1. Examining Reliability and Validity of the Jebsen-Taylor Hand Function Test Among Children With Cerebral Palsy.
Tofani M, Castelli E, Sabbadini M, Berardi A, Murgia M, Servadio A, Galeoto G.


PMID: 32321360


PMID: 32320751


This study explored the role of lesion timing (periventricular white matter versus cortical and deep grey matter lesions) and type of corticospinal tract (CST) wiring pattern (contralateral, bilateral, ipsilateral) on white matter characteristics of the CST, medial lemniscus, superior thalamic radiations and sensorimotor transcallosal fibers in children with unilateral cerebral palsy (CP), and examined the association with upper limb function. Thirty-four children (mean age 10 years 7 months ± 2 years 3 months) with unilateral CP underwent a comprehensive upper limb evaluation and diffusion weighted imaging (75 directions, b value 2800). Streamline count, fractional anisotropy and mean diffusivity were extracted from the targeted tracts and asymmetry indices were additionally calculated. Transcranial magnetic stimulation was applied to assess the CST wiring pattern. Results showed a more damaged CST in children with cortical and deep grey matter lesions (N = 10) and ipsilateral CST projections (N = 11) compared to children with periventricular white matter lesions (N = 24; p < 0.02) and contralateral CST projections (N = 9; p < 0.025), respectively. Moderate to high correlations were found between diffusion metrics of the targeted tracts and upper limb function (r = 0.45-0.72; p < 0.01). Asymmetry indices of the CST and sensory tracts could best explain bimanual performance (74%, p < 0.0001) and unimanual capacity (50%, p = 0.004). Adding lesion timing and CST
wiring pattern did not further improve the model of bimanual performance, while for unimanual capacity lesion timing was additionally retained (58%, p = 0.0002). These results contribute to a better understanding of the underlying neuropathology of upper limb function in children with unilateral CP and point towards a clinical potential of tractography.

PMID: 32318818

Fonseca M, Gasparutto X, Leboeuf F, Dumas R, Armand S.


Clinical gait analysis is widely used in clinical routine to assess the function of patients with motor disorders. The proper assessment of the patient's function relies greatly on the repeatability between the measurements. Marker misplacement has been reported as the largest source of variability between measurements and its impact on kinematics is not fully understood. Thus, the purpose of this study was: 1) to evaluate the impact of the misplacement of the lateral femoral epicondyle marker on lower limb kinematics, and 2) evaluate if such impact can be predicted. The kinematic data of 10 children with cerebral palsy and 10 aged-match typical developing children were included. The lateral femoral epicondyle marker was virtually misplaced around its measured position at different magnitudes and directions. The outcome to represent the impact of each marker misplacement on the lower limb was the root mean square deviations between the resultant kinematics from each simulated misplacement and the originally calculated kinematics. Correlation and regression equations were estimated between the root mean square deviation and the magnitude of the misplacement expressed in percentage of leg length. Results indicated that the lower-limb kinematics is highly sensitive to the lateral femoral epicondyle marker misplacement in the anterior-posterior direction. The joint angles most impacted by the anterior-posterior misplacement were the hip internal-external rotation (5.3° per 10 mm), the ankle internal-external rotation (4.4° per 10 mm) and the knee flexion-extension (4.2° per 10 mm). Finally, it was observed that the lower the leg length, the higher the impact of misplacement on kinematics. This impact was predicted by regression equations using the magnitude of misplacement expressed in percentage of leg length. An error below 5° on all joints requires a marker placement repeatability under 1.2% of the leg length. In conclusion, the placement of the lateral femoral epicondyle marker in the antero-posterior direction plays a crucial role on the reliability of gait measurements with the Conventional Gait Model.

PMID: 32330162

5. Comparative analysis of power, work and muscle activation during weight-stack and iso-inertial flywheel resistance exercise in young adults with cerebral palsy.


INTRODUCTION: The development of efficient resistance exercise protocols to counteract muscle dysfunction in cerebral palsy is warranted. Whether individuals with cerebral palsy are able to perform iso-inertial resistance (flywheel) exercise in a comparable manner to typically developed subjects has never been experimentally tested. DESIGN: A comparative, controlled study. SUBJECTS: Eight young ambulatory adults with cerebral palsy (mean age 19 years; Gross Motor Function Classification System (GMFCS) I-III) and 8 typically developed control subjects (mean age 21 years). METHODS: Subjects performed acute bouts on the weight-stack and flywheel leg-press device, respectively. Range of motion, electromyography, power, work and muscle thickness (ultrasound) data were collected. RESULTS: Subjects with cerebral palsy were able to produce a greater eccentric/concentric peak power ratio on the flywheel (p < 0.05 vs ratio in weight-stack), however absolute values were lower (p < 0.05 vs weight-stack). Typically developed subjects produced more power per mm of thigh muscle than the cerebral palsy group, independent of leg, device and action. DISCUSSION: Subjects with cerebral palsy could not elicit the eccentric overload seen in typically developed subjects. Furthermore, peak power production per mm muscle was markedly reduced in both legs in subjects with cerebral palsy. In conclusion, this comparative study of weight-stack and flywheel exercise does not support the implementation of the current iso-inertial protocol for young adults with cerebral palsy.

PMID: 32318745


AIM: To compare the prevalence of mental disorders (MDs) in a cohort of children and adolescents with and without cerebral palsy (CP) and to explore whether there is an association between MDs and the Gross Motor Function Classification System (GMFCS) level. METHOD: A register-linkage follow-up study of 10- to 16-year children with CP (identified in the Danish National Cerebral Palsy Registry, n = 893), and 2627 children without CP, matched by gender and age. Information on MDs was obtained from the National Patient Registry in Denmark and based on ICD-10-codes. Conditional logistic regression was performed in order to compare the prevalence of MDs. RESULTS: The prevalence of MDs was significantly higher in children and adolescents with CP (22.4%, CI 19.8-25.2%) compared with controls (6.3%, CI 5.5-7.3%). Intellectual disability was statistically significantly associated with motor function (odds ratio (OR) 4.55, CI 2.81-7.36 for GMFCS levels IV-V compared to GMFCS level I), but there were no statistically significant association between motor function and autism spectrum disorders, ADHD or affective disorders. INTERPRETATION: Our findings emphasize that follow-up of children with CP should include screening for both cognitive dysfunction and other mental disorders. The motor function does not predict the risk of other mental disorders than intellectual disability in children and adolescents with CP.

PMID: 32327392


Purpose: Adults with cerebral palsy experience challenges related to lifelong disability, such as stress, fatigue, pain and emotional issues. E-health services can be delivered regardless of residence and level of functioning. The aim of this pilot study was to explore the potential benefits and feasibility of a mindfulness-based program delivered to adults with cerebral palsy via group video conferencing. Methods: Six adults with cerebral palsy received an 8 week mindfulness group-based program via video conferencing. A multiple single-case study design was applied, including quantitative and qualitative elements. Pain was assessed 16 times through the study period. Questionnaires were administered to gather data on pain catastrophizing, stress, fatigue, emotional distress, positive and negative affect, and quality of life. A focus group interview addressed experiences with the intervention and the mode of delivery. Results: The participants' pain levels showed varied trajectories. Pain catastrophizing and negative affect were statistically significant decreased. Qualitative data indicated benefits from mindfulness in coping and stress management. The video conferencing delivery was evaluated as feasible, with no major adverse effects. Conclusion: Since the pilot study had a small sample size, potential treatment benefits should be interpreted with caution. However, this pilot study provides important information in the planning of future larger and controlled studies on mindfulness-based interventions programs via video conferencing for adults with cerebral palsy and other persons living with long-term disability.

PMID: 32318010


Over 275,000 infants are born very preterm in the US each year. Fifty percent of infants born very preterm will have some degree of neurological dysfunction limiting their ability to keep up with their typically developing peers. Clinical rehabilitation for these high-risk infants has not kept pace with advances in basic science or developmental theory. OBJECTIVE: The aim of this project is to study the effect of a physical therapy intervention provided in the first months of life on developmental outcomes of infants born very preterm. Secondary aims are to investigate the impact of intervention timing on the efficacy and
impact of the intervention on infants with and without cerebral palsy. DESIGN: This study is a multisite longitudinal controlled trial comparing developmental outcomes from infants in the SPEEDI_Late or SPEEDI_Early group to a usual care group. SETTING: Urban and rural areas surrounding 2 academic medical centers. PARTICIPANTS: There will be 90 preterm infants enrolled in this study born at ≥29 weeks of gestation. INTERVENTION: SPEEDI is a developmental intervention provided by a collaboration between a physical therapist and parent to support a child's motor and cognitive development. MEASUREMENTS: The primary outcome measure is the Bayley Scale of Infant and Toddler Development Cognitive and Gross Motor Scaled Scores. Secondary measures include behavioral coding of early problem solving skills, the Gross Motor Function Measure (GMFM), and Test of Infant Motor Performance (TIMP). LIMITATIONS: This study is powered to detect group differences between those receiving the study intervention and those receiving usual care. CONCLUSION: This study is a step towards understanding the impact of intensive developmental intervention in the first months of life. 

PMID: 32329778

9. General Movement Assessment from videos of computed 3D infant body models is equally effective compared to conventional RGB video rating.


BACKGROUND: General Movement Assessment (GMA) is a powerful tool to predict Cerebral Palsy (CP). Yet, GMA requires substantial training challenging its broad implementation in clinical routine. This inspired a world-wide quest for automated GMA. AIMS: To test whether a low-cost, marker-less system for three-dimensional motion capture from RGB depth sequences using a whole body infant model may serve as the basis for automated GMA. STUDY DESIGN: Clinical case study at an academic neurodevelopmental outpatient clinic. SUBJECTS: Twenty-nine high risk infants were assessed at their clinical follow-up at 2-4 month corrected age (CA). Their neurodevelopmental outcome was assessed regularly up to 12-31 months CA. OUTCOME MEASURES: GMA according to Hadders-Algra by a masked GMA-expert of conventional and computed 3D body model (“SMIL motion”) videos of the same GMs. Agreement between both GMAs was tested using dichotomous and graded scaling with Kappa and intraclass correlations, respectively. Sensitivity and specificity to predict CP at ≥12 months CA were assessed. RESULTS: Agreement of the two GMA ratings was moderate-good for GM-complexity (κ = 0.58; ICC = 0.874 [95%CI 0.730; 0.941]) and substantial-good for fidgety movements (FM; Kappa = 0.78, ICC = 0.926 [95% CI 0.843; 0.965]). Five children were diagnosed with CP (four bilateral, one unilateral CP). Five infants were rated as mildly abnormal with FM. GM-complexity and somewhat less FM, of both conventional and SMIL motion videos predicted bilateral CP comparably to published literature. CONCLUSIONS: Our computed infant 3D full body model is an attractive starting point for automated GMA in infants at risk of CP.

PMID: 32304982

Carter B, Bennett CV, Jones H, Bethel J, Perra O, Wang T, Kemp A.


AIM: To link routinely collected health data to a cerebral palsy (CP) register in order to enable analysis of healthcare use by severity of CP. METHOD: The Northern Ireland Cerebral Palsy Register was linked to hospital data. Data for those on the CP register born between 1st January 1981 and 31st December 2009 and alive in 2004 were extracted, forming a CP cohort (n=1684; 57% males, 43% females; aged 0-24y). Frequencies of healthcare events, and the reasons for them, were reported according to CP severity and compared with those without CP who had had at least one hospital attendance in Northern Ireland within the study period. RESULTS: Cases of CP represented 0.3% of the Northern Ireland population aged 0 to 24 years but accounted for 1.6% of hospital admissions and 1.6% of outpatient appointments. They had higher rates of elective admissions and multi-day hospital stays than the general population. Respiratory conditions were the most common reason for emergency admissions. Those with most severe CP were 10 times more likely to be admitted, and four times more likely to attend outpatients, than those with mild CP. INTERPRETATION: Linkage between a register and routinely collected healthcare data provided a confirmed cohort of cases of CP that was sufficiently detailed to analyse healthcare use by disease severity.
PMID: 32314347


OBJECTIVE: To specifically report on ataxic-hypotonic cerebral palsy (CP) using registry data and to directly compare its features with other CP subtypes. METHODS: Data on prenatal, perinatal, and neonatal characteristics and gross motor function (Gross Motor Function Classification System [GMFCS]) and comorbidities in 35 children with ataxic-hypotonic CP were extracted from the Canadian Cerebral Palsy Registry and compared with 1,804 patients with other subtypes of CP. RESULTS: Perinatal adversity was detected significantly more frequently in other subtypes of CP (odds ratio [OR] 4.3, 95% confidence interval [CI] 1.5-11.7). The gestational age at birth was higher in ataxic-hypotonic CP (median 39.0 weeks vs 37.0 weeks, p = 0.027). Children with ataxic-hypotonic CP displayed more intrauterine growth restriction (OR 2.6, 95% CI 1.0-6.8) and congenital malformation (OR 2.4, 95% CI 1.2-4.8). MRI was more likely to be either normal (OR 3.8, 95% CI 1.4-10.5) or to show a cerebral malformation (OR 4.2, 95% CI 1.5-11.9) in ataxic-hypotonic CP. There was no significant difference in terms of GMFCS or the presence of comorbidities, except for more frequent communication impairment in ataxic-hypotonic CP (OR 4.2, 95% CI 1.5-11.6). CONCLUSIONS: Our results suggest a predominantly genetic or prenatal etiology for ataxic-hypotonic CP and imply that a diagnosis of ataxic-hypotonic CP does not impart a worse prognosis with respect to comorbidities or functional impairment. This study contributes toward a better understanding of ataxic-hypotonic CP as a distinct nosologic entity within the spectrum of CP with its own pathogenesis, risk factors, clinical profile, and prognosis compared with other CP subtypes.

PMID: 32309031

Bray N, Spencer LH, Edwards RT.


INTRODUCTION: Mobility impairment is the leading cause of disability in the UK. Individuals with congenital mobility impairments have unique experiences of health, quality of life and adaptation. Preference-based outcomes measures are often used to help inform decisions about healthcare funding and prioritisation, however the applicability and accuracy of these measures in the context of congenital mobility impairment is unclear. Inaccurate outcome measures could potentially affect the care provided to these patient groups. The aim of this systematic review was to examine the performance of preference-based outcome measures for the measurement of utility values in various forms of congenital mobility impairment. METHODS: Ten databases were searched, including Science Direct, CINAHL and PubMed. Screening of reference lists and hand-searching were also undertaken. Descriptive and narrative syntheses were conducted to combine and analyse the various findings. Results were grouped by condition. Outcome measure performance indicators were adapted from COSMIN guidance and were grouped into three broad categories: validity, responsiveness and reliability. Screening, data extraction and quality appraisal were carried out by two independent reviewers. RESULTS: A total of 31 studies were considered eligible for inclusion in the systematic review. The vast majority of studies related to either cerebral palsy, spina bifida or childhood hydrocephalus. Other relevant conditions included muscular dystrophy, spinal muscular atrophy and congenital clubfoot. The most commonly used preference-based outcome measure was the HUI3. Reporting of performance properties predominantly centred around construct validity, through known group analyses and assessment of convergent validity between comparable measures and different types of respondents. A small number of studies assessed responsiveness, but assessment of reliability was not reported. Increased clinical severity appears to be associated with decreased utility outcomes in congenital mobility impairment, particularly in terms of gross motor function in cerebral palsy and lesion level in spina bifida. However, preference-based measures exhibit limited correlation with various other condition-specific and clinically relevant outcome measures. CONCLUSION: Preference-based measures exhibit important issues and discrepancies relating to validity and responsiveness in the context of congenital mobility impairment, thus care must be taken when utilising these measures in conditions associated with congenital mobility impairments.

PMID: 32318840
13. Retinal ganglion cell topography predicts visual field function in spastic cerebral palsy.
Jacobson L, Lennartsson F, Nilsson M.


The aim of this study was to evaluate the use of optical coherence tomography (OCT) to identify and assess visual field defects caused by primary damage to the optic radiation in individuals with spastic cerebral palsy (CP). Ten individuals with spastic CP (six females, four males, with a median age of 21 years [range 17-38y]) had their brain lesions documented with conventional magnetic resonance imaging (MRI) and diffusion-weighted MRI fibre tractography. Their macular ganglion cell layer (GCL) and inner plexiform layer (IPL) were examined with OCT and their visual fields were plotted. All participants had good visual acuity and were able to cooperate with the MRI and OCT examinations, as well as undergoing reliable perimetry. We found focal thinning of the GCL+IPL and corresponding homonymous visual field defects in individuals with brain damage affecting the optic radiation. We used GCL+IPL sector asymmetry as a sensitive OCT parameter to identify focal visual field defects. We observed no such sector asymmetry in GCL+IPL, or focal visual field defects, in individuals with normal MRI optic radiation imaging. Lesions affecting the optic radiation cause retrograde trans-synaptic degeneration of retinal ganglion cells. OCT examination of the GCL in the macula identified corresponding focal damage to the optic radiation in individuals with spastic CP and can be used to predict focal visual field defects. WHAT THIS PAPER ADDS: Spastic cerebral palsy (CP) may be associated with damage to the optic radiation. Damage to the optic radiation causes retrograde trans-synaptic degeneration (RTSD). RTSD can be mapped using optical coherence tomography. Ganglion cell topography can predict visual field defects in individuals with spastic CP.

PMID: 32314356

14. Cerebral palsy after very preterm birth - an imaging perspective.
Gano D, Cowan FM, de Vries LS.


Neonatal brain imaging undoubtedly can provide the most accurate information from which to determine whether cerebral palsy is likely to affect an individual infant born preterm. The sensitivity and specificity of that information is different between cranial ultrasound and MRI, depending on what approaches and sequences are used and the timing of the examinations. In this chapter we highlight the changing incidence of different patterns of brain injury in the preterm newborn and present a comparison of cranial ultrasound and MRI for predicting cerebral palsy in preterm infants affected by the commoner intracranial pathologies.

PMID: 32317152

15. Heart Rate Variability in Children and Adolescents with Cerebral Palsy - A Systematic Literature Review.


Cardiac autonomic dysfunction has been reported in patients with cerebral palsy (CP). The aim of this study was to assess the existing literature on heart rate variability (HRV) in pediatric patients with CP and a special attention was paid to the compliance of the studies with the current HRV assessment and interpretation guidelines. A systematic review was performed in PubMed, Web of Science, and Cumulative Index to Nursing and Allied Health Literature (CINAHL) databases searched for English language publications from 1996 to 2019 using Medical Subject Headings (MeSH) terms "heart rate variability" and "cerebral palsy" in conjunction with additional inclusion criteria: studies limited to humans in the age range of 0-18 years and empirical investigations. Out of 47 studies, 12 were included in the review. Pediatric patients with CP presented a significantly higher resting heart rate and reduced HRV, different autonomic responses to movement stimuli compared to children with normal development, but also reduced HRV parameters in the children dependent on adult assistance for mobility compared to those generally independent. None of the included studies contained the necessary details concerning RR intervals acquisition and HRV measurements as recommended by the guidelines. Authors of HRV studies should follow the methodological
guidelines and recommendations on HRV measurement, because such an approach may allow a direct comparison of their results.

PMID: 32316278

Limsakul C, Noten S, Selb M, Stam HJ, van der Slot WMA, Roebroeck ME.


OBJECTIVE: To identify areas of functioning in adults with cerebral palsy that are considered relevant by experts, in order to develop an International Classification of Functioning, Disability and Health (ICF) Core Set for adults with cerebral palsy.

PARTICIPANTS: Experts from various professional backgrounds worldwide who had experience working with adults with cerebral palsy for ≥2 years and were able to complete the survey in the English language. METHODS: A cross-sectional study using an international internet-based survey. The experts were asked to address relevant areas of functioning in adults with cerebral palsy. These areas of functioning were then linked to the ICF and the frequencies analysed. RESULTS: A total of 126 experts from 32 countries completed the survey. From the responses, 217 unique second-level ICF categories were identified. The three most frequently mentioned categories were "design, construction and building products and technology of buildings for public use (e150, 77%) and private use" (e155, 67%), followed by "sensation of pain" (b280, 62%). CONCLUSION: The broad diversity of ICF categories reported by the experts emphasize the known heterogeneity of cerebral palsy and the variety of functioning in adulthood. They also reported on many environmental factors, illustrating the importance of person-environment interactions. These findings provide information about relevant issues for use in developing an ICF Core Set for adults with cerebral palsy.

PMID: 32313963

17. The Effect of Cerebral Palsy Disease Severity, Socioeconomic Status, and Educational Background on Selective Percutaneous Myofascial Lengthening Reoperation Rates.
Faraji M, Yngve D.


Cerebral palsy (CP) is a neuro-developmental disorder. Spastic CP is the most common type of CP and is characterized by contractures of the extremities. Selective Percutaneous Myofascial Lengthening (SPML) is a minimally invasive procedure practiced by a handful of physicians in the US, and it decreases contractures and increases the range of motion in individuals with spastic CP. This study wanted to examine if there was an association between CP severity, socioeconomic status, and reoperation rates. This study used electronic medical records (EMR) to include 626 patients with spastic CP who had surgeries between January 2006 and December 2012. The zip codes from the EMR were used to determine the inflation-adjusted mean income and educational qualification (a high school education or higher) of the community via the US Census Bureau. Disease severity before the initial surgery was determined by using the functional mobility scale in the EMR to compute the Gross Motor Function Classification System (GMFCS) level. Then the data was graphed and averages were taken for the reoperation versus the no-reoperation populations, and Student's t-tests were run to determine statistical significance. The data showed that communities with higher education and income tended to reoperate more often. The higher number of reoperations in affluent communities could mean that either more affluent communities are better educated and know the benefits of bringing their children back for reoperation or that they require further education about physical therapy after the initial surgery to decrease the incidence of reoperation. This retrospective study is a level 2 study looking at the socioeconomic and educational backgrounds and disease severity and their association with reoperation rates.

PMID: 32313777
18. [Cervical myelopathy in the hyperkinetic form of cerebral palsy: combination of botulinum therapy with surgical treatment]. [Article in Russian; Abstract available in Russian from the publisher]  
Korsunskaya LL, Mikliaev OO, Matyazhova NA, Sidorenko NA, Romensky AO, Torgovyi DI, Kuzmishchenko IV, Krapro JA, Torgovaya MV.  
The article describes the case of cervical myelopathy with tetraparesis and sphincter disorders, as a complication of cervical dystonia in a patient with hyperkinetic form of cerebral palsy. Left-side laterocollis in combination with the same side laterocaput was noted. Myelopathy symptoms progressed gradually over one year. The main clinical problems were: the inability to conduct a qualitative MRI study due to hyperkinesis, which required anesthesia, and the high risk of perioperative complications and relapses of cervical myelopathy. Before the surgery, botulinum therapy of cervical dystonia with abobotulotoxin in the total dose 1000ED was administered that led to regression of hyperkinesis. Microsurgical decompression of the spinal canal with the installation of fixation system at the level of C7-Th1 vertebrae was performed. After surgery, the neck was fixed with a Philadelphia collar. There were no complications after surgery or displacement of the stabilizing structure. This case report indicates the possibility of development of cervical myelopathy in cervical dystonia and demonstrates the need of pre - and post-operative botulinum therapy of cervical dystonia to prevent possible complications and relapses in the postoperative period.  
PMID: 32307417

Zaino NL, Steele KM, Donelan JM, Schwartz MH.  
AIM: To determine whether energy consumption changes after selective dorsal rhizotomy (SDR) among children with cerebral palsy (CP). METHOD: We retrospectively evaluated net nondimensional energy consumption during walking among 101 children with bilateral spastic CP who underwent SDR (59 males, 42 females; median age [5th centile, 95th centile] 5y 8mo [4y 2mo, 9y 4mo]) compared to a control group of children with CP who did not undergo SDR. The control group was matched by baseline age, spasticity, and energy consumption (56 males, 45 females; median age [5th centile, 95th centile] 5y 8mo [4y 1mo, 9y 6mo]). Outcomes were compared at baseline and follow-up (SDR: mean [SD] 1y 7mo [6mo], control: 1y 8mo [8mo]). RESULTS: The SDR group had significantly greater decreases in spasticity compared to matched controls (-42% SDR vs -20% control, p<0.001). While both groups had a modest reduction in energy consumption between visits (-12% SDR, -7% control), there was no difference in change in energy consumption (p=0.11) or walking speed (p=0.56) between groups. INTERPRETATION: The SDR group did not exhibit greater reductions in energy consumption compared to controls. The SDR group had significantly greater spasticity reduction, suggesting that spasticity had minimal impact on energy consumption during walking in CP. These results support prior findings that spasticity and energy consumption decrease with age in CP. Identifying matched control groups is critical for outcomes research involving children with CP to account for developmental changes.  
PMID: 32306392

Brain Imaging Behav. 2020 Apr 18. doi: 10.1007/s11682-020-00295-6. [Epub ahead of print]  
Periventricular white matter injury (PWMI) is a common cause of spastic cerebral palsy (SCP). Diffusion tensor imaging (DTI) shows high sensitivity but moderate specificity for predicting SCP. The limited specificity may be due to the diverse and extensive brain injuries seen in infants with PWMI. We enrolled 72 infants with corrected age from 6 to 18 months in 3 groups: PWMI with SCP (n = 20), non-CP PWMI (n = 19), and control (n = 33) groups. We compared DTI-based brain network properties among the three groups and evaluated the diagnostic performance of brain network properties for SCP in PWMI infants. Our results show abnormal global parameters (reduced global and local efficiency, and increased shortest path length),
and local parameters (reduced node efficiency) in the PWMI with SCP group. On logistic regression, the combined node efficiency of the bilateral precentral gyrus and right middle frontal gyrus had a high sensitivity (90%) and specificity (95%) for differentiating PWMI with SCP from non-CP PWMI, and significantly correlated with the Gross Motor Function Classification System scores. This study confirms that DTI-based brain network has great diagnostic performance for SCP in PWMI infants, and the combined node efficiency improves the diagnostic accuracy.

PMID: 32306282

**Prevention and Cure**

Lin J, Niimi Y, Clausi MG, Kanal HD, Levison SW.  

Neonatal hypoxic-ischemic encephalopathy remains the most important neurological problem of the newborn. Delays in diagnosing perinatal brain injuries are common, preventing access to acute therapies. Therefore, there is a critical need for therapeutic strategies that are beneficial when delivered beyond 24 h after birth. Here we show that Leukemia Inhibitory Factor (LIF) functions as an essential injury-induced neurotrophic cytokine in the CNS and that non-invasively administering LIF as late as 3 days after a hypoxic-ischemic insult improves neurological function. Using a mouse model of late preterm brain injury we show that astroglial and reactivity to hypoxia-ischemia was diminished at 3 days of recovery, but then exacerbated at 2 weeks of recovery in LIF haplodeficient mice. There also were significantly more CD68+/Iba-1+ cells in the ipsilateral striatum in LIF-Het mice compared to WT mice at 2 weeks of recovery. This desynchronized glial response was accompanied by increased neuronal cell death in the striatum and neocortex (Fluorograde C), hypomyelination (reduced MBP staining and thinner external capsule), increased extent of brain damage (Nissl) and diminished neurological function on sensorimotor tests. To our surprise, injured LIF-Het mice had ~7-fold higher IGF-1 levels than injured WT mice at 3 days after HI injury. Intranasally administered LIF activated the Jak-Stat-3 pathway both within the subventricular zone and the neocortex at 30 min after administration. When delivered with a delay of 3 days after the insult, intranasal LIF reduced the extent of brain injury by ~60%, attenuated astrogliosis and microgliosis in striatum, improved subcortical white matter thickness, increased numbers of Olig2+ cells in corpus callosum and improved performance on sensorimotor tests at 2 weeks of recovery. These studies provide key pre-clinical data recommending LIF administration as a neuroprotectant and regenerative cytokine and they highlight the feasibility of pursuing new therapeutics targeting the tertiary phase of neurodegeneration for hypoxic-ischemic encephalopathies.

PMID: 32320698

Sowmithra S, Jain NK, Datta I.  

In hypoxic-ischemic encephalopathy, the Neural Progenitors (NPs) of the developing brain fail to replenish the oligodendrocyte progenitor cells lost during hypoxic-ischemic injury (HII). Here, we aim to examine the influence of HII on the vulnerability of human NPs derived from human embryonic stem cells (hESCs) with regard to cell survival and oxidative stress, followed by assessment of cellular deregulation through measuring glutathione-levels, basal-calcium, glutamate-release and intracellular-calcium [Ca2+]i response under KCl and ATP stimulation. NPs were further evaluated for their fundamental-potential of self-renewal & proliferation, neural and glial progenitor pool and migration. Oxygen-glucose-deprivation (OGD) of 90mins was sub-lethal for NPs yet significantly increased ROS generation, oxidative-stress susceptibility and decreased glutathione-levels, along with a rise in glutamate release, basal [Ca2+]i and KCl and ATP-induced [Ca2+]i. Distinct increase in gene-expression for K+ leak channel(TASK1), purinergic-receptor P2X7 and decrease of voltage-gated Kv-channels Kv1.5, Kv4.2 & Kv4.3 were observed. OGD-insulted NPs showed reduced migration-potential and decline in glial-progenitor population. Our present study thus demonstrates for the first time that brief exposure of OGD does not reduce the neural progenitor population, its
proliferation and self-renewal but can induce significant alteration in oxidative-stress susceptibility, glutamate release, $[\text{Ca}^{2+}]_i$ response to physiological stimulus, migration and glial-progenitor pool. We thus infer that treatment strategies need to target repair of NPs of the developing brain that is affected during intra-partum asphyxia leading to varying neurologic complications such as seizure, mental retardation and/or cerebral palsy.

PMID: 32326841