of cardiovascular disease (CVD), risk factors of CVD, and CVD-related mortality in adults with cerebral palsy (CP). METHOD: A systematic review was conducted by searching the PubMed, Embase, MEDLINE (Ovid), Cochrane, and CINAHL databases. Selection criteria included adults with CP aged 18 years or over. Methodological quality was assessed using the Newcastle-Ottawa scale for observational studies. Data were reported descriptively. RESULTS: Nineteen studies met the inclusion criteria. Only one study reported directly on the presence of CVD in adults with CP, which found adults with CP reported greater CVD conditions than adults without CP (15.1 vs 9.1%, $p<0.001$). The most commonly reported risk factor of CVD in adults with CP was overweight/obesity. Five studies included data on CVD-related mortality in persons with CP, where CVD-related and circulatory system-related deaths were elevated and more common at a younger age in adults with CP than in the general population. INTERPRETATION: The prevalence of CVD and the risk of death because of CVD in this population seems increased, though the knowledge base is fragmented by studies that are small in size and geographically isolated. Further research is required to understand prevalence of risk factors among adults with CP, in particular overweight/obesity. WHAT THIS PAPER ADDS: Overweight and obesity are risk factors of cardiovascular disease (CVD) that are commonly reported in adults with cerebral palsy (CP). CVD-related and circulatory system-related deaths are elevated in individuals with CP compared to the general population.

PMID: 30221763

12. Standards of Virtual Reality Application in Balance Training Programs in Clinical Practice: A Systematic Review.
Juras G, Brachman A, Michalska J, Kamieniarz A, Pawłowski M, Hadamus A, Białoszewski D, Błaszczyk J, Słomka KJ.

Games Health J. 2018 Sep 21. doi: 10.1089/g4h.2018.0034. [Epub ahead of print]

OBJECTIVE: To determine the effect of virtual reality (VR) games on improving balance in different groups of neurological patients with a particular focus on the study quality and to determine the gold standard in VR training in these groups. MATERIALS AND METHODS: A systematic review of controlled trials published between January 2009 and December 2017 was conducted. The PubMed, SCOPUS, SPORTDiscus, and Medline databases were searched. Studies involved patients with stroke or Parkinson's disease or children with cerebral palsy. The Physiotherapy Evidence Database (PEDro) scale was used to assess the methodological quality of the included studies. RESULTS: A total of 20 studies met the inclusion criteria. The PEDro scores ranged from 4 to 8 points. Analysis of the rehabilitation programs revealed a very large discrepancy in the planned volume of exercises in different subgroups of patients. CONCLUSIONS: Overall, the comparison of VR interventions between conventional rehabilitation and no intervention exhibited significantly better results. However, these results should be interpreted with great caution due to the large diversity of the systems, games, and training volume used in the VR therapy. In all included studies, only several articles included objective methods to assess the effect of VR. In addition, most of the articles showed a high risk of bias, such as a lack of randomization and blinding or a small sample size. That is why further well-designed randomized control trials are required to evaluate the influence of VR on balance in different groups of neurological patients.

PMID: 30239217

13. The influence of prior pronunciations on sensorimotor cortex activity patterns during vowel production.
Salari E, Freudenburg ZV, Vansteensel MJ, Ramsey N.

J Neural Eng. 2018 Sep 21. doi: 10.1088/1741-2552/aae329. [Epub ahead of print]

Objective; In recent years, brain-computer interface (BCI) systems have been investigated for their potential as a communication device to assist people with severe paralysis. Decoding speech sensorimotor cortex activity is a promising avenue for the generation of BCI control signals, but is complicated by variability in neural patterns, leading to suboptimal decoding. We investigated whether neural pattern variability associated with sound pronunciation can be explained by prior pronunciations and determined to what extent prior speech affects BCI decoding accuracy. Approach; Neural patterns in speech motor areas were evaluated with electrocorticography in five epilepsy patients, who performed a simple speech task that involved pronunciation of the /i/ sound, preceded by either silence, the /a/ sound or the /u/ sound. Main results; The neural pattern related to the /i/ sound depends on previous sounds and is therefore associated with multiple distinct sensorimotor patterns, which is likely to reflect differences in the movements towards this sound. We also show that these patterns still contain a commonality that is distinct from the other vowel sounds (/a/ and /u/). Classification accuracies for the decoding of different sounds do increase, however, when the multiple patterns for the /i/ sound are taken into account. Simply including multiple forms of the /i/ vowel in the training set for the creation of a single /i/ model performs as well as training individual models for each /i/ variation. Significance; Our results are of interest for the development of BCIs that aim to decode speech sounds from the sensorimotor cortex, since they argue that a multitude of cortical activity patterns associated with speech movements can be reduced to a basis set of models which reflect meaningful language units (vowels), yet it is important to account for the variety of neural patterns associated with a single sound in the training process.

PMID: 30238924

14. Association between bronchopulmonary dysplasia and cerebral palsy in children: a meta-analysis.
Gou X, Yang L, Pan L, Xiao D.

BMJ Open. 2018 Sep 19;8(9):e020735. doi: 10.1136/bmjopen-2017-020735.

OBJECTIVE: To investigate the association between bronchopulmonary dysplasia (BPD) and the risk of cerebral palsy (CP) in children. DATA SOURCES: We used EMBASE, PubMed and Web of Science to conduct a meta-analysis of studies published before 1 September 2017, written in English whose titles or abstracts discussed an association between BPD and CP. STUDY SELECTION: Observational studies, for example, case-control and cohort studies were included. DATA EXTRACTION AND SYNTHESIS: All review stages were conducted by two reviewers independently. Data synthesis was undertaken via meta-analysis of available evidence. MAIN OUTCOMES AND MEASURES: The prevalence of developing CP was measured after

exposure to BPD. RESULTS: Among 1234 initially identified studies, we selected those that addressed an association between BPD and CP according to our preselected inclusion criteria. Our meta-analysis included 11 studies. According to a random effect model, BPD was significantly associated with CP (ORs 2.10; 95% CI 1.57 to 2.82) in preterm infants. Factors explaining differences in the study results included study design, the definition of BPD, the time of diagnosis of CP and whether the studies adjusted for potential confounders. CONCLUSION: This study suggests that BPD is a risk factor for CP. Further studies are required to confirm these results and to detect the influence of variables across studies.

PMID: 30232102

15. Acquired undescended testis and possibly associated testicular torsion in children with cerebral palsy or neuromuscular disease.
Ito T, Matsui F, Fujimoto K, Matsuyama S, Yazawa K, Matsumoto F, Shimada K.

J Pediatr Urol. 2018 Aug 23. pii: S1477-5131(18)30482-0. doi: 10.1016/j.jpurol.2018.08.015. [Epub ahead of print]

INTRODUCTION: Torsion of an undescended testis (UDT) associated with cerebral palsy (CP) and neuromuscular disease (NMD) is an uncommon condition that is not well recognized by primary care physicians or healthcare providers. OBJECTIVE: The objective of this study was to highlight the clinical importance of torsion of a UDT in children with CP and NMD. MATERIALS AND METHODS: Eleven children with testicular torsion of a UDT operated on at the study institute between 1991 and 2015 were identified. The records of seven children (63.6%) associated with CP or NMD were retrospectively reviewed. Clinical findings of testicular torsion were assessed along with the treatment outcome and testicular salvageability. RESULTS: All seven children were not identified with a UDT by public health checkup for infant and young children. No children with CP or NMD had torsion of a descended testis during the present study period. Median age at surgery was 15 years (range, 1-20 years). The testis location was at the external inguinal ring in five patients, in the inguinal canal in one, and in the superficial inguinal pouch in one. Of the contralateral testes, four were a UDT, one was a retractile testis, and two were descended testes. Orchiectomy was performed in six patients (85.7%). In the remaining patients, the testis was preserved but became atrophic. DISCUSSION: This study demonstrated that children with CP or NMD may be affected with torsion of a UDT with peak at around puberty with the poor salvage rate, even if the testes appear descended in infancy and young children. Shortcomings of this study were the retrospective design and a small series of children undergoing surgery for torsion of a UDT. CONCLUSION: Pediatric urologists need to educate primary care physicians and healthcare providers in the recognition of acquired UDTs and possibly associated testicular torsion in children with CP and NMD. Genital examination should be continued regularly until adolescence in these children to detect acquired UDT. These children should be referred to pediatric urologists to promote surgery as soon as the diagnosis of acquired UDT is carried out. It is believed that it is perhaps the best approach to prevent loss of the testis in children with CP and NMD.

PMID: 30219308

16. Impact of social disadvantage on cerebral palsy severity.
Woolfenden S, Galea C, Smithers-Sheedy H, Blair E, Mcintyre S, Reid S, Delacy M, Badawi N; Australian Cerebral Palsy Register Group; CP Quest.

Dev Med Child Neurol. 2018 Sep 17. doi: 10.1111/dmcn.14026. [Epub ahead of print]

AIM: To investigate the impact of socio-economic disadvantage on indicators of cerebral palsy (CP) severity - motor impairment, intellectual disability, and the presence of severe comorbidities - in children with CP in Australia. METHOD: Data from the Australian Cerebral Palsy Register were analysed. Socio-economic disadvantage was assessed using maternal age, maternal country of birth, and a measure of neighbourhood socio-economic status (SES) at the time of the child's birth. Descriptive bivariate analysis, trend analysis, risk ratios, and mediation analysis were undertaken to examine the impact of disadvantage on the indicators of CP severity. RESULTS: A socio-economic gradient was demonstrated with an increasing proportion of children with non-ambulant status, at least moderate intellectual disability, and the presence of severe comorbidities (having epilepsy, functional blindness, bilateral deafness, and/or no verbal communication) with decreasing neighbourhood SES, adolescent motherhood, and maternal minority ethnicity. INTERPRETATION: In Australia, socio-economic disadvantage at birth impacts adversely on CP severity at age 5 years. By identifying that socio-economically disadvantaged children with CP are at greater risk of more severe functional outcomes, we can inform targeted interventions at the family and neighbourhood level to reduce these inequities for children with CP. WHAT THIS PAPER ADDS: Socio-economic disadvantage is associated with increased severity of cerebral palsy functional outcomes. This encompasses low neighbourhood socio-economic status, adolescent motherhood, and maternal minority ethnicity.

PMID: 30221759

Prevention and Cure

17. Neurotherapeutic Capacity of P7C3 Agents for the Treatment of Traumatic Brain Injury.
Blaya MO, Wasserman JM, Pieper AA, Sick TJ, Bramlett HM, Dietrich WD.

Neuropharmacology. 2018 Sep 17. pii: S0028-3908(18)30672-5. doi: 10.1016/j.neuropharm.2018.09.024. [Epub ahead of print]

Traumatic brain injury (TBI) is a significant public health problem around the world. A promising area of research is the characterization of small, drug-like molecules that have potent clinical properties. One pharmacotherapeutic agent in particular, an aminopropyl carbazole called P7C3, was discovered using an in vivo screen to identify new agents that augmented the net magnitude of adult hippocampal neurogenesis. P7C3 greatly enhanced neurogenesis by virtue of increasing survival rates of immature neurons. The potent neuroprotective efficacy of P7C3 is likely due to enhanced nicotinamide phosphoribosyltransferase (NAMPT) activity, which supports critical cellular processes. The scaffold of P7C3 was found to have favorable pharmacokinetic properties, good bioavailability, and was nontoxic. Preclinical studies have shown that administration of the P7C3-series of neuroprotective compounds after TBI can rescue and reverse detrimental cellular events leading to improved functional recovery. In several TBI models and across multiple species, P7C3 and its analogues have produced significant neuroprotection, axonal preservation, robust increases in the net magnitude of adult neurogenesis, protection from injury-induced LTP deficits, and improvement in neurological functioning. This review will elucidate the exciting and diverse therapeutic findings of P7C3 administration in the presence of a complex and multifactorial set of cellular and molecular challenges brought forth by experimental TBI. The clinical potential and broad therapeutic applicability of P7C3 warrants much needed investigation into whether these remedial effects can be replicated in the clinic. P7C3 may serve as an important step forward in the design, understanding, and implementation of pharmacotherapies for treating patients with TBI.

PMID: 30236963

18. Inflammasome Proteins in Serum and Serum-Derived Extracellular Vesicles as Biomarkers of Stroke.
Kerr N, García-Contreras M, Abbassi S, Mejias NH, Desousa BR, Ricordi C, Dietrich WD, Keane RW, de Rivero Vaccari JP.

Front Mol Neurosci. 2018 Sep 4;11:309. doi: 10.3389/fnmol.2018.00309. eCollection 2018.

The inflammasome is a key contributor to the inflammatory innate immune response after stroke. We have previously shown that inflammasome proteins are released in extracellular vesicles (EV) after brain and spinal cord injury. In addition, we have shown that inflammasome proteins offer great promise as biomarkers of central nervous system (CNS) injury following brain trauma. In the present study, we used a Simple Plex Assay (Protein Simple), a novel multi-analyte automated microfluidic immunoassay platform, to analyze serum and serum-derived EV samples from stroke patients and control subjects for inflammasome protein levels of caspase-1, apoptosis-associated speck-like protein containing a caspase-recruitment domain (ASC), Interleukins (IL)-1β, and (IL)-18. Receiver operator characteristic (ROC) curves with associated confidence intervals obtained from the analysis of serum samples revealed that the area under the curve (AUC) for ASC was 0.99 with a confidence interval between 0.9914 and 1.004, whereas the AUC for caspase-1, IL-1β, and IL-18 were 0.75, 0.61, and 0.67, respectively. Thus, these data indicate that ASC is a potential biomarker of stroke and highlight the role of the inflammasome in the inflammatory response after brain ischemia.

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19. Preventing Childhood and Lifelong Disability: Maternal Dietary Supplementation for Perinatal Brain Injury.
Shaw OEF, Yager JY.

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The majority of brain injuries that lead to cerebral palsy, developmental disability, and mental health disorders have their onset in utero. These lifelong conditions come with great economic and emotional burden as they impact function in nearly all domains of affected individuals' lives. Unfortunately, current therapeutic options are limited. There remains a focus on rescue, rehabilitation, and regeneration after the injury has occurred, rather than aiming to prevent the initial injury. Prevention would imply treating the mother during pregnancy to alter the fetal environment and in turn, treat the fetus. Fear of harming the

developing fetus remains as a result of errors of the past such as the release of thalidomide. In this review, we outline evidence from animal studies and clinical trials that have explored maternal dietary supplementation with natural health products (including nutraceuticals and functional foods) for perinatal brain injury prevention. Namely, we discuss magnesium sulphate, creatine, choline, melatonin, resveratrol and broccoli sprouts/sulforaphane. Although clinical trials have only been completed in this realm for magnesium sulphate, results in animal models have been promising, suggesting that this is a productive avenue for further research. Natural health products may provide safe, effective, affordable, and easily accessible prevention of fetal brain injury and resulting lifelong disabilities.

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