Background: Paradoxical kinesia (PK) in patients with idiopathic Parkinson disease (IPD) is a sudden and brief period of mobility induced by emotional or physical stress.

Objective: To evaluate improvements in mobility after an earthquake for patients with IPD classified as Hoehn and Yahr Stage 3 to 5.

Methods: 31 IPD patients attending a movement disorders clinic located near an area that experienced a major earthquake (6.0 on the Richter scale) were evaluated. The patients had been followed up for 3 to 9 years on a regular basis at the clinic. Of the 31 patients, 14 with IPD classified as Hoehn and Yahr Stage 3 to 5 were included in the study. These patients and their relatives were interviewed, and all patients had been examined after the earthquake. One patient was Stage 5 and bedridden, 10 had severe freezing episodes, and all had motor fluctuations and moderate dyskinesias. The Mini-Mental Status Examination score was <24 for all patients. Twelve patients had rapid eye movement (REM) sleep behavior disorder, 10 had severe nocturnal akinesia, 13 had fluctuating cognition, and 10 had visual hallucinations. All patients were routinely assessed by the United Parkinson's Disease Rating Scale (UPDRS), Mini-Mental Status Examination (MMSE), and Freezing of Gait Questionnaire every 2 to 3 months.

Results: All 14 patients could escape during or immediately after the earthquake, which occurred at 3:30 A.M. Eleven patients were the first in the house to be alerted by the quake and were able to alert relatives and run out of collapsing buildings. Six accomplished this from the third or fourth floor, and 9 caregivers were actually helped by the patients. Patients reported improvement in their mobility lasting several days. For 5 patients, motor improvements were recorded on the UPDRS at 2 and 5 months after the quake. There was no difference in the treatment of these 5 patients, and there was no change in cognitive scores. The disappearance or reduction of freezing was 1 of the major effects of PK.

Conclusions: All patients with moderate to severe IPD experienced PK in response to a major earthquake and were able to survive.

Reviewer's Comments: PK is an interesting but poorly understood phenomenon. It is thought to result from stimulation of noradrenergic pathways, activation of cerebellar circuitry, or activation of basal ganglia reserves. It is interesting that all patients in the more severe phases of this disease had this response and that the response lasted up to 5 months. This suggests that it is much more common than I would have predicted. It is also of interest that freezing was reduced or disappeared, as this is also surmised to be due to noradrenergic dysfunction. (Reviewer-John Schwankhaus, MD).
SICS Stenting Complications Related to Procedure

In-Hospital Complication Rates After Stent Treatment of 388 Symptomatic Intracranial Stenoses: Results From the INTRASTENT Multicentric Registry.

Kurre W, Berkefeld J, et al:

Stroke 2010; 41 (March): 494-498

In patients with symptomatic atherosclerotic intracranial stenoses treated with stents, no clinical feature was associated with an increased adverse event rate, nor was any characteristic of the treated arterial lesion.

**Objective:** To track technical success and complications in patients with symptomatic atherosclerotic intracranial stenoses (SICS) treated with stents.

**Design:** Partly retrospective, partly prospective multicenter registry.

**Participants:** Patients with SICS treated by elective stent placement.

**Methods:** Choices of stent, angiography technique, and stent deployment technique were left to individual treating physicians. Patients received aspirin and clopidogrel after the procedure. Data collected included: presenting syndrome (stroke or TIA), demographics, stroke risk factors, modified Rankin scale before procedure and at discharge, and stenosis characteristics (location, percentage of luminal narrowing, and length). Technical failure was defined as failure to place the stent or to reduce the treated stenosis to <50%. Outcomes included “non-disabling events” (TIAs or strokes leaving the patient with a modified Rankin scale [mRS] of 0 to 1), disabling events (strokes resulting in mRS of 2+), and death. Unfortunately, non-disabling events were not clearly separated into true strokes and TIAs. Postprocedural intracranial hemorrhage (ICH) was not systematically sought, but it was identified only in patients who had postprocedural scans prompted by symptoms. Patients were followed up only to discharge.

**Results:** 388 stenoses were treated during 374 procedures in 372 patients. The cohort was 75% male and was about equally divided between patients aged ≤66 years and those aged >66 years. Approximately 64% presented with stroke, and 36% presented with TIA. The cohort had the expected high incidence of comorbidities, including hypertension, diabetes, lipid disorders, tobacco use, and coronary atherosclerosis. Nearly all (85%) had severe stenosis (>70%) of the target vessel. Overall, about 10% of the procedures ended in technical failure. Rates of non-disabling and disabling events were about 5% each, while the death rate was about 2%. Therefore, about 12.5% of patients had some type of adverse event associated with the procedure, while 7% died or had a disabling stroke. The ICH rate was 3.5% and was responsible for about half of deaths and disabilities. No clinical feature was associated with an increased adverse event rate, nor was any characteristic of the treated arterial lesion. Attempts to treat middle cerebral artery stenosis were associated with increased rates of ICH; most of the ischemic strokes that were attributed to occlusion of perforating arteries arising from the treated segment were associated with basilar artery procedures.

**Conclusions:** The complications noted were inherent to the procedure and not associated with any particular patient or lesion characteristic.

**Reviewer's Comments:** In view of the lack of evidence of efficacy for intracranial stents, I will refer patients meeting criteria to the randomized controlled trial now being conducted in the United States, which examines both technical aspects and efficacy. (Reviewer-James W. Schmidley, MD).

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Keywords: Intracranial Atherosclerosis, Arterial Stents, Complications

Print Tag: Refer to original journal article
Autobiographical Memory Most Impaired in TEA

Remote Memory Deficits in Transient Epileptic Amnesia.

Milton F, Muhlert N, et al:

Brain 2010; 133 (May): 1368-1379

In transient epileptic amnesia, severely impaired memory for autobiographical events extends across the entire lifespan.

**Objective:** To define the nature of the memory deficit in transient epileptic amnesia (TEA).

**Methods:** 14 patients had witnessed episodes of transient amnesia with intact cognitive functions other than memory. Evidence for epilepsy was based on epileptiform abnormalities on EEG, concurrent other clinical features such as lip-smacking or olfactory hallucinations, or response to anticonvulsant therapy. All patients were receiving anticonvulsant medication and had been seizure-free for at least 18 months. Neuropsychological testing for anterograde memory included immediate and delayed recall and recognition of a prose passage, delayed copying of the Rey-Osterrieth figure, and a paired associates learning test. Remote autobiographical memory was tested by having patients recall a unique autobiographical event lasting <0.5 day for each decade of their lives, with attention paid to event, place, time, and perceptual and emotional details and scoring for “episodic richness.” Where possible, accuracy was verified by spouses. Additionally, remote autobiographical memory was assessed using the Crovitz Interview in which patients described a personal event connected to a particular high frequency noun such as “table” or “ship.” Personal semantic memory was assessed using questions about personal facts for each decade, such as friends, home addresses, jobs, and family events. Public semantic memory was assessed using tests such as whether a famous person was dead or alive, whether a famous event was real or fictitious, and whether recently invented words such as “Wi-Fi” could be defined. Patients were compared to healthy control subjects.

**Results:** Most seizures were brief and frequent. MRI in 13 did not show major structural pathology. Patients performed normally on tests of anterograde memory. In contrast, memory for autobiographical events was impaired across the entire lifespan. Personal semantic memory was impaired to a lesser degree, and public semantic memory was impaired only mildly for recent decades.

**Conclusions:** TEA is associated with “focal retrograde amnesia,” which is an inability to retrieve memories that have been successfully acquired in the past. These findings might reflect subtle structural pathology in the hippocampus, as described in volumetric studies. Such interpretation would be consistent with the view that semantic but not episodic memory becomes independent of the hippocampus over time. Alternatively, the findings might reflect propagation of epileptiform activity through a network of brain regions responsible for long-term memory.

**Reviewer's Comments:** Much is yet to be learned about where long-term memories reside in the brain and the role of the hippocampus in their retrieval. (Reviewer-John C. Brust, MD).

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Keywords: Transient Epileptic Amnesia, Remote Memory, Autobiographical Memory, Focal Retrograde Amnesia

Print Tag: Refer to original journal article
Early postoperative tapering of antiepileptic drugs (AED), seizure occurrence before AED reduction, normal preoperative MRI, and longer disease duration predict greater risk of relapse after postoperative AED withdrawal.

**Background:** Most data regarding the success of epilepsy surgery have been accumulated from patients undergoing surgery for mesial temporal lobe epilepsy, which is reported to be quite successful with long-term follow-up.

**Objective:** To determine the prevalence of successful withdrawal of antiepileptic drugs (AED) and to identify predictors of seizure recurrence after AED reduction after neocortical resectional epilepsy surgery.

**Design:** Retrospective case review.

**Participants:** 223 consecutive patients who had undergone resectional surgery for intractable neocortical epilepsy. Of these patients, 100 had neocortical temporal lobe epilepsy, 69 had frontal lobe epilepsy, 23 had parietal lobe epilepsy, 25 had occipital lobe epilepsy, and 6 had multifocal epilepsy.

**Methods:** All subjects underwent video EEG monitoring, brain MRI, PET scanning, intracarotid amobarbital test, and ictal/interictal SPECT when possible. Surgery consisted of simple lesionectomy or lobectomy in patients with MRI lesions that correlated well with ictal scalp EEG and semiology. The mean period of observation was 84.4 months (range, 24-152 months) after surgery and was 72.6 months (range, 12-138 months) after initial AED reduction.

**Results:** AED reduction was attempted in 147 patients (66%), 78 of whom (53%) had seizure recurrence after initial reduction. Discontinuation of AED was achieved in 73 patients (33%), and 59 of these (81%) remained seizure-free until final assessment. On multivariate analysis, the independent significant risk factors for seizure recurrence included AED tapering earlier than the ninth postoperative month, the absence of focal lesions on MRI, seizures occurring between surgery and AED reduction, and duration of epilepsy >11 years. The incidence and hazard ratio of seizure recurrence increased with an increasing number of these risk factors. Overall, 27.4% of these patients were seizure-free without drugs, and 26.9% were seizure-free with drugs.

**Conclusions:** The complete cure rate of intractable neocortical epilepsy by resectional surgery was 27.4%, although another 27% of subjects were seizure-free with continued AED treatment. Risk factors for recurrence of seizures after decrease in AED treatment include early tapering before 9 months, normal MRI preoperatively, seizure occurrence before AED reduction, and epilepsy duration >11 years. For patients whose AED reductions started >2 years postoperatively, the relapse rate was only 33.3%.

**Reviewer’s Comments:** This study indicates that overall results after neocortical epilepsy surgery may be equivalent to those achieved with temporal lobectomy for mesial temporal lobe epilepsy. The results suggest that early epilepsy surgery might be better to prevent the presumed secondary epileptogenesis in epilepsy with continued seizures, although there is currently no general agreement on such an assumption. Overall, about a quarter of patients with neocortical epilepsy can be cured with surgery and another quarter can be rendered seizure-free with continued AED treatment. (Reviewer-W. Steven Metzer, MD).

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**Keywords:** Neocortical Resectional Epilepsy Surgery, AED Withdrawal, Predicting Seizure Recurrence

**Print Tag:** Refer to original journal article
Hyperfamiliarity for faces (HFF) may be more common than suggested by the literature. Lesions causing HFF are more often left-sided and most often involve the temporal lobe.

**Background:** Hyperfamiliarity for faces (HFF) is a disorder in which unfamiliar people or faces appear familiar.

**Objective:** To report the findings of 4 cases of HFF seen by the authors as well as 5 other cases from the literature.

**Case Report:** An illustrative case was that of a 62-year-old right-handed attorney who had developed partial epilepsy at age 31 years. Seizures involved severe anxiety, palpitations, déjà vu, and a “bad nightmare.” A subsequent convulsion led to medical attention. Phenytoin controlled the generalized but not the partial seizures. MRI showed a nonenhancing mass of the left parahippocampal gyrus/hippocampus. Video EEG showed a left temporal seizure focus. During some seizures, the attorney felt that a complete stranger was someone he had known for the past 20 years.

**Results:** Three of the 4 cases had pathologic findings most extensive in the left temporal area. HFF occurred after tonic-clonic seizures in 2, during simple partial seizures in 1, and in the setting of increased simple partial seizures (but not during seizures) in the other. All 9 cases occurred in adults with seizures. The duration of HFF was seconds to minutes in the ictal case and 2 days to 7 years in the others. Lesions or seizure foci were on the left in 5, bilateral in 2, and unknown in 2. Six of the 7 cases with known localization were localized to the temporal lobe. Known lesions included remote trauma in 1, stroke in 2, and low-grade tumor in 1. Two had persistent HFF after a seizure. These 2 had no abnormalities on MRI and no history of remote head injury, so the etiology was unknown. While HFF appeared to be due to a post-ictal phenomenon in several cases, the etiology in the persistent cases remains unknown.

**Conclusions:** Lesions causing HFF are more often left-sided and most often involve the temporal lobe. Epilepsy and seizures were present in all cases. HFF is thought to be more common than reported.

**Reviewer's Comments:** Studies have identified the hippocampus as important for recollection and the perirhinal cortex as important for feelings of familiarity. Hyperfamiliarity, such as déjà vu, can occur through stimulation of the amygdala, hippocampus, and perirhinal cortex, especially on the right side. HFF may result from left temporal dysfunction impairing detection of specific facial features while at the same time disinhibiting right temporal regions that falsely signal familiarity. (Reviewer-John Schwankhaus, MD).
Thermal Hypoesthesia Distinguishes Primary, Secondary RLS

Thermal Hypoaesthesia Differentiates Secondary Restless Legs Syndrome Associated With Small Fibre Neuropathy From Primary Restless Legs Syndrome.

Bachmann CG, Rolke R, et al:

Brain 2010; 133 (March): 762-770

Thermal hypoesthesia is present in restless legs syndrome (RLS) secondary to small fiber neuropathy but it is not present in idiopathic RLS.

Objective: To assess whether quantitative sensory testing could differentiate primary restless legs syndrome (RLS) from secondary RLS associated with small fiber neuropathy.

Methods: RLS was diagnosed in 34 patients using standard criteria. All had an urge to move the legs usually accompanied or caused by uncomfortable or unpleasant sensations in the legs. The urge to move began or worsened during periods of rest or inactivity, was partially or totally relieved by movement as long as the activity continued, and was worse at night than during the day. Three men and 18 women (age 53 ±8 years) had idiopathic RLS. One man and 12 women (age 63 ±8 years) had secondary RLS with small fiber neuropathy, suspected on examination and confirmed by skin biopsy.

Results: In the primary RLS group, only 1 patient reported shooting pain, which responded completely to dopaminergic therapy. In the secondary RLS group, except for 1 patient who reported only numbness, all patients reported positive symptoms (usually pain) which did not respond to dopaminergic therapy. Patients in the secondary RLS group preferentially responded to neuropathic pain medication, including gabapentin and pregabalin. A positive family history was found in two-thirds of idiopathic RLS patients and one-third of secondary RLS patients. All patients underwent quantitative sensory testing that consisted of 13 parameters involving thermal, painful, and vibratory sensation. Patient groups were compared to each other and to healthy control subjects. The main findings were that both groups had hyperalgesia to pinprick, but only the secondary RLS group had marked loss of small fiber function, with hypoesthesia to both cold and warm stimuli. Patients with idiopathic RLS did not show loss of any sensory function and had lower vibratory detection thresholds and pressure-pain thresholds.

Conclusions: While both idiopathic and secondary RLS have hyperalgesia, increased thermal detection thresholds distinguish RLS secondary to small-fiber neuropathy from idiopathic RLS. A common physiological abnormality in both groups might be sensitization or disinhibition of dorsal horn circuits underlying nociceptive transmission. In the case of idiopathic RLS, disinhibition might be the result of malfunctioning dopamine-influenced descending regulatory pathways. In the case of small-fiber neuropathy, sensitization or disinhibition might follow a shift in the balance of excitatory and inhibitory influences resulting from peripheral nerve injury or inflammation.

Reviewer’s Comments: The authors' speculation as to different mechanisms of sensitization or disinhibition is consistent with the fact that most patients with idiopathic RLS have symptomatic improvement taking levodopa or a dopamine agonist, whereas most patients with RLS secondary to small-fiber neuropathy do not. (Reviewer-John C. Brust, MD).

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Keywords: Primary vs Secondary Restless Legs Syndrome, Small Fiber Neuropathy, skin biopsy

Print Tag: Refer to original journal article
In obstetric brachial plexus palsy, recovery of elbow flexion, shoulder external rotation, and forearm supination by age 3 months strongly predicts complete recovery.

**Background:** Most newborn infants with obstetric brachial plexus palsy (OBPP or Erb palsy) will have a complete recovery, but some will have lifelong functional deficits.

**Objective:** To evaluate and identify the incidence of OBPP in newborn infants, the early prognostic indicators that predict recovery, and the functional outcome at age 18 months.

**Design/Participants:** A prospective study of all infants born in western Sweden during a 2-year study interval.

**Methods:** Those with OBPP were identified by a neonatologist and were then followed up by a physiotherapist with serial examinations during the first week after birth and again at 2 weeks and 3, 6, 12, and 18 months of age. If the exam was normal at age 3 months, then the 6-month and 12-month visits were skipped, and the final examination was performed at 18 months. A standard protocol was used to record muscle strength, range of motion, and hand preference at each visit. Established scales were used to assess functional skills at age 18 months, and the severity of OBPP was classified.

**Results:** OBPP was identified in 114 of 38,749 newborn infants. The affected infants included 70 boys and 44 girls. The incidence of OBPP was 2.9/1000 live births. The incidence of OBPP for vaginal deliveries was 3.6/1000 live births. Complete recovery of function had occurred by age 3 months in 50% of newborns and by age 18 months in 82%. The prevalence of persistent deficits due to OBPP at age 18 months was approximately 0.5/1000 infants. At age 3 months, the best predictor of complete recovery was elbow flexion (predictive value, 100%) followed by shoulder external rotation (predictive value, 99%) and forearm supination (predictive value, 96%). Of 18 children with persistent impaired function at age 18 months, the degree of impairment was mild in 5, moderate in 11, and severe in 2. Surgery on damaged nerves had been performed on 3 children.

**Conclusions:** OBPP occurs in about 3 per 1000 live births, and residual deficits persist at 18 months in 0.5 per 1000. Recovery of elbow flexion, shoulder external rotation, and forearm supination by age 3 months is strongly predictive of complete recovery.

**Reviewer's Comments:** Approximately 80% of children with OBPP will experience complete recovery of function. Examination at age 3 months can be used to predict recovery. (Reviewer-Gregory B. Sharp, MD).
Chronic cerebrospinal venous insufficiency as a cause of multiple sclerosis is unproven and does not justify invasive intervention at this time.

Background: A vascular surgeon in Italy has reported that multiple sclerosis (MS) patients have stenosis of the internal jugular veins rarely found in other neurologic disorders and normal subjects. It is postulated that the resulting chronic cerebrospinal venous insufficiency (CCSVI) somehow leads to the development of MS. Angioplasty and/or stenting opens the stenosis in 100% of cases. Some patients improve, mostly in the relapsing-remitting MS cohort. Although the findings are unconfirmed, MS chat rooms on the Web have spread the news, and the demand for the stenting procedure has skyrocketed among MS patients. Some surgeons have accommodated these patients, alarming many other physicians that an expensive, unproven, and potentially dangerous therapy has been unleashed. While anecdotal claims of improvement abound on the Internet, less is said of the procedure’s potential dangers, such as stent migration to the heart. A panel of MS experts has reviewed these developments and issued a position paper.

Objective: To examine CCSVI for any technical or conceptual shortcomings, to evaluate its relationship with MS pathophysiology, and to identify the research that must be completed before stenting can be recommended. Technical Shortcomings: Technically, there are no standardized Doppler criteria for abnormal venous return, and others have reported internal jugular valve insufficiency in 29% to 38% of healthy volunteers. The ultrasound studies behind CCSVI are not detailed and include no reference standard such as MRI for intracranial vascular evaluation. Lack of MRI disallows for any correlation between plaque topography and refluxing veins. The angioplasty study suffers from small sample size, unblinded neurologic evaluations, restenoses in 47%, inconsistent MRI protocols, concomitant disease-modifying therapies, and a lack of controls, all of which undermine any interpretation of “efficacy” attributed to angioplasty. Conceptual Shortcomings: CCSVI should worsen with age, but the inflammation associated with MS actually subsides. Known causes of cerebral venous hypertension (cerebral venous thrombosis, pseudotumor cerebri, radical neck dissection, pulmonary hypertension) do not increase the risk for MS. Although optic neuritis is common among MS patients, venous stasis retinopathy is not. Genes known to increase risk of MS and other autoimmune diseases have no association with venous disease. CCSVI cannot help explain the geographic distribution of MS or the role of vitamin D and EBV infection in MS.

Conclusions: Invasive, potentially dangerous endovascular procedures for MS patients should be avoided until the appropriate studies have been completed, analyzed, and debated in the scientific community.

Reviewer’s Comments: The cerebral veins in MS are known to be abnormal. Inflammatory cells show a perivenular not a peri-arteriolar distribution. Perhaps local venous congestion is a necessary condition for all the other better-studied risk factors of MS to play out their pathophysiologic roles. Alternatively, the venous anomalies could be secondary to other disease processes in MS or simply an epiphenomenon. (Reviewer-Michael Jacewicz, MD).

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Keywords: Chronic Cerebral Venous Insufficiency

Print Tag: Refer to original journal article
In patients presenting with low back pain, high psychiatric comorbidities, high-intensity fear avoidance behavior, and greater degrees of somatization predict persistent disabling low back pain.

**Objective:** To determine if patient characteristics, findings on exam, or symptom questionnaires can predict whether a patient with acute low back pain (LBP) will develop persistent disabling LBP (PDLBP).

**Methods:** Studies from the literature were included if they evaluated patients who had acute LBP for <8 weeks and prospectively assessed the ability of patient characteristics, exam findings, or results from various symptom questionnaires to accurately predict which patients would go on to develop PDLBP at 3 months and/or 1 year. Only findings from the clinical evaluation were used (no radiographic studies were considered). Twenty studies evaluating >10,000 patients were ultimately used in this analysis. Sensitivities, specificities, and likelihood ratios (LRs) were calculated. A positive LR was defined as the odds of developing PDLBP if the characteristic/attribute was present. A negative LR was defined as the odds of developing PDLBP in patients without the characteristic. Age, gender, education, smoking status, body mass index, general level of health, psychiatric comorbidities, prior episodes of LBP, intensity of pain, degree of impairment, level of job satisfaction, level of physical demands involved, work/compensation/litigation status, and fear avoidance behavior (FAB) were considered. FAB means not doing something for fear it will worsen pain or further injure the spine. Exam findings considered were the presence or absence of radiculopathy and evidence of somatization, including the Waddell signs. Several risk assessment questionnaires based on symptoms were also examined.

**Results:** High psychiatric comorbidity, high levels of FAB, and greater degrees of somatization were associated with LRs near 2.0. Low overall health status and low work satisfaction were associated with LRs of approximately 1.5. Radiculopathy, a physically demanding job, and receiving or seeking workers compensation were associated with significant LRs, but all were <1.5. Age, BMI, gender, education, and prior episodes of LBP were not (or just barely) significant. As expected, the studies were heterogeneous, with about one-third analyzing workers compensation populations and the rest analyzing primary care populations. Outcome measures also varied widely, with some concentrating on work or disability and others focusing on pain and overall functioning. The findings were similar regardless of the population evaluated, the outcome evaluated, or the duration of acute low back pain (0-4 weeks vs 4-8 weeks).

**Conclusions:** Not one of the various questionnaires was sufficiently powerful to be recommended for routine use. Research is needed on optimal early intervention strategies aimed at individuals with acute LBP who are likely to go on to PDLBP.

**Reviewer’s Comments:** No clinician who sees patients with LBP will be surprised by these findings, except perhaps the lack of association between BMI and PDLBP. I was left with the impression that early interventions to nip FAB and persistent inactivity in the bud are most likely to be fruitful. (Reviewer-James W. Schmidley, MD).

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Keywords: Back Pain, Disability, Risk Prediction

Print Tag: Refer to original journal article
During stroke recovery, the topological structure of the motor-related network undergoes dynamic reorganization.

**Background:** Following stroke, cortical reorganization may contribute to restoration of motor function. Recent cognitive neurological studies of neuroplasticity and cortical reorganization have focused on “graph theory” and “small-world networks” assessed through functional MRI (fMRI).

**Objective:** To identify dynamic changes in the functional organization of the motor execution network during stroke recovery.

**Design:** Longitudinal prospective controlled study.

**Participants:** 10 right-handed patients (mean age, 48.3 years) with left subcortical infarcts with residual motor deficit were included. There were also 3 age-matched cohort normal control groups.

**Methods:** The 10 stroke subjects underwent resting-state fMRI about 1 week, 2 weeks, 1 month, 3 months, and 1 year after their stroke. Clinical recovery was monitored using the Modified Rankin Scale, the Barthel Index, and the NIH Stroke Scale. fMRI focused on a total of 21 regions of interest 10 mm in diameter, including bilateral primary motor cortex, bilateral premotor cortex, bilateral superior parietal lobule, basal ganglia, thalamus, and anterior inferior cerebellum.

**Results:** There was a progressive clinical recovery process in motor deficits related to stroke, which significantly correlated with increased regional “centrality” within the network in the ipsilesional primary motor area and the contralesional cerebellum. The ipsilesional cerebellum showed decreased regional “centrality.” The results indicated a shift toward random networks over time, associated with clinical improvement. Connectivity between ipsilesional primary motor cortex and contralesional key motor areas were significantly increased; most of these connectivities significantly correlated with the degree of motor recovery.

**Conclusions:** The topological structure of the motor-related network undergoes dynamic reorganization during stroke recovery. The increased “betweenness” in ipsilesional primary motor cortex and contralesional cerebellum may contribute to stroke recovery.

**Reviewer’s Comments:** As pointed out by the authors, this study expands our understanding of the spectrum of changes occurring in the brain after stroke and opens up a new avenue for investigating lesion-induced network plasticity. This is a difficult paper to read, and much of the discussion of this research is beyond the scope of this review. However, my recent experience at the Cognitive Neurology Session of the Annual American Academy of Neurology meeting indicates that this is a very important area of research. (Reviewer-W. Steven Metzer, MD).

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**Keywords:** Stroke, Motor Restoration, Function Reorganization, Small-World Networks

**Print Tag:** Refer to original journal article
Although felbamate should be used with caution, it can be very effective in the treatment of some children with severe intractable epilepsy.

**Background:** Most typically, felbamate is used sparingly in the treatment of epilepsy due to the potential risk for the development of aplastic anemia or hepatic failure. In general, the treating physician must always consider the potential benefit versus risk when prescribing any medication. With felbamate, the clinician may ask if the potential benefit ever outweighs the risk. To date, 34 cases of aplastic anemia have been reported in patients exposed to felbamate. The complete diagnostic criteria for aplastic anemia were met in 23 cases, and felbamate was determined to be the definite or most likely etiologic agent in 14 cases. The youngest patient who has developed aplastic anemia on felbamate was 13 years of age. Since 1994, there have been 40,000 new patient exposures to felbamate and only 1 case of associated aplastic anemia. There have been a total of 18 reported cases of hepatic failure in 9 children and 9 adults taking felbamate. Of these, 7 cases and 1 death were determined to be likely related to felbamate. It is notable that the risk of hepatic failure and death in children, especially under 2 years of age, is much higher with the use of valproate than with felbamate.

**Objective:** To note the efficacy of felbamate in the treatment of children with intractable epilepsy.

**Methods:** 38 children with medically refractory epilepsy who had been treated with felbamate at a single pediatric center were retrospectively identified. Felbamate was typically initiated as adjunctive therapy, and the dosage was titrated to 30 to 100 mg/kg per day in divided doses (2 to 3 times daily).

**Results:** Approximately 60% (n=22) of these children who were treated with felbamate had Lennox-Gastaut syndrome, 6 had myoclonic-astatic epilepsy of Doose, 5 had other forms of symptomatic generalized epilepsy, and 5 had symptomatic localization-related epilepsy. As a general rule, most of these children had frequent seizures, multiple seizure types, and had been treated with multiple antiepileptic drugs. Just over 60% of patients experienced a >50% reduction in seizure frequency in response to felbamate, and 15% became seizure-free, including 4 of 6 with myoclonic-astatic epilepsy of Doose. None of these children experienced serious adverse events. One patient discontinued use due to the development of tics. There were no cases of aplastic anemia or hepatic failure.

**Reviewer’s Comments:** There is a significant risk for the development of aplastic anemia and hepatic failure associated with felbamate treatment, and it is never indicated as initial therapy or for benign forms of epilepsy in children. It is an appropriate consideration to use felbamate when the potential benefit likely outweighs the risk in children with devastating forms of epilepsy and uncontrolled seizures. (Reviewer-Gregory B. Sharp, MD).

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Keywords: Felbamate, Epilepsy

Print Tag: Refer to original journal article
Antihistamines are commonly overused to treat upper respiratory infection symptoms in young children and may possibly contribute to an increased risk for febrile seizures.

**Background:** Antihistamines are often given to children with upper respiratory infections at an age when febrile seizures may occur. Histaminergic neurons are involved in many regulatory processes and have a wide distribution within the central nervous system. High histamine levels increase seizure threshold, so antihistamines may produce the opposite effect. Histamine 1 and histamine 3 receptor binding may decrease epileptiform activity. There have been reports of antihistamines being linked to seizures in children without epilepsy. Febrile seizures are frequently seen in the United States, but are twice as common in Japan. **Objective:** To determine if antihistamines increase the occurrence and duration of febrile seizures in young children. **Design:** Retrospective study. **Participants:** 49 children with febrile seizures who were admitted to a single center in Japan. All had relatively prolonged febrile seizures that contributed to the decision to admit. **Methods:** Seizure duration and the time from fever detection to seizure onset were determined and compared between simple and complex febrile seizure groups. Medication history that specifically documented antihistamine use was recorded. **Results:** One of the criteria for a simple febrile seizure is duration <20 minutes. For this and other reasons, there were more children admitted with complex febrile seizures (n=35) than simple febrile seizures (n=14). Antihistamines had been given to 23 of these children. The time from detection of fever to seizure onset was shorter in children who received an antihistamine (3 hours) than in those who did not (4 hours). In addition, seizure duration was longer in children who received an antihistamine (40 minutes) than in those who did not (30 minutes). These findings were statistically significant, and, in general, held true in the groups of children with simple and complex febrile seizures. **Conclusions:** Antihistamines may lower the seizure threshold and increase seizure duration in a sick child who is at risk for febrile seizures. **Reviewer's Comments:** Hypothetically, antihistamines given to children during febrile illnesses may contribute to the occurrence of febrile seizures. To adequately evaluate the relationship between antihistamine use and febrile seizures, a larger case-control study would need to be performed that included a more typical group of children with febrile seizures. Febrile seizures are most commonly of short duration, and most children with febrile seizures are not admitted to the hospital. (Reviewer-Gregory B. Sharp, MD).

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Keywords: Antihistamines, Febrile Seizures

Print Tag: Refer to original journal article
Although Effective, Avoid Quinine for Muscle Cramps

Assessment: Symptomatic Treatment for Muscle Cramps (An Evidence-Based Review).
Katzberg HD, Khan AH, So YT:
Neurology 2010; 74 (February 23): 691-696

Quinine is modestly effective for muscle cramps but is so toxic that it should be avoided. Diltiazem and vitamin B complex may be effective.

**Background:** Muscle cramps are involuntary, painful contractions of a muscle or muscle group. In 2006, the Food and Drug Administration, citing dangerous side effects, disapproved quinine as the major treatment of cramps or for any disease other than malaria.

**Objective:** To review the literature on symptomatic treatment of cramps.

**Methods:** EMBASE and MEDLINE were searched for prospective treatment trials of muscle cramps not caused by pregnancy, medical conditions such as cirrhosis and renal failure, or physiologic stresses such as excessive exercise and dehydration. A study was graded “class I” if it was a high-quality randomized, controlled trial (RCT) and “class II” if it was a prospective matched-group cohort study or if it was an RCT lacking adequate randomization or blinding, or liable to attrition or outcome ascertainment bias. A recommendation was graded “level A” (treatment definitely effective, ineffective, safe, or unsafe), “level C” (treatment possibly effective, ineffective, safe, or unsafe), or “level U” if data were inadequate.

**Results:** Of the 24 studies found, most (13) involved quinine 200-500 mg qhs. Two class I and 2 class II studies showed efficacy of a small magnitude, and 2 class II studies showed no efficacy. Serious side effects were rare (2% to 4% of patients) and included hemolytic-uremic syndrome, hypoglycemia, and cardiac arrhythmia. Minor side effects occurred often (up to 20% of patients) and included cinchonism (headache and tinnitus) and bitter taste. No studies of quinine water (“tonic”) were found. Gabapentin was the only other drug for which a class-I study (negative) was found. Single class-II studies showed modest benefit from vitamin B complex (including vitamin B6 30 mg/day), diltiazem, and naftidrofuryl (unavailable in the United States), but no benefit was demonstrated with magnesium or vitamin E. Data were inadequate from a class-II study of calf stretching to prevent cramps. No studies of carbamazepine, oxcarbazepine, phenytoin, or baclofen were found.

**Conclusions:** Quinine is modestly effective for muscle cramps, but it is so toxic that it should be avoided unless cramps are disabling and unresponsive to other agents and the patient understands how serious the side effects may be (level A). Diltiazem and vitamin B complex may be effective (level C). Data for calf stretching are inadequate (level U).

**Reviewer's Comments:** Muscle cramps are a common symptom in patients with and without neuromuscular disease. Quinine, the most effective treatment, is too toxic to use routinely, and no other drug has convincing evidence of efficacy in either the literature or personal experience. (Reviewer-Marc D. Winkelman, MD).

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Keywords: Muscle Cramp, Symptom Management, Treatment Guideline, Quinine

Print Tag: Refer to original journal article
Children With ADHD More Likely to Also Have Epilepsy

Epilepsy in Children With Attention-Deficit/Hyperactivity Disorder.


It is known that children with epilepsy have an increased risk for attention-deficit/hyperactivity disorder (ADHD), and children with ADHD appear to have a greater incidence and severity of epilepsy.

**Background:** Previous studies have shown an increased risk for attention-deficit/hyperactivity disorder (ADHD) in pediatric epilepsy patients. However, there are few studies that have examined the risk of seizures in children with ADHD.

**Objective:** To examine the incidence of epilepsy in children with ADHD compared to those without ADHD, and to compare the characteristics of epilepsy in children with and without ADHD.

**Participants:** The study initially included 5718 participants identified from school records for every child born in Rochester, Minnesota, from 1976 to 1982.

**Methods:** A 5-step approach was performed to identify cases of ADHD. Subjects with a diagnosis of autism, severe mental retardation, schizophrenia, or other psychotic disorder were excluded. For each identified ADHD case, 2 controls without ADHD were selected from the same birth cohort. All ADHD cases and controls were screened for medical diagnostic index codes indicative of seizure activity. A retrospective review of the medical records from birth until the last medical examination preceding age 20 years was performed.

**Results:** There were 358 children with a diagnosis of ADHD and 728 controls. A positive seizure history was identified in 23 children with ADHD and 32 controls. There was no difference between the 2 groups in the incidence of single unprovoked, febrile or other provoked seizures. Children with ADHD were 2.7 times more likely to have epilepsy than were controls, although statistical significance was not reached. Those with ADHD and epilepsy were also more likely to have earlier seizure onset, and there was a trend toward more frequent seizures. Among those who met research criteria for ADHD, children with epilepsy were less likely to be treated with stimulant medication. There was also a trend toward a greater decline in cognitive function over time in the group with, compared to those without epilepsy.

**Reviewer's Comments:** Although statistical significance was not reached, there were compelling trends to indicate a greater incidence and severity of epilepsy among children with ADHD. The physician should be aware of the increased risk of seizures in children with ADHD, as well as the increased risk for ADHD in children with epilepsy. (Reviewer-Gregory B. Sharp, MD).

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Keywords: Epilepsy, Attention-Deficit/Hyperactivity Disorder

Print Tag: Refer to original journal article
Blood, CSF Markers and MRI Lesions Distinguish SCS

Spinal Cord Sarcoidosis: Clinical and Laboratory Profile and Outcome of 31 Patients in a Case-Control Study.

Cohen-Aubart F, Galanaud D, et al:

Medicine 2010; 89 (March): 133-140

Spinal cord MRI as well as blood and cerebrospinal fluid markers help to distinguish spinal cord sarcoidosis from other causes of myelopathies.

Background: Neurological manifestations of sarcoidosis occur in 5% to 15% of patients and may affect any part of the central and peripheral nervous systems. Spinal cord sarcoidosis (SCS) is rare but is often included in the differential diagnosis of patients presenting with subacute myelopathy.

Objective: To describe the clinical, laboratory, and imaging features of SCS and to compare them to myelopathies of other causes.

Design: Multicenter, retrospective case-control study from 2 tertiary hospitals in France.

Methods: Patients fulfilling the following 4 criteria for SCS were included: (1) signs of myelopathy; (2) intramedullary lesion; (3) biopsy evidence of noncaseating granuloma or 30% to 50% lymphocytes on bronchioalveolar lavage (CD4/CD8 >3.5); and (4) no alternative diagnosis. The control group consisted of patients with myelopathy and intramedullary lesions due to other causes, including multiple sclerosis (n=7), neuromyelitis optica (n=4), spondylotic myelopathy (n=3), infections (n=2), Sjögren syndrome (n=1), tumor (n=1), and idiopathic (n=12).

Results: This study included 31 SCS patients (22 biopsy-proven cases) and 30 controls. Their demographic and clinical features were similar except for radicular pain being more common in the SCS group (45%) than in controls (7%, P=0.004). Men were slightly more common in the SCS group (65%) than in the control group (53%, P=0.055). Spinal cord involvement was the initial manifestation of sarcoidosis in 28 patients (90%). In 22 patients, systemic involvement, mostly of the liver (n=10) and both the lung and mediastinal lymph nodes (n=17), was detected, while in 9 patients, SCS was isolated. Elevated C-reactive protein or LDH levels and lymphopenia were significantly more common in SCS (P<0.0001). CSF pleocytosis, high protein, and low glucose were significantly more common in SCS (P=0.01, P=0.04, and P=0.006, respectively). Low CSF glucose was seen in 6 of 20 SCS patients and in 0 of 23 controls. Serum and CSF angiotensin converting enzyme levels were not significantly different in both groups. MRI cord T2-weighted lesions extended across more vertebral bodies in SCS compared to controls (mean 6 vs 1.9; P=0.0001) and had longer medullary enhancement (mean 2.47 vs 0.45; P=0.003) and meningeal enhancement (mean 3.7 vs 0.2; P=0.01). The lesions in SCS were more often central than in controls (P=0.004). Mediastinal and peripheral lymph node and spinal cord biopsy had the highest diagnostic yield. Most patients (83%) responded to corticosteroids, but 50% had side effects. Most were ultimately treated with immunosuppressive agents with 33% to 75% efficacy rates.

Conclusions: Spinal cord MRI and blood and CSF markers are useful in the accurate diagnosis of SCS.

Reviewer’s Comments: This nice study should assist neurologists when considering SCS in the differential diagnosis of patients presenting with subacute myelopathies. The abnormal blood and CSF markers and long central cord lesion should raise the suspicion of SCS. (Reviewer-Bashar Katirji, MD).

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Keywords: Spinal Cord Sarcoidosis

Print Tag: Refer to original journal article
Brain MRI Improves Infective Endocarditis Diagnosis

Effect of Early Cerebral Magnetic Resonance Imaging on Clinical Decisions in Infective Endocarditis: A Prospective Study.

Duval X, Iung B, et al:


Brain MRI is important in detecting subclinical lesions and influencing diagnosis and management of patients with suspected infective endocarditis.

Background: Infectious endocarditis (IE) is a serious disorder with high mortality and morbidity rates, particularly when associated with neurologic complications. These consist of ischemic and hemorrhagic infarcts, mycotic aneurysms, and abscesses. The latter were reported in 20% to 40% of patients, while earlier autopsies found brain lesions in up to 90% of patients. Prospective studies of brain MRI in IE detected brain lesions in 65% to 80% of patients and in 30% of patients with no neurologic symptoms.

Objective: To determine whether early brain MRI affects diagnostic accuracy of IE and its clinical management.

Design: Prospective study conducted at a French tertiary care center between June 2005 and October 2008.

Methods: All patients with suspected IE were examined by a cardiologist and an infectious disease specialist prior to a brain MRI, done within 7 days of inclusion. Detailed neurologic, skin, and mucosal examinations, with special attention to Osler nodes, were performed. The examiners classified patients as “definite IE,” “possible IE,” and “excluded” based on Duke criteria. The examiners returned in 24 hours and reclassified their diagnosis based on MRI findings. All patients underwent blood cultures and echocardiograms. At discharge, a final diagnosis was made based on new event, surgery, and microbiology.

Results: 130 patients were included in the study. MRI revealed abnormality in 106 patients (82%), including all 16 patients with neurologic symptoms (100%) and 90 patients without neurological symptoms (79%). Ischemic lesions were seen in 68 patients, microhemorrhages were seen in 74, and silent mycotic aneurysms were seen in 10. At entry, 77 patients were classified as “definite IE,” 50 were classified as “possible IE,” and 3 were classified as “excluded.” After MRI, 101 patients were classified as “definite IE,” and 29 were classified as “possible IE.” Based on MRI, 17 of 53 (32%) nondefinite patients were upgraded into definite (n=14) or possible categories (n=3). At discharge, there was a minimal change in diagnosis: 105 definite and 25 possible. After MRI, treatment was modified in 24 of 130 patients (18%): 18 underwent surgery, 5 had a change in antibiotics, and 1 had a change in anticoagulation therapy.

Conclusions: MRI detects brain lesions in many IE patients with no neurological symptoms, improves diagnostic accuracy, and changes clinical management.

Reviewer’s Comments: This study is unique because it confirmed that MRI, a well-established sensitive tool in cerebrovascular disease, improves diagnostic accuracy and sometimes changes management in patients with suspected IE. I imagine that the number of patients without clinical neurologic manifestations would not be as low as 12% if a neurologist had participated in the clinical assessment. (Reviewer-Bashar Katirji, MD).

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Keywords: Infective Endocarditis, Early Cerebral MRI

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Etiology, Presentation, Prognosis Vary for cSAH

Atraumatic Convexal Subarachnoid Hemorrhage: Clinical Presentation, Imaging Patterns, and Etiologies.

Kumar S, Goddeau RP Jr, et al:
Neurology 2010; 74 (March 16): 893-899

Atraumatic subarachnoid hemorrhage over the cerebral convexity is most commonly caused by reversible cerebral vasoconstriction syndrome in young people and by cerebral amyloid angiopathy in older patients.

**Background:** Determining for the cause of small, focal, cerebral convexity (“convexal”) subarachnoid hemorrhage (cSAH), not due to trauma or aneurysm, is a frequent problem of inpatient neurology. **Objective:** To study the clinical and imaging features of cSAH and to determine the causes of cSAH. **Design:** Retrospective review of medical records, neuroimaging studies, and follow-up data for patients at an academic stroke program. **Participants:** All inpatients from 2003 to 2008 with brain imaging showing cSAH not caused by trauma. Patients with intracerebral bleeding or large SAH spreading into fissures or basal cisterns were excluded. **Results:** 29 of 389 patients with nontraumatic SAH (7%) met the inclusion criteria. The study group included 13 men and 16 women (age range, 29-87 years; median age, 58 years). The hemorrhages occupied 1 to 3 adjacent sulci, but they occupied only 1 sulcus in most patients (83%). The areas most often involved were the frontal lobe (51%) and anterior parietal regions (21%). Of the 29 patients, 21 had 1 of 2 diseases: the younger ones (age <60 years) had reversible cerebral vasoconstriction syndrome (RCVS or Call-Fleming syndrome), and the older ones (age >60 years) had cerebral amyloid angiopathy (CAA). Those with RCVS (n=11) presented with headache, which was severe (“worst ever” or thunderclap onset) and long-lasting (mean, 6 days). Angiograms showed segmental constriction of cerebral cortical arteries and no aneurysm. The RCVS patients recovered fully and did not relapse. The patients with CAA (n=10) presented differently: they had transient focal neurologic symptoms and no headache. Sensory symptoms (numbness) spread slowly from 1 part of the body to another (range, 5-20 minutes), like a migraine aura, and the authors speculated that cortical spreading depression might be the mechanism. Motor symptoms resembled TIA. MRI of the head showed extensive leukoaraiosis, microbleeds, and superficial siderosis, consistent with CAA. During follow-up, 4 of these patients had cerebral hemorrhages, and 3 died. The 8 patients without RCVS or CAA had a variety of diseases, including posterior reversible encephalopathy syndrome, infective endocarditis, and immune-mediated thrombocytopenia. Unlike earlier studies, this one did not report seizures, postpartum angiopathy, amphetamine, ephedrine, or cocaine toxicity, vasculitis, cortical vein or dural sinus thrombosis, or cavernoma. **Conclusions:** Convexal SAH has many possible causes, but RCVS is the most common in young people, and CAA is the most common cause in the elderly. **Reviewer’s Comments:** The other type of nontraumatic nonaneurysmal SAH (perimesencephalic or pretruncal SAH) differs from cSAH in that most, if not all, cases appear to be due to rupture of small veins. (Reviewer-Marc D. Winkelman, MD).

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Keywords: Convexity Subarachnoid Hemorrhage, Imaging Features, Etiology

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