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Interventions and Management

1. J Child Neurol. 2012 Oct 30. [Epub ahead of print]

The Relationship Between Gross Motor Function and Manual Ability in Cerebral Palsy.

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A retrospective cohort study was conducted to describe the relationship between gross motor function and manual ability in children with cerebral palsy and explore differences between cerebral palsy subtypes and associated comorbidities. Children with cerebral palsy born between 1999 and 2008 were included from the Registre de la Paralyse Cérébrale de Québec identifying 332 children. The overall agreement between Gross Motor Function Classification System and Manual Ability Classification Scale Levels was moderate (κ 0.457, standard error 0.034) with a strong positive correlation (Spearman rho of 0.820, standard error 0.023). This agreement was moderate among children with spastic quadriplegia and dyskinetic cerebral palsy, fair in children with spastic diplegia, and poor in children with spastic hemiplegia. Children with cognitive impairment showed a higher correlation than those without cognitive impairment. The correlation between gross motor function and manual ability in children with CP varies based on neurologic subtype and cognitive level.

[PMID: 23112248](#) [PubMed - as supplied by publisher]

2. Am J Phys Med Rehabil. 2012 Sep 5. [Epub ahead of print]

Pediatric Arm Function Test: Reliability and Validity for Assessing More-Affected Arm Motor Capacity in Children with Cerebral Palsy.

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OBJECTIVE: Although there are several validated upper-extremity measures in young children with cerebral palsy, none of these primarily assess the capacity to carry out actions and tasks with the more-affected arm. To address

this need, we developed the Pediatric Arm Function Test (PAFT), which involves the behavioral observation of how children use their more-affected arm during structured play in a laboratory or clinic. This article evaluates the reliability and validity of the PAFT Functional Ability scale. DESIGN: In study 1, a total of 20 children between 2 and 8 yrs old with a wide range of upper-extremity hemiparesis caused by cerebral palsy completed the PAFT on two occasions separated by 3 wks. In study 2, a total of 41 children between 2 and 6 yrs old with similar characteristics completed the PAFT and received a grade reflecting the severity of more-affected arm motor impairment. RESULTS: In study 1, the PAFT test-retest reliability correlation coefficient was 0.74. In study 2, convergent validity was supported by a strong inverse correlation ($r = -0.6$, $P < 0.001$) between the PAFT scores and the grade of impairment. CONCLUSIONS: The PAFT Functional Ability scale is a reliable and valid measure of more-affected arm motor capacity in children between 2 and 6 yrs old with cerebral palsy. It can be used to measure upper-extremity neurorehabilitation outcome.

[PMID: 23103486](#) [PubMed - as supplied by publisher]

3. Am J Occup Ther. 2012 Nov;66(6):682-90. doi: 10.5014/ajot.2012.004556.

Effect of robotic-assisted three-dimensional repetitive motion to improve hand motor function and control in children with handwriting deficits: a nonrandomized phase 2 device trial.

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OBJECTIVE. We explored the efficacy of robotic technology in improving handwriting in children with impaired motor skills. METHOD. Eighteen participants had impairments arising from cerebral palsy (CP), autism spectrum disorder (ASD), attention deficit disorder (ADD), attention deficit hyperactivity disorder (ADHD), or other disorders. The intervention was robotic-guided three-dimensional repetitive motion in 15-20 daily sessions of 25-30 min each over 4-8 wk. RESULTS. Fine motor control improved for the children with learning disabilities and those ages 9 or older but not for those with CP or under age 9. All children with ASD or ADHD referred for slow writing speed were able to increase speed while maintaining legibility. CONCLUSION. Three-dimensional, robot-assisted, repetitive motion training improved handwriting fluidity in children with mild to moderate fine motor deficits associated with ASD or ADHD within 10 hr of training. This dosage may not be sufficient for children with CP.

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4. Am J Occup Ther. 2012 Nov;66(6):672-81. doi: 10.5014/ajot.2012.004622.

Functional impact of constraint therapy and bimanual training in children with cerebral palsy: a randomized controlled trial.

de Brito Brandão M, Gordon AM, Mancini MC.

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OBJECTIVE. We compared children's self-care performance and caregivers' perception of children's performance on functional goals established for children with hemiplegic cerebral palsy (CP) after unimanual constraint-induced movement therapy (CIMT) or hand-arm bimanual intensive training (HABIT). METHOD. Sixteen children with CP were randomized to the CIMT or HABIT group. Interventions lasted for 15 days, 6 hr/day, totaling 90 hr. We used the Pediatric Evaluation of Disability Inventory and the Canadian Occupational Performance Measure (COPM) to assess the children's daily functioning and mixed analyses of variance to compare group means on functional test scores before and after intervention. RESULTS. Both groups showed significant improvements on functional measures. Group \times Assessment interaction in COPM performance revealed greater improvements for the HABIT group after intervention ($p = .04$). CONCLUSION. The results suggest that specificity of training exists only for

performance of specific goals established by parents and that both CIMT and HABILIT can be used to increase children's daily functioning.

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[PMID: 23106987](#) [PubMed - in process]

5. BMJ Open. 2012 Oct 31;2(6). pii: e001807. doi: 10.1136/bmjopen-2012-001807. Print 2012.

Can manual ability be measured with a generic ABILHAND scale? A cross-sectional study conducted on six diagnostic groups.

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OBJECTIVES: Several ABILHAND Rasch-built manual ability scales were previously developed for chronic stroke (CS), cerebral palsy (CP), rheumatoid arthritis (RA), systemic sclerosis (SSc) and neuromuscular disorders (NMD). The present study aimed to explore the applicability of a generic manual ability scale unbiased by diagnosis and to study the nature of manual ability across diagnoses. **DESIGN:** Cross-sectional study. **SETTING:** Outpatient clinic homes (CS, CP, RA), specialised centres (CP), reference centres (CP, NMD) and university hospitals (SSc). **PARTICIPANTS:** 762 patients from six diagnostic groups: 103 CS adults, 113 CP children, 112 RA adults, 156 SSc adults, 124 NMD children and 124 NMD adults. **PRIMARY AND SECONDARY OUTCOME MEASURES:** Manual ability as measured by the ABILHAND disease-specific questionnaires, diagnosis and nature (ie, uni-manual or bi-manual involvement and proximal or distal joints involvement) of the ABILHAND manual activities. **RESULTS:** The difficulties of most manual activities were diagnosis dependent. A principal component analysis highlighted that 57% of the variance in the item difficulty between diagnoses was explained by the symmetric or asymmetric nature of the disorders. A generic scale was constructed, from a metric point of view, with 11 items sharing a common difficulty among diagnoses and 41 items displaying a category-specific location (asymmetric: CS, CP; and symmetric: RA, SSc, NMD). This generic scale showed that CP and NMD children had significantly less manual ability than RA patients, who had significantly less manual ability than CS, SSc and NMD adults. However, the generic scale was less discriminative and responsive to small deficits than disease-specific instruments. **CONCLUSIONS:** Our finding that most of the manual item difficulties were disease-dependent emphasises the danger of using generic scales without prior investigation of item invariance across diagnostic groups. Nevertheless, a generic manual ability scale could be developed by adjusting and accounting for activities perceived differently in various disorders.

[PMID: 23117570](#) [PubMed - in process]

6. Exp Brain Res. 2012 Dec;223(4):517-24. doi: 10.1007/s00221-012-3278-2. Epub 2012 Sep 29.

Movement analysis and EEG recordings in children with hemiplegic cerebral palsy.

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Impaired hand function is often the most disabling symptom in children with hemiplegic cerebral palsy (CP). Literature provides a wide number of studies dealing either with the kinematics or the cerebral correlates of the impairment. Nevertheless, few studies exist merging both aspects together. The aim of this study is the integrated analyses of time and spatial parameters of both the affected and less-affected sides and of the EEG signal, recorded during the movement execution, for the quantitative description of the pointing gesture in children with CP. The participants (pathological and control subjects) were asked to execute a pointing task simultaneously with the recording by an optoelectronic system and an electroencephalographer. Kinematic data were processed for the extraction of several synthetic indexes, to be correlated with parameters derived from frequency analysis of the electroencephalographic signal. Kinematic results showed statistical differences (1) between the affected and the less-affected arms in patients and (2) between the less-affected arm in patients and the normal arm in controls.

Further differences were found in kinematics with respect to bilateral or ipsilateral motor control, extracted from EEG. Given the different behavior evidenced by either ipsilateral or contralateral reorganization, and considering the role of feedback and feed-forward contributions to motor programming, some hypotheses emerged about the motor control during pointing task in CP.

[PMID: 23111429](#) [PubMed - in process]

7. J Hand Surg Am. 2012 Nov;37(11):2400-3. doi: 10.1016/j.jhssa.2012.08.033.

Technique of forearm osteotomy for pediatric problems.

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Correction of a rigid forearm deformity in children is often desired in congenital radioulnar synostosis, brachial plexus palsy, cerebral palsy, or posttraumatic torsional deformity. Osteotomies at the diaphyseal level present difficulties with maintenance of reduction, whether or not internal or pin fixation is used. The stabilizing and healing potential of the periosteum in these cases can be used to advantage in the correction of these deformities.

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8. Neuropediatrics. 2012 Nov 1. [Epub ahead of print]

Application of Pediatric Balance Scales in Children with Cerebral Palsy.

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9. PLoS One. 2012;7(10):e47474. doi: 10.1371/journal.pone.0047474. Epub 2012 Oct 26.

Risk factors associated with death in in-hospital pediatric convulsive status epilepticus.

Loddenkemper T, Syed TU, Ramgopal S, Gulati D, Thanaviratananich S, Kothare SV, Alsheklee A, Koubeissi MZ.

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OBJECTIVE: To evaluate in-patient mortality and predictors of death associated with convulsive status epilepticus (SE) in a large, multi-center, pediatric cohort. **PATIENTS AND METHODS:** We identified our cohort from the KID Inpatient Database for the years 1997, 2000, 2003 and 2006. We queried the database for convulsive SE, associated diagnoses, and for inpatient death. Univariate logistic testing was used to screen for potential risk factors. These risk factors were then entered into a stepwise backwards conditional multivariable logistic regression procedure. P-values less than 0.05 were taken as significant. **RESULTS:** We identified 12,365 (5,541 female) patients with convulsive SE aged 0-20 years (mean age 6.2 years, standard deviation 5.5 years, median 5 years) among 14,965,571 pediatric inpatients (0.08%). Of these, 117 died while in the hospital (0.9%). The most frequent additional admission ICD-9 code diagnoses in addition to SE were cerebral palsy, pneumonia, and respiratory failure. Independent risk factors for death in patients with SE, assessed by multivariate calculation, included near drowning (Odds ratio [OR] 43.2; Confidence Interval [CI] 4.4-426.8), hemorrhagic shock (OR 17.83; CI 6.5-49.1), sepsis (OR 10.14; CI 4.0-25.6), massive aspiration (OR 9.1; CI 1.8-47), mechanical ventilation >96 hours (OR 5.6; CI 1.75-14.6), transfusion (OR 8.25; CI 4.3-15.8), structural brain lesion (OR 7.0; CI 3.1-16), hypoglycemia (OR 5.8; CI 1.75-14.6).

19.2), sepsis with liver failure (OR 14.4; CI 5-41.9), and admission in December (OR3.4; CI 1.6-4.1). African American ethnicity (OR 0.4; CI 0.2-0.8) was associated with a decreased risk of death in SE. **CONCLUSION:** Pediatric convulsive SE occurs in up to 0.08% of pediatric inpatient admissions with a mortality of up to 1%. There appear to be several risk factors that can predict mortality. These may warrant additional monitoring and aggressive management.

[PMID: 23110074](#) [PubMed - in process] PMID: PMC3482185

10. Arch Phys Med Rehabil. 2012 Oct 24. pii: S0003-9993(12)01061-1. doi: 10.1016/j.apmr.2012.10.007. [Epub ahead of print]

Reported eating ability of young children with cerebral palsy: is there an association with gross motor function?

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OBJECTIVE: To examine the association between parent-reported ability of young children with cerebral palsy (CP) to eat different food textures and gross motor functional abilities. **DESIGN:** Prospective, longitudinal, representative cohort study. **SETTING:** Community and tertiary pediatric hospital settings. **PARTICIPANTS:** One hundred and seventy children (110 males, 65%) were assessed on 396 occasions (range 1-4 occasions), including 67 at 1yr 6 mo (49 males), 99 at 2 yrs (66 males), 111 at 2 yrs 6 mo (71 males) and 119 at 3 yrs (64 males). **INTERVENTIONS:** Not applicable **MAIN OUTCOME MEASURES:** Gross motor function was determined using the Gross Motor Function Classification System (GMFCS). Parent-reported eating ability was determined using four items of the Pediatric Evaluation of Disability Inventory (PEDI). The association between capability to eat food textures and GMFCS level was examined using generalized estimating equations. **RESULTS:** GMFCS levels at initial presentation were: I=62; II=32. III=24; IV=22; and V=30. Reported capability to eat cut up/chunky and "all textures" of table foods decreased significantly as GMFCS level increased. Decreased capability to eat pureed/blended and ground/lumpy foods compared to GMFCS I was significantly associated with GMFCS levels IV-V only. **CONCLUSION:** Reported attainment of eating skills was closely associated with GMFCS in young children with CP across age levels. These results emphasize the need for early oral motor and feeding screening in young children with CP across gross motor functional abilities.

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11. J Surg Res. 2012 Apr 18. pii: S0022-4804(12)00276-4. doi: 10.1016/j.jss.2012.03.064. [Epub ahead of print]

Need for subsequent fundoplication after gastrostomy based on patient characteristics.

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BACKGROUND: Gastrostomy tube placement is common in children. Many of the conditions associated with need for gastrostomy are also associated with gastroesophageal reflux. It is not clear how many patients without complicated reflux will subsequently require a fundoplication or which conditions increase this risk. Therefore, we performed a two-center review to determine the disease-specific propensity for fundoplication after gastrostomy tube placement. **METHODS:** The data set was retrospectively collected from two centers from 2000 to 2008. All patients underwent gastrostomy tube placement without fundoplication owing to the surgeon's discernment that fundoplication was not needed at the time. Pearson's correlation was used to evaluate the influence of patient variables and operative approach against the subsequent need for fundoplication. Significance was defined as two-tailed $P \leq 0.01$. Logistic regression analysis was used to evaluate independence. **RESULTS:** A total of 684 patients

underwent gastrostomy tube placement only, of which 124 were open, 282 laparoscopic, and 278 endoscopic (percutaneous endoscopic gastrostomy). The mean patient age was 2.9 years. Subsequent fundoplication was performed in 62 patients (9.1%). The mean interval to fundoplication was 20.7 months. Cerebral palsy and anoxic brain injury had the most significant correlation with subsequent fundoplication. These were also independent predictors. The laparoscopic approach had a negative correlation with the subsequent need for fundoplication. **CONCLUSIONS:** The low incidence of subsequent fundoplication in children who undergo gastrostomy tube placement justifies conservative use of fundoplication in the absence of complicated reflux. Those with cerebral palsy and anoxic brain injury appeared to have the greatest risk of the need for subsequent fundoplication.

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Prevention and Cure

12. *Metab Brain Dis.* 2012 Oct 27. [Epub ahead of print]

Promising outcomes in glutaric aciduria type I patients detected by newborn screening.

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Glutaric aciduria type I (GA-I) is an inborn error of lysine and tryptophan metabolism. Clinical manifestations of GA-I include dystonic or dyskinetic cerebral palsy, but when the symptoms occur, treatment is not effective. In Taiwan, newborn screening for GA-I started in 2001; we wish to evaluate the outcomes of patients detected through newborn screening. Newborns diagnosed with GA-I by abnormal dried blood spot glutarylcarnitine (C5DC) levels followed in our hospital were included in this study. They were treated with special diets, carnitine supplements, and immediate stress avoidance. Six patients were included in this study. All patients were treated prior to reaching 1 month of age. They were followed up with for 4 to 9 years. One patient had encephalopathic crisis episodes prior to turning 1 year old that caused pallidal lesions. Another patient had a chronic progressive disease during infancy that caused bilateral putamen lesions. These two patients had delayed development, but their brain lesions were resolved. The other four patients ran uneventful courses. They had normal intelligence, ranged between average to low average level and their brain magnetic resonance imaging showed only high intensity over deep white matter. Patients with GA-I diagnosed by newborn screening have promising outcomes, though the risks of disease progression prior to 1 year of age remain significant.

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13. *J Child Neurol.* 2012 Oct 30. [Epub ahead of print]

Two-Year Follow-Up Study on Neurodevelopmental Outcomes After Term Intrapartum Asphyxia Using Age and Stages Questionnaire.

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Birth asphyxia is one of the multiple causes of neonatal encephalopathy. The objective of this study was to evaluate neurodevelopmental outcomes of newborn term infants with definitive asphyxia. Thirty infants met study criteria for asphyxia. The 5-year incidence of asphyxia was estimated to be 5.5 in 1000. According to the Age and Stage Questionnaire, 10.5% of 6-month-old infants, 14.3% of 12- and 18-month-old infants, and 5.3% of 24-month-old infants had neurodevelopmental delay in gross motor function in the absence of cerebral palsy. In 7.3% of 18-month-old infants, neurodevelopmental delay in problem-solving ability was observed. Higher values of Apgar score

and bicarbonate levels were associated with higher Age and Stage Questionnaire total score. Delivery type, maternal age, gravidity of mother, and existence of mother disease during pregnancy were also associated with lower Age and Stage Questionnaire total score in different stages of life.

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14. Cereb Cortex. 2012 Oct 31. [Epub ahead of print]

Anatomic and Molecular Development of Corticostriatal Projection Neurons in Mice.

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Corticostriatal projection neurons (CStrPN) project from the neocortex to ipsilateral and contralateral striata to control and coordinate motor programs and movement. They are clinically important as the predominant cortical population that degenerates in Huntington's disease and corticobasal ganglionic degeneration, and their injury contributes to multiple forms of cerebral palsy. Together with their well-studied functions in motor control, these clinical connections make them a functionally, behaviorally, and clinically important population of neocortical neurons. Little is known about their development. "Intratelenchephalic" CStrPN (CStrPN(i)), projecting to the contralateral striatum, with their axons fully within the telencephalon (intratelenchephalic), are a major population of CStrPN. CStrPN(i) are of particular interest developmentally because they share hodological and axon guidance characteristics of both callosal projection neurons (CPN) and corticofugal projection neurons (CFuPN); CStrPN(i) send axons contralaterally before descending into the contralateral striatum. The relationship of CStrPN(i) development to that of broader CPN and CFuPN populations remains unclear; evidence suggests that CStrPN(i) might be evolutionary "hybrids" between CFuPN and deep layer CPN-in a sense "chimeric" with both callosal and corticofugal features. Here, we investigated the development of CStrPN(i) in mice-their birth, maturation, projections, and expression of molecular developmental controls over projection neuron subtype identity.

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15. J Inherit Metab Dis. 2012 Oct 30. [Epub ahead of print]

Ammonia toxicity to the brain.

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Hyperammonemia can be caused by various acquired or inherited disorders such as urea cycle defects. The brain is much more susceptible to the deleterious effects of ammonium in childhood than in adulthood. Hyperammonemia provokes irreversible damage to the developing central nervous system: cortical atrophy, ventricular enlargement and demyelination lead to cognitive impairment, seizures and cerebral palsy. The mechanisms leading to these severe brain lesions are still not well understood, but recent studies show that ammonium exposure alters several amino acid pathways and neurotransmitter systems, cerebral energy metabolism, nitric oxide synthesis, oxidative stress and signal transduction pathways. All in all, at the cellular level, these are associated with alterations in neuronal differentiation and patterns of cell death. Recent advances in imaging techniques are increasing our understanding of these processes through detailed in vivo longitudinal analysis of neurobiochemical changes associated with hyperammonemia. Further, several potential neuroprotective strategies have been put forward recently, including the use of NMDA receptor antagonists, nitric oxide inhibitors, creatine, acetyl-L-carnitine, CNTF or inhibitors of MAPKs and glutamine synthetase. Magnetic resonance imaging and spectroscopy will ultimately be a powerful tool to measure the effects of these neuroprotective approaches.

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16. J Neuroinflammation. 2012 Oct 30;9(1):247. [Epub ahead of print]**Rod microglia: elongation, alignment, and coupling to form trains across the somatosensory cortex after experimental diffuse brain injury.**

Ziebell JM, Taylor SE, Cao T, Harrison JL, Lifshitz J.

BACKGROUND: Since their discovery, the morphology of microglia has been interpreted to mirror their function, with ramified microglia constantly surveying the micro-environment and rapidly activating when changes occur. In 1899, Franz Nissl discovered what we now recognize as a distinct microglial activation state, microglial rod cells (Stabchencellen), which he observed adjacent to neurons. These rod-shaped microglia are typically found in human autopsy cases of paralysis of the insane, a disease of the pre-penicillin era, and best known today from HIV-1-infected brains. Microglial rod cells have been implicated in cortical 'synaptic stripping' but their exact role has remained unclear. This is due at least in part to a scarcity of experimental models. Now we have noted these rod microglia after experimental diffuse brain injury in brain regions that have an associated sensory sensitivity. Here, we describe the time course, location, and surrounding architecture associated with rod microglia following experimental diffuse traumatic brain injury (TBI). **METHODS:** Rats were subjected to a moderate midline fluid percussion injury (mFPI), which resulted in transient suppression of their righting reflex (6 to 10 min). Multiple immunohistochemistry protocols targeting microglia with Iba1 and other known microglia markers were undertaken to identify the morphological activation of microglia. Additionally, labeling with Iba1 and cell markers for neurons and astrocytes identified the architecture that surrounds these rod cells. **RESULTS:** We identified an abundance of Iba1-positive microglia with rod morphology in the primary sensory barrel fields (S1BF). Although present for at least 4 weeks post mFPI, they developed over the first week, peaking at 7 days post injury. In the absence of contusion, Iba1-positive microglia appear to elongate with their processes extending from the apical and basal ends. These cells then abut one another and lay adjacent to cytoarchitecture of dendrites and axons, with no alignment with astrocytes and oligodendrocytes. Iba1-positive rod microglial cells differentially express other known markers for reactive microglia including OX-6 and CD68. **CONCLUSION:** Diffuse traumatic brain injury induces a distinct rod microglia morphology, unique phenotype, and novel association between cells; these observations entice further investigation for impact on neurological outcome.

[PMID: 23111107](#) [PubMed - as supplied by publisher]**17. Rev Neurol (Paris). 2012 Apr;168 Suppl 3:S36-44. doi: 10.1016/S0035-3787(12)70045-0.****Pathophysiology of spasticity [Article in French]**

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The term "spasticity" describes the velocity-dependent increase in tonic stretch reflexes. The symptom is commonly seen in patients with injury to the central nervous system. It is rarely isolated but, instead, part of a set of symptoms that is sometimes confusing. However, the pathophysiology of the symptom has evolved over the past three decades, and it is now considered part of a global process that includes not only spinal reflex loop modifications, but also changes in the biomechanical properties of muscle fibers. Finally, recent studies of changes in the membrane properties of motor neurons and the occurrence of plateau potential have opened new perspectives. This review aims to describe these new pathophysiological models.

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18. Science. 2012 Oct 26;338(6106):491-5. doi: 10.1126/science.1218071.

Glial progenitor cell-based treatment and modeling of neurological disease.

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The diseases of myelin are among the most prevalent and disabling conditions in neurology. These diseases include both the vascular and inflammatory demyelinating disorders of adulthood, as well as the childhood leukodystrophies and cerebral palsy. These fundamentally glial disorders may be amenable to treatment by glial progenitor cells (GPCs), which give rise to astroglia and myelin-producing oligodendrocytes. Given the development of new methods for generating and isolating human GPCs, the myelin disorders may now be compelling targets for cell-based therapy. In addition, the efficient engraftment and expansion of human GPCs in murine hosts has led to the development of human glial chimeric mouse brains, which provides new opportunities for studying the species-specific roles of human glia in cognition, as well as in disease pathogenesis.

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