Sánchez MB, Loram I, Holmes P, Darby J, Butler PB.


BACKGROUND: Physical therapy evaluations of motor control are currently based on subjective clinical assessments. Despite validation, these can still be inconsistent between therapists and between clinics, compromising the process of validating a therapeutic intervention and the subsequent generation of evidence-based practice (EBP) guidelines. EBP benefits from well-defined objective measurements that complement existing subjective assessments. RESEARCH QUESTION: The aim of this study was to develop an objective measure of head/trunk control in children with Cerebral Palsy (CP) using previously developed video-based methods of head/trunk alignment and absence of external support and compare these with the existing subjective Segmental Assessment of Trunk Control (SATCo). METHODS: Twelve children with CP were recruited and an average of 3 (±1.1) SATCo tests performed per child. The full SATCo was concurrently video-recorded from a sagittal view; markers were placed on specific landmarks of the head, trunk and pelvis to track and estimate head/trunk segment position. A simplified objective rule was created for control and used on videos showing no external support. This replicated the clinical parameters and enabled identification of the segmental-loss-of-control. The subjectively and objectively identified segmental-loss-of-control were compared using a Pearson Correlation Coefficient. RESULTS: An angular-threshold of 17° from alignment showed the minimum bias between the subjectively and the objectively measured segmental-loss-of-control (mean error =0.11 and RMSE = 1.5) and a significant correlation (r = 0.78, r² = 0.61, p < .01). SIGNIFICANCE: This study showed that simple objective video-based measurements can be used to reconstruct the subjective assessment of segmental head/trunk control. This suggests that a clinically-friendly video-based objective measure has future potential to complement subjective assessments and to assist in the generation of EBP guidelines. Further development will increase the information that can be extracted from video images and enable generation of a fully automated objective measure.

PMID: 30558945

Lieber RL, Fridén J.


Skeletal muscle contractures represent the permanent shortening of a muscle-tendon unit, resulting in loss of elasticity and, in extreme cases, joint deformation. They may result from cerebral palsy, spinal cord injury, stroke, muscular dystrophy and other neuromuscular disorders. Contractures are the prototypic and most severe clinical presentation of increased passive mechanical muscle force in humans, often requiring surgical correction. Intraoperative experiments demonstrate that high muscle passive force is associated with sarcomeres that are abnormally stretched, although otherwise normal, with fewer
sarcomeres in series. Further, changes in the amount and arrangement of collagen in the extracellular matrix (ECM) also increase muscle stiffness. Structural light and electron microscopy studies demonstrate that large bundles of collagen, referred to as perimysial cables, may be responsible for this increased stiffness and are regulated by interaction of a number of cell types within the ECM. Loss of muscle satellite cells (SCs) may be related to changes in both sarcomeres and ECM. Future studies are required to determine the underlying mechanism for changes in muscle SCs and their relationship (if any) to contracture. A more complete understanding of this mechanism may lead to effective nonsurgical treatments to relieve and even prevent muscle contractures.

PMID: 30571285

3. The influence of maximum isometric muscle force scaling on estimated muscle forces from musculoskeletal models of children with cerebral palsy.


BACKGROUND: Musculoskeletal models do not include patient-specific muscle forces but rely on a scaled generic model, with muscle forces left unscaled in most cases. However, to use musculoskeletal simulations to inform clinical decision-making in children with cerebral palsy (CP), inclusion of subject-specific muscle forces is of utmost importance in order to represent each child's compensation mechanisms introduced through muscle weakness. RESEARCH AIM: The aims of this study were to (i) evaluate if maximum isometric muscle forces (MIMF) in musculoskeletal models of children with CP can be scaled based on strength measurements obtained with a hand-held-dynamometer (HHD), (ii) evaluate the impact of the HHD based scaling approach and previously published MIMF scaling methods on computed muscle forces during gait, and (iii) compare maximum muscle forces during gait between CP and typically developing (TD) children. METHODS: Strength and motion capture data of six CP and motion capture data of six TD children were collected. The HHD measurements to obtain hip, knee and ankle muscle strength were simulated in OpenSim and used to modify MIMF of the 2392-OpenSim model. These muscle forces were compared to the MIMF scaled on the child's body mass and a scaling approach, which included the body mass and muscle-tendon lengths. OpenSim was used to calculate peak muscle forces during gait. RESULTS: Ankle muscle strength was insufficient to reproduce joint moments during walking when MIMF were scaled based on HHD. During gait, peak hip and knee extensor muscle forces were higher and peak ankle dorsiflexor forces were lower in CP compared to TD participants. SIGNIFICANCE: HHD measurements can be used to scale MIMF for the hip and knee muscle groups but underestimate the force capacity of the ankle muscle groups during walking. Muscle-tendon-length and mass based scaling methods affected muscle activations but had little influence on peak muscle forces during gait.

PMID: 30558934

4. Synergy complexity during maximal voluntary isometric contractions.
Goudriaan M, Shuman BR, Steele KM, Molenaers G, Goemans N, Desloovere K.


PMID: 30558932

5. Is ferritin estimation and optimisation important in cerebral palsy children undergoing single event multilevel surgery?
Mohan R, Unnikrishnan PN, George H, Bass A, Dhotare SVR, Sampath JS.


PMID: 30568342


Background and purpose - Gait analysis is indicated in children with cerebral palsy (CP) to identify and quantify gait deviations. One particularly difficult-to-treat deviation, crouch gait, can progress in adolescence and ultimately limit the ability to ambulate. An objective quantitative assessment is essential to early identify progressive gait impairments in children with CP. 3-dimensional gait analysis (3D GA) is considered the gold standard, although it is expensive, seldom available, and unnecessarily detailed for screening and follow-up. Simple video assessments are time-consuming when processed manually, but more convenient if used in conjunction with video processing algorithms; this has yet been validated in CP. We validate a 2-dimensional markerless (2D ML) assessment of knee joint flexion/extension angles of the gait cycle in children and young adults with CP. Patients and methods - 18 individuals, mean age 15 years (6.5-28), participated. 11 had bilateral, 3 unilateral, 3 dyskinetic, and 1 ataxic CP. In the Gross Motor Function Classification System, 6 were at level I, 11 at level II, and 1 at level III. We compared 2D ML, using a single video camera with computer processing, and 3D GA. RESULTS: The 2D ML method overestimated the knee flexion/extension angle values by 3.3 to 7.0 degrees compared with 3D GA. The reliability within 2D ML and 3D GA was mostly good to excellent. Interpretation - Despite overestimating, 2D ML is a reliable and convenient tool to assess knee angles and, more importantly, to detect changes over time within a follow-up program in ambulatory children with CP.

PMID: 30558517

7. Pre-operative hamstring length and velocity do not explain the reduced effectiveness of repeat hamstring lengthening in children with cerebral palsy and crouch gait.
Osborne M, Mueske NM, Rethlefsen SA, Kay RM, Wren TAL.


BACKGROUND: Hamstring lengthening surgery (HSL) is often performed to correct crouch gait in patients with cerebral palsy (CP). However, crouch can recur over time, and repeat HSL may be ineffective. One possible reason is that the hamstrings in repeat HSL patients are neither short nor lengthening slowly and would therefore not benefit from HSL. RESEARCH QUESTION: This study aimed to determine whether the hamstrings are short and/or slow preoperatively only in patients with primary, and not repeat, HSL. METHODS: We compared pre- and postoperative dynamic semimembranosus muscle-tendon lengths for children with CP who had primary (N = 15) or repeat (N = 8) HSL to a group of control participants (N = 10). Outcome measures were compared between visits (pre- vs. postoperative) and groups (control, primary HSL, repeat HSL) using mixed model analysis. RESULTS: Preoperatively, hamstrings were shorter and slower than normal on average in both HSL groups (p < 0.001); all but 3 limbs (primary 26/28, repeat 13/14) had hamstrings that were shorter and/or slower than controls by more than two standard deviations. Postoperative improvements were observed in the primary HSL group for popliteal angle, initial contact knee flexion, minimum stance knee flexion, and dynamic hamstring length (p ≤ 0.001). The repeat HSL group improved only in dynamic hamstring length (p = 0.004) and worsened in passive knee extension (p = 0.01) and minimum hip flexion in stance (p = 0.04). Hamstrings in both surgical groups on average remained shorter and slower than controls postoperatively (p ≤ 0.001). SIGNIFICANCE: The fact that repeat HSL is less effective in improving knee motion is not due to a lack of short or slow hamstrings preoperatively. However, in recurrent crouch, short or slow hamstrings do not usually indicate hamstring dysfunction, and correction of other deformities such as rotational malalignment, fixed knee flexion contractures, patella alta, weak calf muscles, and/or loose heelcords should be considered rather than repeat HSL.

PMID: 30572181

8. Quantitative Assessment of Muscle Strength Following "Slow" Surgical Lengthening of the Medial Hamstring Muscles in Children With Cerebral Palsy.
Davids JR, Cung NQ, Sattler K, Boakes JL, Bagley AM.


BACKGROUND: Classic teaching for surgical lengthening of muscle contractures in children with cerebral palsy (CP) has emphasized complete correction of the deformity acutely, with immobilization of the targeted muscles in the fully corrected position. Clinical experience has led to the impression that the muscles are invariably weakened by this approach. We have developed an alternative technique for correction of contractures called slow surgical lengthening (SSL). The goal of the study was to determine the physical examination, kinematic, and muscle strength outcomes following SSL of the medial hamstring muscles in children with CP. METHODS: The study group included 41 children with CP who underwent SSL of the medial hamstring muscles as part of a comprehensive single-event multilevel surgery, who had preoperative and 1-year postoperative evaluations in our Motion Analysis Center, which included quantitative assessment of isometric and isokinetic muscle strength. RESULTS: All subjects were Gross Motor Function Classification System I and II. Mean age at the time of surgery was 10.8 years. The mean popliteal angle improved by 16.2 degrees (P<0.001) following SSL of the medial hamstrings. Sagittal plane
kinematics following SSL of the medial hamstrings showed improvement of knee extension at initial contact of 10.2 degrees (P<0.001), decrease of peak knee flexion in mid-swing of 3.6 degrees (P=0.014), improved minimum knee flexion in stance of 4.9 degrees (P=0.002), and no significant change in mean anterior pelvic tilt (P=0.123). Mean peak isometric knee flexion torque remained unchanged from preoperative to postoperative studies (P=0.154), whereas mean peak isokinetic knee flexion torque significantly increased by 0.076 Nm/kg (P=0.014) following medial hamstring SSL. DISCUSSION: SSL was developed based upon clinical experience and improved understanding of the pathophysiology of skeletal muscle in children with CP. The SSL technique allows the tendinous tissue to separate spontaneously at the time of recession, but does not force further acute lengthening by intraoperative manipulation, thereby minimizing the damage to the underlying muscle. It is broadly believed that muscle weakness is inevitable following surgical lengthening. The current study shows that the SSL technique does not cause weakness. LEVEL OF EVIDENCE: Level IV-therapeutic.

PMID: 30570590

O'Sullivan R, Munir K, Keating L.


BACKGROUND: Toe-walking is a normal variant in children up to 3 years of age but beyond this a diagnosis of idiopathic toe-walking (ITW) must be considered. ITW is an umbrella term that covers all cases of toe-walking without any diagnosed underlying medical condition and before assigning these diagnosis potential differential diagnoses such as cerebral palsy, peripheral neuropathy, spinal dysraphism and myopathy must be ruled out. Gait laboratory assessment (GLA) is thought to be useful in the evaluation of ITW, and kinematic, kinetic and electromyography features associated with ITW have been described. However, the longer term robustness of a diagnosis based on GLA has not been investigated. The primary aim of this study was to examine if a diagnosis of ITW based on GLA features persisted. METHODS: All patients referred to a national gait laboratory service over a ten year period with queried ITW were sent a postal survey to establish if a diagnosis of ITW which had been offered following GLA persisted over time. The gait and clinical parameters differentiating those reported as typical ITW and not-typical ITW following GLA were examined in the survey respondents. RESULTS: Of 102 referrals to the laboratory with queried ITW, a response rate of 40.2% (n = 41) was achieved. Of the respondents, 78% (n = 32) were found to be typical of ITW following GLA and this diagnosis persisted in the entire group at an average of 7 years post GLA. The other nine subjects were reported as not typical of ITW following GLA and 44.4% (n = 4) received a subsequent differential diagnosis. The clinical examination and gait analysis features differentiating these groups were consistent with previous literature. CONCLUSION: GLA appears to be a useful objective tool in the assessment of ITW and a diagnosis based on described features persists in the long-term.

PMID: 30553151

10. The development of anticipatory action planning in children with unilateral cerebral palsy.
Krajenbrink H, Crichton A, Steenbergen B, Hoare B.


Background Previous studies suggest that compromised bimanual performance experienced by children with unilateral cerebral palsy (CP) is not only due to difficulties in action execution but may also be a result of impaired anticipatory action planning. Aims The effect of age and side of hemiplegia were examined and the relationship between anticipatory action planning, unimanual capacity and bimanual performance was explored. Methods and procedures Using a multi-centre, prospective, cross-sectional observational design, anticipatory action planning was analyzed in 104 children with unilateral cerebral palsy, aged 6-12 years, using the sword task. Outcomes and results Anticipatory action planning did not improve with age in children with unilateral CP, aged between 6-12 years. No differences were found between children with left or right hemiplegia. Finally, anticipatory action planning was not related to unimanual capacity or bimanual performance. Conclusion and implications This study demonstrates anticipatory action planning, measured using the sword task, does not improve with age in children with unilateral CP and is not related to bimanual performance or laterality. Future studies of anticipatory action planning in children with unilateral CP should consider using measures that require effective anticipatory action planning for successful task completion rather than end state comfort.

PMID: 30557847
11. Developmental Trajectories and Reference Percentiles for the 6-Minute Walk Test for Children With Cerebral Palsy.
Fiss AL, Jeffries L, Bjornson K, Avery L, Hanna S, Westcott McCoy S.

PURPOSE: The purposes of this study were to document longitudinal developmental trajectories in 6-minute walk test (6MWT) distances and to develop age-specific reference percentiles for children across different Gross Motor Function Classification System (GMFCS) levels. METHODS: A TOTAL OF: 456 children with cerebral palsy ages 3 to 12 years of, GMFCS levels I to III participated. Children's motor function was classified on the GMFCS, and children completed the 6MWT 2 to 5 times in 2 years. RESULTS: Longitudinal developmental trajectories support that 6MWT distances increase with age followed by a tapering, as children approach their functional limit relative to their GMFCS level. Reference percentile graphs were created to monitor change over time. CONCLUSIONS: The 6MWT longitudinal developmental trajectories, reference percentiles, and interpretation of percentile change should assist collaborative and proactive intervention planning relative to functional walking capacity for children with cerebral palsy. Comment in Commentary on "Developmental Trajectories and Reference Percentiles for the 6-Minute Walk Test for Children With Cerebral Palsy". [Pediatr Phys Ther. 2019]

PMID: 30557281

12. Commentary on "Developmental Trajectories and Reference Percentiles for the 6-Minute Walk Test for Children With Cerebral Palsy".
Maher C, Kuszczakowski K.

Comment on Developmental Trajectories and Reference Percentiles for the 6-Minute Walk Test for Children With Cerebral Palsy. [Pediatr Phys Ther. 2019]

PMID: 30557282

Hösl M, Böhm H, Eck J, Döderlein L, Arampatzis A.

BACKGROUND: Patients with spastic Cerebral Palsy are prone to equinus deformities, likely affected by short and inextensible plantarflexor muscles. Manual stretching is a popular treatment but its effectiveness concerning joint mobility, muscle-tendon morphometrics and walking function is debated. Eccentric exercise by backward-downhill treadmill training could be a therapeutic alternative for ambulatory patients improving gait and muscle function. RESEARCH QUESTION: What are the effects of eccentric training by backward-downhill treadmill training and plantarflexor stretching concerning gait and muscle function in patients with spastic Cerebral Palsy? METHODS: 10 independent ambulators with spastic Cerebral Palsy (12 [SD 4] years old, 2 uni- and 8 bilaterally affected) participated in a randomized crossover-study. One group started with manual static stretching, the other one with backward-downhill treadmill training. Each treatment period lasted 9 weeks (3 sessions per week). Pre and post treatments, 3D gait was assessed during comfortable and during fastest possible walking. Ultrasonography and dynamometry were used to test plantarflexor strength, passive joint flexibility, as well as gastrocnemius morphometrics, stiffness and strain on muscle-tendon and joint level. RESULTS: When comparing both treatments, backward-downhill treadmill training lead to larger single stance dorsiflexion at comfortable walking speed (+2.9°, P = 0.041) and faster maximally achievable walking velocities (+0.10 m/s, P = 0.017). Stretching reduced knee flexion in swing, particularly at faster walking velocities (-5.4°, P = 0.003). Strength, ankle joint flexibility, as well as stiffness on muscle-tendon and joint level were not altered, despite similar increases in passive muscle and fascicle strain with both treatments (P ≤ 0.023). SIGNIFICANCE: Backward-downhill treadmill training can be an effective gait treatment, probably improving coordination or reducing dynamic stretch sensitivity. More intense BDTT might be necessary to further alter muscle-tendon properties. Manual static plantarflexor stretching may not be optimal in Cerebral Palsy patients with high ambulatory status.

PMID: 30558918

Iturricastillo A, Granados C, Reina R, Sarabia JM, Romarate A, Yanci J.


PURPOSE: This study analyzes the relationship between mean propulsive velocity (MPV) of the bar and relative load (%1RM) in the bench press exercise, as well as determining the relationship of power variables (i.e. Mean Power (MP), Mean Propulsive Power (MPP) and Peak Power (PP)) in change of direction ability (CODA), linear sprint and RSA performance. METHODS: Nine Spanish First Division wheelchair basketball (WB) players participated in the study. All participants performed an isoinertial bench press (BP) test in free execution mode, 505 change of direction ability test (505 CODA), linear sprint test (20 m), and Repeated Sprint Ability Test (RSA). RESULTS: A nearly perfect and inverse relationship was observed for the BP exercise between the %1RM and MPV ($r = - .97; R^2 = .945; P < 0.001$). The maximum loads for MP, MPP and PP were obtained between 48.1 - 59.4% of the 1RM. However, no significant correlations were observed between strength and wheelchair performance. CONCLUSIONS: WB players with different functional impairments showed a nearly perfect and inverse relationship for the BP exercise between the %1RM and MPV, thus the MPV could be used to estimate the %1RM. This finding has important practical applications for velocity-based resistance training in which coaches would be able to prescribe and monitor training load. Conversely, the absence of association between BP performance and field tests might be due to other factors such as wheelchair-user interface, trunk muscular activity or propulsion technique apart from strength variables.

PMID: 30569792

15. Annual Injection of Zoledronic Acid Improves Bone Status in Children with Cerebral Palsy and Rett Syndrome.

Wiedemann A, Renard E, Hernandez M, Dousset B, Brezin F, Lambert L, Weryha G, Feillet F.


Osteoporosis is a common complication of cerebral palsy and Rett's syndrome. It is responsible for multiple fractures, bone pain, and impaired quality of life. In case of Rett's syndrome, a specific dysfunction of osteoblasts causes bone fragility. We observed the effects of annual zoledronic acid (ZA) infusion in a cohort of children with cerebral palsy and Rett's syndrome. 27 children under 18 years (19 with cerebral palsy and 8 girls with Rett syndrome confirmed by MCEP2 mutation) were treated with an annual injection of 0.1 mg/kg (max 4 mg) of ZA. Calcium and vitamin D were combined in all patients from the first injection of ZA. Dental examination was performed before treatment. Data were analyzed retrospectively. Bone mineral density was measured at diagnosis and yearly thereafter. Bone mass density (BMD) is decreased in patient with cerebral palsy and RS. One year after injection of ZA, we observe an increase of Lumbar spine BMD from -2.99 to -2.14 SD (p < 0.0001) and femoral BMD from -4.26 to -3.32 SD (p < 0.001) In the subgroup of patient with Rett syndrome, we also observe an increase from -3.27 to 2.50 SD (p = 0.018) of Lumbar spine BMD. No fractures have been observed in our cohort since the first infusion. Side effects (flu-like syndrome and hypocalcemia) were more common in younger patients and after the first infusion. No serious complications were noticed. This study confirms the efficacy and the safety of an annual injection of ZA to improve bone status in children with cerebral palsy and Rett syndrome. No severe adverse effects were observed.

PMID: 30554334

16. The Hidden Resources of Occupational Therapy: A Conversation With Rhoda Erhardt, MS, OTR/L, FAOTA.

Erhardt R, Gillenwaters K.


Kary Gillenwaters, MA, OTR/L, is currently a consultant and facilitator of the See Me as a Person and Re-Igniting the Spirit of Caring programs at Creative Health Care Management. Her career in health care spans rural and urban settings, and pediatric to geriatric clients and families. Rhoda Erhardt, MS, OTR/L, FAOTA, is an occupational therapy consultant in private practice. She has provided evaluation and consultation services to families, health agencies, educational systems, and corporations, and published and lectured extensively in the United States and overseas on hand skills, vision, eye-hand coordination, and feeding problems in children with cerebral palsy, and handwriting and perceptual problems in children with learning disabilities. Kary and Rhoda talk about the resources occupational therapists bring to the health-care team, as well as how OTs identify and maximize the resources of clients and their families.

PMID: 30567966
17. Symptoms of Feeding Problems in Preterm-born Children at 6 Months to 7 years Old.
Park J, Thoyre SM, Pados BF, Gregas M.


OBJECTIVES: Describe symptoms of feeding problems in children born very preterm (<32 weeks gestation) and moderate to late preterm (32-37 weeks gestation) compared to children born full-term; explore the contribution of medical risk factors to problematic feeding symptoms. METHODS: The sample included 57 very preterm, 199 moderate to late preterm, and 979 full-term born children at 6 months to 7 years old. Symptoms of feeding problems were assessed using the Pediatric Eating Assessment Tool (PediEAT) and compared between groups after accounting for the child's age and/or sex. With the sample of preterm children, we further analyzed 11 medical factors as potential risk factors affecting a child's feeding symptoms: feeding problems in early infancy and conditions of oxygen requirement past 40 weeks of postmenstrual age, congenital heart disease, structural anomaly, genetic disorder, cerebral palsy, developmental delay, speech-language delay, sensory processing disorder, vision impairment or symptoms of gastroesophageal reflux. RESULTS: Compared to children born full-term, both very preterm and moderate to late preterm born children had significantly higher scores on the PediEAT total scale and all four subscales. More severe symptoms were noted in very preterm children, particularly in the areas of Physiologic Symptoms and Selective/Restrictive Eating. Among preterm children, all 11 medical factors were found to be associated significantly with increased symptoms of feeding problems. CONCLUSION: Compared to children born full-term, preterm born children demonstrated greater symptoms of feeding problems regardless of their current age, suggesting children born preterm may require more careful monitoring of feeding throughout childhood.

PMID: 30562308

18. Delays in the reading and spelling of children with cerebral palsy: Associations with phonological and visual processes.
Criffer V, Messer D, Sheehy K.


BACKGROUND: This investigation addresses the question of whether there exists a significant discrepancy in the cognitive abilities of children with cerebral palsy (CP) who, despite the presence of age appropriate communication and language, have reading and spelling delays. AIMS: We wanted to discover whether there was a relationship between the phonological and visual perceptual abilities of children with CP and their progress in reading and spelling. METHODS AND PROCEDURES: Fifteen children with CP (aged between 6:9 years and 11:6 years) were assessed on reading and spelling; communication and language; non-verbal reasoning; phonological processing; and visual perception. OUTCOMES AND RESULTS: Ten of the children had very weak reading and spelling skills. Five children had (mostly) age appropriate scores of reading and spelling. No differences were found between these two groups in non-verbal reasoning or communication and language. However, phonological abilities, visual sequential memory and perception of visuospatial relationships were found to be related to reading and spelling. CONCLUSIONS AND IMPLICATIONS: The findings suggest that children with CP are at risk for reading and spelling delays when they have poor phonological processing, visual sequential memory and perception of visuospatial relationships. The implications of the findings for classroom practice are discussed.

PMID: 30553174

Subki AH, Mukhtar AM, Saggaf OM, Ali RA, Khalifa KA, Al-Lulu DM, Alsallum MS, Bokhary DH, Baabdullah AM, Kassar SM, Jan BM, Hindi MM, Jan MM.


BACKGROUND: Epilepsy is a common neurological disorder in childhood. However, there have been limited studies on its impact on the oral health of affected children. Our study aimed to assess the oral health of children with epilepsy in the city of Jeddah, Saudi Arabia, as perceived by their mothers. METHODS: We conducted a cross-sectional study in three hospitals. We included children 2-18 years old with physician-confirmed epilepsy diagnosis. We assessed parental perception of dental status and need for dental care using a standardized questionnaire that was completed by the mothers. To adjust for potential confounding variables, we used univariate and multivariate logistic regression. RESULTS: We included 96 children with
epilepsy in our study. Their mean age was 6.4±3.4 years. In 55.2% (n=53), dental status was rated as bad, and in 84.4% (n=81) a need for dental care was expressed. Cerebral palsy (OR 5.06, 95% CI 1.28-19.99; P=0.021), motor disability (OR 6.41, 95% CI 1.12-36.73; P=0.037), referral from a pediatric neurology clinic to a dentist (OR 10.755, 95% CI 3.290-35.151; P<0.001), and irregular brushing of teeth (OR 5.397, 95% CI 1.536-18.961; P=0.009) were significantly associated with increased risk of perceived bad dental status. Perception of the child as being overweight (OR 0.117, 95% CI 0.034-0.400; P=0.001) was significantly associated with decreased risk of perceived bad dental status. Motor disability (OR 5.73, 95% CI 1.64-20.04; P=0.006) was significantly associated with increased parental expression of need for dental care. CONCLUSION: In most children with epilepsy, perceived dental status was bad and there was a high expressed need for dental care. Interventions to improve the dental health of children with epilepsy should focus on those with cerebral palsy and motor disability.

PMID: 30568526

20. Dantrolene.
Ratto D, Joyner RW.


Dantrolene sodium (sold under a variety of trade names) is a postsynaptic muscle relaxant with multiple indications in the fields of anesthesiology and neurology. Among the many indications for the use of dantrolene, its primary indication, and FDA approved usage in both children and adults, is for the treatment of malignant hyperthermia: the very rare, but life-threatening disorder triggered by general anesthesia. Malignant hyperthermia is a reaction to the volatile halogenated anesthetics, or depolarizing muscle relaxants, causing sustained muscle contraction, hyperthermia, rhabdomyolysis, and hypercarbia; potentially leading to intraoperative patient demise. These symptoms develop as a response to the anesthetic agents acting on defective ryanodine receptors (calcium channels in muscle cell sarcoplasmic reticulum). Given the mechanism of action, dantrolene acts as an antagonist to these receptors, therefore halting and preventing the further progression of the symptoms of malignant hyperthermia. Even though the incidence of susceptibility to malignant hyperthermia is estimated to be 1:50,000-100,000,[1] it is required, according to the Malignant Hyperthermia Association of the United States, that any facility that administers malignant hyperthermia triggering agents (Isoflurane, desflurane, sevoflurane, and succinylcholine) should stock dantrolene in their facilities at all times. Other FDA approved uses for dantrolene include muscle spasticity disorders as seen with upper motor neuron disorders including stroke, spinal cord injury, cerebral palsy, and multiple sclerosis. It is the only FDA approved oral peripherally acting antispasmodic medication for these disorders.Dantrolene is also used for the treatment of neuromuscular malignant syndrome (given its similarity in presentation and symptoms to malignant hyperthermia) as well as for the overdose of 2,4-dinitrophenol (A banned "fat burner" medication that interrupts ATP synthesis and causes hyperthermia). However, these are considered off-label uses.Recently, dantrolene has been studied in the treatment of vasospasm following aneurysmal subarachnoid hemorrhage. Single dose administration of intravenous dantrolene was found to decrease arterial vasospasm although this remains an off-label use.[2] Interestingly, research on Alzheimer's disease has shown that increased intracellular calcium release modulates amyloid genetic processing in the brain, thereby promoting memory loss. Ryanodine receptors have been identified as a possible culprit of this phenomenon. Given this information, Dantrolene may serve as a potential future treatment for Alzheimer's disease, although further studies are required to test this hypothesis before it can be recommended for this use.[3]

PMID: 30571019

[No authors listed]


PMID: 30557292

22. Cerebral palsy to cerebral palsy spectrum disorder: Time for a name change?
Shevell M.

Words matter. In utilizing language in a medical context, we should strive to communicate succinctly and clearly, conveying both continuity and understanding. This article seeks to put forward the error in continuing to use the term "cerebral palsy," implying a unitary disease phenomenon, when the heterogeneous nature of this entity is self-evident. In an analogous fashion to that which occurred with autism (another neurodevelopmental disability), the transition in nomenclature to "cerebral palsy spectrum disorder" is put forward for the community's consideration.

PMID: [30568002](#)

23. Pathogenic copy number variants that affect gene expression contribute to genomic burden in cerebral palsy.


Cerebral palsy (CP) is the most frequent movement disorder of childhood affecting 1 in 500 live births in developed countries. We previously identified likely pathogenic de novo or inherited single nucleotide variants (SNV) in 14% (14/98) of trios by exome sequencing and a further 5% (9/182) from evidence of outlier gene expression using RNA sequencing. Here, we detected copy number variants (CNV) from exomes of 186 unrelated individuals with CP (including our original 98 trios) using the CoNIFER algorithm. CNV were validated with Illumina 850 K SNP arrays and compared with RNA-Seq outlier gene expression analysis from lymphoblastoid cell lines (LCL). Gene expression was highly correlated with gene dosage effect. We resolved an additional 3.7% (7/186) of this cohort with pathogenic or likely pathogenic CNV while a further 7.7% (14/186) had CNV of uncertain significance. We identified recurrent genomic rearrangements previously associated with CP due to 2p25.3 deletion, 22q11.2 deletions and duplications and Xp monosomy. We also discovered a deletion of a single gene, PDCD6IP, and performed additional zebrafish model studies to support its single allele loss in CP aetiology. Combined SNV and CNV analysis revealed pathogenic and likely pathogenic variants in 22.7% of unselected individuals with CP.

PMID: [30564460](#)

Ghotra S, Vincer M, Allen VM, Khan N.


OBJECTIVE: To identify the temporal trends, risk factors and outcomes of cystic white matter injury (WMI) detected by ultrasound in a population-based cohort of very preterm infants (VPI) with a minimal risk of selection bias. STUDY DESIGN: All live-born VPIs between 22 and < 31 weeks gestational age born in Nova Scotia, Canada from 1993 to 2013. RESULTS: Cystic WMI was identified in 87 (7%) out of 1184 eligible infants. The gestational age and mortality adjusted prevalence of cystic WMI decreased over time (p = 0.04). In multivariable analysis, chorioamnionitis, antenatal steroids, admission hypothermia, ventilator support, inotropes, and non-Coagulase-negative Staphylococcal and fungal infections were independently associated with cystic WMI. Cerebral palsy was the most common disability in the survivors, however, half of the survivors had none or mild disability. CONCLUSIONS: This cohort study demonstrated a decreasing trend in the incidence of cystic WMI and reported population-based neurological outcomes with cystic WMI, which is important for health-care planning and parental counseling.

PMID: [30552376](#)
25. LncRNA MIAT overexpression reduced neuron apoptosis in a neonatal rat model of hypoxic-ischemic injury through miR-211/GDNF.

OBJECTIVE: To investigate the underlying mechanism of lncRNA myocardial infarction-associated transcript (MIAT) in hypoxic-ischemic (HI)-induced neonatal cerebral palsy. MATERIALS AND METHODS: Neonatal rat model of HI injury was established to detect the motor function. LncRNA MIAT, miR-211, glial cell line-derived neurotrophic factor (GDNF) and caspase-3 expressions were measured by qRT-PCR or western blot. The apoptosis of Neuro2A cells was detected by flow cytometry. RNA immunoprecipitation (RIP) and RNA pull-down assays were performed to confirm the interaction between MIAT and miR-211. RESULTS: Compared with control group, lncRNA MIAT and GDNF were downregulated in striatal tissues of neonatal rats in HI group and oxygen glucose deprivation (OGD)-induced ischemic injury of Neuro2A cells, whereas miR-211 was upregulated in striatal tissues of HI group and OGD-induced ischemic injury of Neuro2A cells. LncRNA MIAT interacted with miR-211, and lncRNA MIAT overexpression reduced neuron apoptosis through miR-211. Besides, GDNF expression was positively regulated by lncRNA MIAT and negatively regulated by miR-211 in Neuro2A cells. In vivo experiment proved MIAT promoted motor function and relieved HI injury. CONCLUSION: MIAT overexpression reduced apoptosis of Neuro2A cells through miR-211/GDNF, which relieved HI injury of neonatal rats.

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26. Administration of Bone Marrow-Derived Mononuclear Cells Contributed to the Reduction of Hypoxic-Ischemic Brain Injury in Neonatal Rats.

Background/Objective: Perinatal hypoxic-ischemia (HI) causes neonatal death and permanent neurological deficits. Cell therapy using various cell sources has been recently identified as a novel therapy for perinatal HI. Among the available types of cell sources, bone marrow-derived mononuclear cells (BMMNCs) have unique features for clinical application. For example, stem cells can be collected after admission, thus enabling us to perform autologus transplantation. This study aimed to investigate whether the administration of BMMNCs ameliorated HI brain injury in a neonatal rat model. Methods: Seven-day-old rats underwent left carotid artery ligation and were exposed to 8% oxygen for 60 min. BMMNCs were collected from the femurs and tibias of juvenile rats using the Ficoll-Hypaque technique and injected intravenously 24 h after the insult (1 × 10^5 cells). Active caspase-3, as an apoptosis marker, and ED1, as an activated microglia/macrophage marker, were evaluated immunohistochemically 48 h after the insult (vehicle, n = 9; BMMNC, n = 10). Behavioral assessments using the rotarod treadmill, gait analysis, and active avoidance tests were initiated 3 weeks after the insult (sham, n = 9, vehicle, n = 8; BMMNC, n = 8). After these behavioral tests (6 weeks after the insult), we evaluated the volumes of their hippocampi, cortices, thalami, striata, and globus palidus. Results: The mean cell densities of the sum of four parts that were positive for active caspase-3 significantly decreased in the BMMNC group (p < 0.05), whereas in the hippocampi, cortices, thalami, and striata cell densities decreased by 42, 60, 56, and 47%, respectively, although statistical significance was not attained. The number of ED1 positive cells for the sum of the four parts also significantly decreased in the BMMNC group compared to the vehicle group (p < 0.05), whereas in each of the four parts the decrease was 35, 39, 47, and 36%, respectively, although statistical significance was not attained. In gait analysis, the BMMNC normalized the contact area of the affected hind paw widened by HI. The volumes of the affected striata and globus palidus were significantly larger in the BMMNC group than in the control group. Conclusion: These results indicated that the injection of BMMNCs ameliorated HI brain injury in a neonatal rat model.

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