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NEUROLOGY ALERT®

A monthly survey of developments in neurologic medicine

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Microdiscectomy or Open Discectomy?

ABSTRACT & COMMENTARY

Source: Hermantin FU, et al. A prospective, randomized study comparing the results of open discectomy with those of video-assisted arthroscopic microdiscectomy. *J Bone Joint Surg Am* 1999;81:958-965.

Sixty patients with single-level lumbosacral intracanalicular disc herniation at L2-3 or lower were prospectively enrolled in this unblinded study comparing open discectomy (n = 30) with video-assisted arthroscopic microdiscectomy (n = 30). Ages ranged from 15 to 67 years, with a mean age of 39.5, and men outnumbered women by 2:1. All patients demonstrated radicular symptoms including a dermatomal pattern of pain consistent with the disc herniation seen on imaging studies, and positive straight-leg raising (Lasegue sign) with or without neurologic deficit. All had failed conservative measures, administered for a minimum of 14 weeks, including rest, nonsteroidal anti-inflammatory medication, physical therapy, exercise, and oral or epidural steroids. None had previous low back surgery and none was involved in litigation or workers' compensation. Exclusionary criteria included diffuse disc bulging with spinal stenosis, a sequestered herniation, drug dependency, or psychological abnormality. Both open laminotomy and arthroscopic microdiscectomy were performed using standard technique that required an overnight admission for the former but not the latter. Patients were followed for up to 42 months following surgery (mean 31 months) and end points included pre- and post-surgical patient self-evaluation, plus neurological evaluation including use of pain medication and ability to return to work.

Post-operatively, open discectomy patients required intravenous morphine for 24 hours, followed by oral percocet, for a mean of 25 days and at last follow-up, six patients (20%) used occasional codeine for pain control. A mean of 49 days was lost from work in this group. None of the arthroscopic microdiscectomy patients required parenteral medication. The mean use of oral analgesics was only seven days, and a mean of 27 days were lost from work. One open discectomy patient developed a dural leak but neither group developed infection or neurovascular injury. Overall, 28 (93%) of open discectomy and 29 (97%) of microdiscectomy patients had an excellent (painfree, unre-

INSIDE

markable examination, return to normal activity) or good outcome (as above with residual back pain modifying occupation). Despite similar outcomes, arthroscopic microdiscectomy patients suffered lower morbidity, required no hospitalization, and returned to work sooner than open discectomy patients. In properly selected patients, arthroscopic microdiscectomy appears to be the treatment of choice for solitary herniated discs of the lumbosacral spine.

COMMENTARY

Why do some patients experience continued pain following disc surgery? *Neurology Alert* overlooked a paper by Nygaard and colleagues (*J Neurol Neurosurg Psychiatry* 1998;64:120-123) that discusses this. The recovery of sensory nerve function was examined in 39 patients following microdiscectomy (25 men and 14 women, mean age 38 years) to determine whether this could be predicted preoperatively. All patients satisfied strict criteria for nerve root compression, including typical radicular pain pattern, positive Lasegue sign, unilateral disc herniation on CT or MRI scan, and surgical confirmation of compression. Exclusionary criteria included previous back surgery, diabetes, other neurological disease, and age older than 60 years. All patients underwent clinical evaluation and quantitative sensory testing (QST) comprising cold, warm, and vibratory detection thresholds prior to and at 6 weeks, 4 months, and 12 months following microdiscectomy. A clinical overall score (COS) encompassing maximum pain, clinical symptoms, and signs was tallied (Haaland AK, et al. *Spine* 1992; 17:1024-1027) and patients were divided into good and poor outcome based on COS less than 250 or COS more than 250, respectively (maximum score = 1000). Twenty healthy volunteers served as controls, and RANOVA and two-tailed tests were used for statistical analysis.

Cold detection threshold improved to normal at 12 months post-operatively, but not at four months, in the good outcome group (P = 0.005), whereas warm detection thresholds improved within six weeks (P = 0.034). No further significant change followed at 12 months. Vibratory threshold improved at 12 months in the good outcome patients but this was not significant. Retrospectively, the poor outcome group preoperatively had significantly higher warm, but not cold or vibratory, detection thresholds. A simple regression analysis demonstrated an association between preoperative warm detection threshold and COS at 12 months (P = 0.031). The varied time course of improvement for cold and warm sensations, transmitted via small myelinated A delta and unmyelinated C fibers, respectively, and the absence of significant improvement for vibratory threshold, transmitted via large myelinated fibers, indicates a range of nerve injury from compression with larger fibers more affected, axonal injury may affect small fibers leading to longer or lesser recovery. Preoperative evidence of C fiber dysfunction is a negative prognostic factor for recovery following surgery and may be responsible for the surgical failures. **—mr**

Neurology Alert, ISSN 0741-4234, is published monthly by American Health Consultants, 3525 Piedmont Rd., NE, Bldg. 6, Suite 400, Atlanta, GA 30305.

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GST Registration Number: R128870672.
Second class postage paid at Atlanta, GA.
POSTMASTER: Send address changes to ***Neurology Alert,*** P.O. Box 740059, Atlanta, GA 30374.

Back issues: $35. Missing issues will be fulfilled by Customer Service free of charge when contacted within one month of the missing issue's date.

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World-Wide Web: http://www.ahcpub.com

Subscription Prices

United States
$209 per year.

Multiple Copies
1-9 additional copies: $188. 10 or more copies: $167.

Canada
Add GST and $30 shipping.

Elsewhere
Add $30 shipping.

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Attention Deficit Disorder: To Treat or Not to Treat?

ABSTRACT & COMMENTARY

Source: Bjederman J, et al. Pharmacotherapy of attention-deficit/hyperactivity disorder reduces risk for substance use disorder. *Pediatrics* 1999;104:e20:http://www.pediatrics.org/cgi/content/full/104/2/e20.

Attention deficit hyperactivity disorder (ADHD) is one of the most common behavioral syndromes encountered in pediatric neurology, with an estimated prevalence of 3-5%. ADHD is characterized by motor overactivity, impulsivity, and inattention,

among other features. The diagnosis of ADHD is often made "by committee" with impressions of parents, teachers, and various clinicians, including neurologists, playing a role. These impressions can be bolstered by psychometric tests, but no test is entirely specific. With these diagnostic uncertainties, particularly in younger patients or in milder cases, the decision to treat patients with ADHD with daily stimulant medications, such as methylphenidate (Ritalin), can be a difficult one.

Two recent papers highlight two potential risks, one short-term and one long-term, of withholding appropriate treatment of ADHD. DiScala and colleagues (DiScala C, et al. *Pediatrics* 1998;102:1415-1421) retrospectively examined the National Pediatric Trauma Registry (NPTR) for injury characteristics of patients diagnosed with ADHD to those with no other pre-existing condition. The NPTR database includes children admitted to the hospital with acute injury, regardless of severity, and includes extensive information on preinjury medical history. DiScala et al found that patients with ADHD (n = 240) were more likely to be injured as pedestrians and bicyclists, and to inflict self-injury than patients without ADHD (n = 21,902). Patients with ADHD in the registry, as compared to patients without ADHD, were more likely to be admitted with Glasgow Coma Scale scores of 9-12 (9.2% vs 3.3%) or scores of less than 8 (7.5% vs 3.4%). It is notable that 80% of the children in the ADHD group had not been receiving regular medication, so that the information largely reflects untreated ADHD.

Biederman and colleagues provide evidence for a less immediate risk of untreated ADHD, namely an increased risk for future substance abuse. This group has published extensively on the longitudinal follow-up of patients with ADHD. This particular study restricted its analysis to male patients older than age 15, and compared three groups: ADHD/medicated (n = 56), ADHD/nonmedicated (n = 19), and non-ADHD groups (n = 137). The groups were examined for the presence of alcohol, marijuana, hallucinogen, cocaine/stimulant, or tobacco use of dependency at baseline and four-year follow-up. Biederman et al found that the incidence of any of the substance abuse disorders at four-year follow-up was 6.3-fold more likely in patients with unmedicated ADHD as compared to the non-ADHD group. Strikingly, stimulant drug treatment of ADHD had a protective effect, bringing the incidence of any substance abuse disorder down to levels comparable to non-ADHD groups. Unmedicated ADHD seemed to have the most powerful effect on future alcohol or cocaine/stimulant use and no significant effect on hallucinogen or tobacco use, so that there may be certain use patterns in these patients.

COMMENTARY

Although these cited studies are complex and their interpretation not completely straightforward, they appear to swing the balance toward early and effective therapy of patients with ADHD. The administration of "speed" to children with ADHD clearly does not breed "junkies" later in life, as was once thought (and many parents still believe).

The side effects and limitations of stimulants are better understood now than a decade or two ago. For example, it is now clear that while the risk of patients developing a tic disorder with methylphenidate treatment may be as high as 10% (Lipkin PH, et al. *Arch Pediatr Adolesc Med* 1994;148:859-861), most cases are transient and only about 1% of patients develop features of Tourette syndrome. Furthermore, methylphenidate can be safely and effectively used in the great majority of patients with chronic tic disorders (Gadow KD, et al. *Arch Gen Psychiatry* 1999;56:330-336), and does not influence the severity of tics in most patients. **—rt**

A Mechanism of Confabulation Revealed

ABSTRACT & COMMENTARY

Source: Schneider A, Ptak R. Spontaneous confabulators fail to suppress currently irrelevant memory. *Nat Neurosc* 1999; 2(7):677-681.

Recognizing confabulation can be useful in the differential diagnosis of amnesia. A new study by Schneider and Ptak suggests that the mechanism underlying spontaneous confabulation may be a deficiency in the ability to suppress activated memory traces that are inappropriate to the current context. In essence, amnesiacs who confabulate may be activating too many memories rather than too few.

Schneider and Ptak examined six amnesiacs who acted according to invented stories (spontaneous confabulators) and compared them to 12 comparably amnesiac patients who did not confabulate, as well as 10 normal controls. Spontaneously confabulating patients had abnormalities in the basal forebrain or medical orbital frontal cortex. The subjects were shown various sets of pictures and asked to identify a target item that appeared recurrently among singly viewed distrators. The same sets of stimuli were used in multiple runs, with previous target items interchanged with distrators. Before each run, subjects were instructed to forget the pictures they

had seen before, and to only identify recurrences within the given run.

On this continuous recognition task, all of the amnesiacs performed significantly worse than controls, making more false-positive responses. However, confabulating amnesiacs showed steeply increasing numbers of false-positive responses as the experiment progressed. When the interval between successive runs was increased to 30 minutes, the false-positive response rate of confabulators remained high. Interference by previously acquired information was most evident when the stimuli represented real world objects, but was also apparent when meaningless designs were used.

Schneider and Ptak concluded that confabulating and nonconfabulating amnesiacs did not differ in their ability to detect new target items, indicating that confabulation is not simply a consequence of failure to saliently represent incoming information. What did distinguish confabulators was their inability to suppress interference arising from previously acquired information. Confabulators may process information encountered 30 minutes ago as though it were part of their experience of the present moment.

COMMENTARY

Schneider and Ptak provide a new slant on the memory-monitoring deficit hypothesis. Based on their findings, spontaneous confabulators may not be able to suppress mental associations that pertain to past events or fully distinguish them from those that arise in the present. Information acquired days, weeks, months, or even years before may intrude into their current thinking, leading to the bizarre, false ideas that constitute confabulations.

This appealing theory explains some but not all of the phenomenology observed in amnesiac confabulators. Perhaps the most famous bedside clinical test for confabulation is the "purple string test," in which the examiner pretends to stretch a string between their own hands, and asks the amnesiac whether they can see the nonexistent purple string. Confabulators, particularly those with acute Korsakoff's syndrome, often state that they see the string and that it appears purple. If suggestive statements and a beguiling hand position are all that one needs to convince the amnesiac patient that they are seeing something that isn't really there, it would seem that confabulation represents more than just a failure to distinguish past from present associations. Confusion about what has been seen in the past vs. the present could be invoked as a partial explanation.

The brain lesions identified in these confabulating amnesiacs were all located in fairly circumscribed locations, distinct from those found in amnesiacs who did not confabulate. The salient areas lie in or near midline structures comprising the anterior limbic system, including the medial orbital frontal cortex and hypothalamus. This confirms that confabulatory amnesia usually arises from dysfunction in midline brain structures, rather than medial temporal and lateral prefrontal areas involved in other forms of forgetfulness. **—nrr**

Which Glioblastoma Multiforme Patient will Become a Long-Term Survivor?

ABSTRACT & COMMENTARY

Source: Scott JN, et al. Which glioblastoma multiforme patient will become a long-term survivor? A population-based study. *Ann Neurol* 1999;46:183-188.

Glioblastoma is the most deadly of all primary brain tumors, with a median survival of 12 months following diagnosis. Long-living (LL) exceptions are thought to exist, however, and Scott and associates provide a well-written description of one relatively tiny group with a prolonged course, a low incidence of the tumor, an unusually slow evolution of symptoms, and, possibly, a favorable reaction to chemotherapy.

Patients were selected from the Alberta Cancer Registry, which, by statute, has required the registration of all cancer patients in that Canadian province since 1941. Patients selected in the present report included all diagnosed glioblastoma multiforme (GBM) cases in the province (n = 689) between 1975 and 1991. Time of onset was taken from that of the first histopathologic diagnosis and subsequent lengths of patients' survivals Scott et al reexamined all previous charts and pathological histology. From those findings, they identified 15 persons (2.2%) from the total who have lived three years or longer from the initial clinical diagnosis. Mean survival times of the LL group amounted to 78.4 ± 13.4 months (range, 38-189 months) compared to the 97.8% remaining of 11.8 ± 1.3 months (range, 0-35 months). The biologic qualities expressed by the long-term GBM survivors [LTGBMSs] were then compared against similar qualities in three short-term control GBM patients of average age, sex, and years following time of diagnosis. The mean age of the LTGBMSs at onset averaged about 10 years younger than their sicker classic GBM confreres (i.e., 43.5 ± 3.3 yrs vs 53 ± yrs of age). They also had higher Karnowski Scale Performance scores when first diagnosed and they were capable of enduring larger brain resections than the clas-

sic GBM controls. Surgically increased post-operative neurological dysfunction is not described.

Table

Items Expressed by LTGBMSs Compared to GBM Controls

	LTGBMSs	GBMCs
	n = 15	n = 43
Karnofsky Performance Status*	86	76.7
Duration of symptoms until histology (wks)*	31 ± 10.2	11.1 ± 3.7
Age at onset (yrs)*	43.5 ± 3.3	53 ± 0.55
Mean survival time (months)*	78.4 ± 13.4	11.8 ± 1.8
Range of survival time (months)*	38-189	0-35
Presenting with seizures	10/15	10/43
Headache, motor signs, mental status change, mood, vision	No difference	
Gross, 'total' resection	6/15	6/43
Treated with radiation, mean cGY 6221	Both	
Treated with chemotherapy (n=)	7/15	0/43

*statistically determined difference

The histological material from the long-term survivors showed mild, but important, differences from the pathological histology found from most glioblastoma patients whose median survival time is about 12 months. Only after the blinded evaluations of all biopsy samples were passed and identified as GBMs did Scott et al's pathologist go back to reevaluate the earlier obtained histological brain tissue of the LTGBMS. Notably, the tissues revealed fewer mitotic figures than the usual GBM, a lower number of Ki-67-positive nuclei (including slower mitoses and reduced proliferations), and, in some cells, a threefold increase in lymphocytic infiltration compared to the number of lymphocytes invading short-lived tumors.

COMMENTARY

Scott et al cite several things that might have lengthened survival in these patients. The LL cohort was younger by a decade from the classic GBM sufferers. They also appear to have been in better neurological health than most patients with classic GBMs when they underwent aggressive surgery. In addition, they also had a longer convalescent time to complete postoperative chemotherapy than was biologically possible for the classic GBM group. However, one-third of the long-term survivors eventually developed radiation dementia and three of the six who lived to an average of at least six years after radiotherapy suffered that complication. Whether chemotherapy applied after surgical and/or radiation therapy influenced the ultimate longevity of these patients can only be guessed at. This report emphasizes the histological variances that were identified as glioblastomas in this particular group. Even before the biopsy and after it as well, however, their early and late progression of symptoms and signs differed from the usual GBM. Why such a difference between groups? It's hard to believe that anything but a different set of nepotistic genes expressed the more favorable course that extended these less stricken lives. **—fp**

Benign Multiple Sclerosis—Does it Exist?

ABSTRACTS & COMMENTARY

Sources: Hawkins SA, McDonnell GV. Benign multiple sclerosis? Clinical course, long-term follow-up, and assessment of prognostic factors. *J Neurol Neurosurg Psychiatry* 1999;67: 148-152; Sorensen TL, et al. Optic neuritis as onset manifestation of multiple sclerosis. A nationwide long-term survey. *Neurology* 1999;53:473-478.

Hawkins and mcdonnell monitored the long-lasting clinical course of 259 patients with multiple sclerosis (MS) in Northern Ireland. One hundred eighty-one of these patients had MS for 10 years or longer, of which 36 (20%) patients with a Kurtze Expanded Disability Scale Score (EDSS) of 3.0 or less were defined as having benign disease. The patients with benign MS were predominantly women (ratio 4.1:1 vs 2.1:1 for nonbenign MS), were younger at onset (25.8 vs 31.2 years), and were more likely to present with optic neuritis or sensory disturbance. Conversely, patients with later onset of MS (> 40 years), male sex, and presenting with motor disturbances were more likely to have a progressive course with a higher EDSS.

In a long-term analysis of 118 MS patients from a similar 1987 study, of the 33 patients defined as benign at onset, 28 were available for follow-up (5 died in the intervening period). Only eight patients (28%) continued to fulfill the criteria for benign MS, all of whom initially had an EDSS score of 2 or less. The mean/median disability score in 1987 of 2.3/3.0 advanced in this benign group to 4.6/5.0, and most patients changed from a relapsing-remitting (RR) course to a secondary progressive (SP) course.

In another long-term survey, Sorensen and colleagues followed 6923 patients in the Danish MS registry from 1949 to 1990. Of the 1282 patients (19%) presenting with optic neuritis (ON), the mean age of onset was 31.1

years, compared with 34.8 years for patients with non-ON manifestations of MS ($P < 0.001$). The mean delay from initial manifestations to clinically definite MS was 6.1 years for ON, and 4.2 for non-ON.

The median survival time from onset of ON in the Danish registry was 40 years in women (compared with 47 years in the age-sex-matched general population) and 30 years in men (compared with 41 years in the general population). The excess death rate was lower for women presenting with ON as an initial manifestation of MS, but not for men with ON, or compared with non-ON presentations in either sex.

COMMENTARY

Longitudinal clinical information from large national health databases has provided an important understanding of the natural history of MS. Such information better enables the neurologist to make an accurate prognostic assessment of MS patients with varied clinical presentations. Thus, less optimal clinical presentations with a greater probability of progressive neurological disability might benefit from early therapeutic intervention.

The eventual neurological disability that occurs at a high rate, even in patients who are initially labeled as benign MS, is sobering. It suggests that, while it may be important for the physician to provide the patient with an optimistic outlook on their disease course, it can be falsely reassuring for both to use misleading labels such as benign MS.

Quantitative MRI data have also documented early subclinical brain atrophy and white matter changes that signal irreversible axonal loss that can occur in the first 10 years of disease preceding the secondary progressive phase of MS (Apatoff BR. *Neurol Alert* 1999;17(9):65-67). Thus, the natural history data presented in these two studies would support the giving of earlier treatment to MS patients with active disease using immunomodulatory agents to minimize long-term disability. **—ba**

Yield of Transcranial Doppler in Acute Cerebral Ischemia

ABSTRACT & COMMENTARY

Source: Alexandrov AV, et al. Yield of transcranial Doppler in acute cerebral ischemia. *Stroke* 1999;30:1604-1609.

The ability to identify the location and severity of arterial obstruction in acute stroke stands crucial in making accurate pathophysiological diagnoses and triaging patients for emergency therapies. Transcranial Doppler (TCD), a portable tool with bedside availability for rapid screening in the emergency setting, can accomplish this goal.

Alexandrov and associates used TCD in 130 consecutive patients with symptoms indicating acute cerebral ischemia. Vascular occlusions were documented in 69% of thrombolysis-eligible patients compared with 24% of patients with strokes and none with TIAs. Of the 130 patients, 84 (65%) also underwent either digital subtraction angiography (DSA), MR angiography (MRA), or CT angiography (CTA). Patients with presumed proximal arterial occlusions were more likely to undergo DSA. Using a combination of DSA, MRA, and CTA, Alexandrov et al found TCD to be 87.5% sensitive and 88.6% specific for detection of a vascular abnormality.

As Alexandrov et al point out, information from TCD may help select patients for angiography and possible intra-arterial thrombolysis. In the Prolyse in Acute Cerebral Thromboembolism Trial (PROACT), 105 thrombolysis-eligible patients with clinically suspected MCA occlusion underwent cerebral angiography, which showed no M1-M2 occlusion in 59 patients (56%). Such unnecessary angiography might be avoided by TCD. Given a negative predictive value of 89%, according to Alexandrov et al, a normal TCD provides reasonable assurance of vessel patency.

COMMENTARY

With the recently reported results of the PROACT showing a significant benefit for intra-arterial pro-urokinase over placebo, intra-arterial thrombolysis with agents such as urokinase or tPA will come into increasing use. It is, therefore, crucial to use techniques such as TCD to make a rapid vascular diagnosis.

Although Alexandrov et al's results are encouraging, few neurologists in the community practice TCD. Results depend on the examiner's skill. Even in the hands of Alexandrov et al, false negatives did occur. Furthermore, the paper does not state how many TCD studies were confirmed by DSA, the only true gold standard in this setting.

Other techniques may be of use. MRA may be performed but can be time consuming and difficult for an agitated acutely ill patient. CTA is another method of rapid diagnosis. It requires a helical CT scanner, present in many ERs, and limited interpretive skill. **—azs** (*Dr. Alan Z. Segal is Assistant Professor, Department of Neurology, Weill-Cornell Medical College, Attending Neurologist, New York Hospital.*)

Functional MRI-BOLD of Visually Triggered Headache in Patients with Migraine

ABSTRACT & COMMENTARY

Source: Cao Y, et al. Functional MRI-BOLD of visually triggered headache in patients with migraine. *Arch Neurol* 1999; 56:548-554.

As neuroimaging advances, so does our understanding of the underlying neurophysiologic events in migraine. Cao and associates used a functional MRI-BOLD oxygenation level dependent contrast (fMRI-BOLD) to study occipital cortex perfusion and activation during visual stimulation of 10 migraine with aura (MwA) patients, two migraine without aura patients (MwoA), and six controls. fMRI-BOLD technique measures relative changes in oxygenation of blood and can, therefore, be used to study brain activation and, indirectly, blood flow. Visual stimulation attempted to trigger migraine using an alternating red-green projected checkerboard through MRI, compatible mirrored goggles. Six MwA patients developed headache. Only two of the six experienced visual changes associated with the headache. Two MwoA patients developed headache and neither had visual changes. The mean time from visual stimulation to the onset of the headache was 7.3 ± 5.2 minutes. Suppression of occipital cortical activation was recorded in six of the eight triggered headache subjects, which included one person in the MwoA group. Suppression of activation was noted to be both bilateral and unilateral and did not correlate to the intensity of the headache or the location of the head pain. The rate of propagation of the suppression ranged from 2.9 to 6.0 mm/min (mean ± SD, 4.1 ± 1.3). It was noted that four of six subjects with headache and no visual changes still recorded spreading activation. In six of eight triggered headache subjects the occipital cortical neuronal suppression was associated with an increase in the baseline intensity. The increase in baseline intensity on BOLD images reflects vasodilation and hyperoxia.

COMMENTARY

fMRI-BOLD imaging proves to be another valuable technique in unlocking the neurophysiologic and neurovascular secrets of migraine. Cao et al make several important conclusions that are worth reiterating. First, visually triggered headache in migraine patients is associated with spreading suppression. The rate of this change is consistent with the 2 mm/min cortical spreading depression of Leao and the clinically observed spreading scotoma of Lashley. It is interesting to note that six of the eight subjects with spreading suppression did not report visual changes. Cao et al also observed that the spreading suppression was associated with initial activation in the occipital cortex. However, the question of whether the origin of this phenomenon is neuronal or vascular remains unanswered by the current techniques. **—jr**

Deep Brain Stimulation for Parkinson's Disease

ABSTRACT & COMMENTARY

Source: Ardouin C, et al. Bilateral subthalamic or pallidal stimulation for Parkinson's disease affects neither memory nor executive functions: A consecutive series of 62 patients. *Ann Neurol* 1999;46:217-223.

The last three years have seen an explosion of interest in deep brain stimulation for Parkinson's disease. Of the possible targets, only pallidal and subthalamic nucleus (STN) stimulation address the major cardinal symptoms of bradykinesia, rigidity, and tremor. Although implantation of a deep brain stimulator into the internal palladium or STN is not currently approved in the United States, these procedures, and in particular STN stimulation, are being performed at academic centers and in clinical practice. Ardouin and colleagues' review of the effects of bilateral stimulation on memory and executive functions is particularly important, as neurologists struggle with the question of who should and who should not undergo these procedures.

Pooling patients implanted with bilateral STN or pallidal stimulators in Grenoble and Paris, 62 consecutive Parkinson's patients underwent a battery of neuropsychological tests before and after bilateral implantation of electrodes. Patients who underwent implantation were relatively young (average age < 55), with at least 12 years of Parkinson's symptoms. All responded to levodopa, with characteristic severe motor fluctuations. In the "on" state, patients were independent, and in the "off" state they were incapacitated (Hoehn and Yahr > 4/5). Electrodes were implanted in a single operative sitting using neuroradiologic landmarks and an intraoperative microelectrode recording to define placement. All patients sustained a dramatic benefit in motor performance, although the benefit was greater in the STN group. Patients

implanted with STN stimulators were also able to substantially reduce their daily requirement for levodopa to assess the late effects of bilateral stimulation. Patients with prior cognitive disturbance or hallucinations should probably not be considered as candidates. The conservative view would hold that STN stimulation should be performed in academic centers where resources are available for continuous neurological followup. The desperation of certain patients to undergo the procedure and the opportunity for considerable financial reimbursement in surgical fees may derail these plans. **—sf** (*Dr. Steven Frucht is Assistant Professor of Neurology, Movement Disorders Division, Columbia-Presbyterian Medical Center.*)

Brief Alert

Tremor Arrest with Thalamic Microinjections

Source: Pahapill PA, et al. Tremor arrest with thalamic microinjections of muscimol in patients with essential tremor. *Ann Neurology* 1999;46:249-252.

The role of interventional therapies for the treatment of movement disorders is rapidly enlarging. In this context, Pahapill and colleagues have reported a pioneering controlled pilot study in six patients with essential tremor. The patients, undergoing stereotactically placed lesions or placement of deep brain stimulators in the ventralis intermedius (Vim) and adjacent thalamic nuclei, received microinjections in the Vim of an inhibitory neurotransmitter (GABA-A) agonist, muscimol. Prior to lesioning and following the characterization of tremor-synchronous cells, microinjections were done in the Vim. The patients were injected with either saline or muscimol, with no effects observed using the saline control. Tremor was suppressed in all patients following the muscimol injection with a relatively long average latency of seven minutes for the full clinical effect to appear. Subsequent tremor suppression lasted an average of nine minutes. Although the microinjection technique has been extensively used in laboratory animals, this study provides the first indication that selective delivery of neurotransmitters to specific anatomical targets may improve the clinician's therapeutic repertoire.

Beyond the present context, Pahapill et al's study provides new insights into the potential mechanisms underlying thalamic lesioning and deep brain stimulation (DBS). Pahapill et al emphasize that the results of the inactivation mimic the effects of thalamotomy or DBS and suggest that GABAergic activation may desynchronize local thalamic networks. This demonstration suggests a potentially wide range of future therapeutic interventions such as combining DBS with directed application of pharmacologic agents. **—ns** *(Dr. Nicholas Schiff is Assistant Professor and Attending Neurologist, Weill-Cornell Medical College and New York Hospital.)*

Correction

The article, "Pain Management for the Elderly and Terminally Ill," in the September 1999 issue of *Neurology Alert* contained two errors. In paragraph two, line four reads "...not all neurologists." The opposite is true—all responses came from members of the Academy of Neurology. Line 12 of the same paragraph reads, "...only about 3% of their patients..." The sentence should read "...about 30% of their patients..." We regret any confusion this may have caused. ❖

CME Questions

18. Which of the following statements is correct?

a. Microdiscectomy is not as effective for the surgical treatment of well-selected single-level intracanalicular lumbar disc herniation as is open laminectomy.
b. Residual pain following microdiscectomy may be due to injury to unmyelinated C fibers at the nerve root level.
c. Cold detection threshold may have positive predictive value in the surgical treatment of lumbar disc disease.
d. Vibratory detection threshold may have positive predictive value in the surgical treatment of lumbar disc disease.

19. Which of the following is *false*? Patients presenting with benign or milder forms of MS are:

a. more likely to present with optic neuritis or sensory disturbance.
b. more commonly female.
c. have a younger age of onset of MS.
d. are rarely going to experience increasing neurologic disability.
e. still have a clinical indication for immunomodulatory therapy.

21. The occurrence of confabulation may indicate:

a. diffuse rather than focal brain pathology.
b. the presence of medial temporal lobe lesion.
c. more severe amnesia than in nonconfabulating patients.
d. a deficit in distinguishing past from present associations.

In Future Issues:

Therapeutic Benefit: Aspirin Revisited in Light of the Introduction of Clopidogrel