Cognition Improves After Carotid Stenting

BY BRUCE K. DIXON
Chicago Bureau

CHICAGO — Carotid artery stenting appeared to improve cognitive function based on the results of what investigators said is the first study to look at perfusion and diffusion-weighted imaging before and after stenting.

"We found that stenting of the carotid artery significantly increased cognitive speed," Dr. Iris Grunwald said at the Radiological Society of North America annual meeting. Studies of brain function following carotid endarterectomy have produced mixed results, and there is no consensus in the literature as to whether carotid intervention improves cognition.

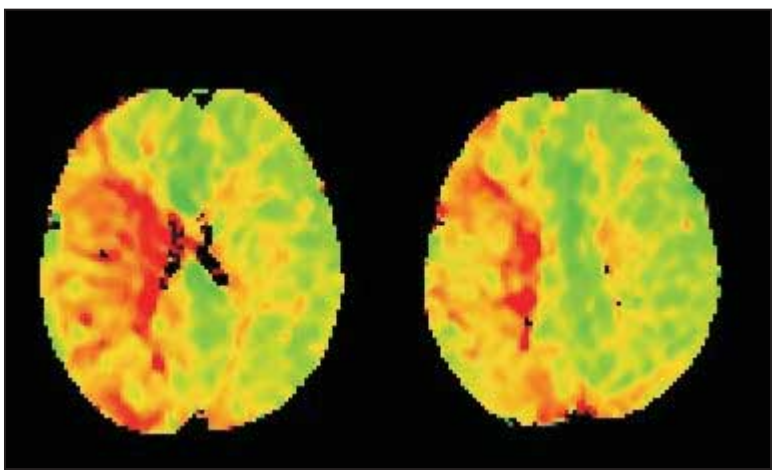
Dr. Grunwald and her colleagues at the Saarland University Clinic in Homburg, performed carotid artery stenting on 29 patients. Mean age was 68 years and mean degree of stenosis was 90%. People were excluded from the study if they had paresis in the upper extremity, impairment in eyesight, and/or hemianopsia. Those with psychiatric disease or insufficient command of language also were excluded.

Stents were implanted in the left carotid artery in 18 patients. All the patients were asymptomatic and right handed. Thus speech-related functions were primarily left-brain functions in these patients, Dr. Grunwald explained.

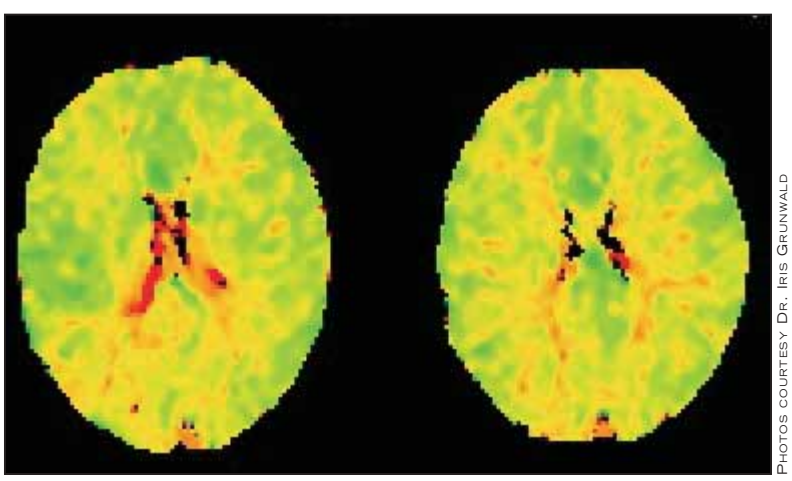
Perfusion and diffusion-weighted magnetic resonance imaging (MRI) was performed 24 hours before and 48 hours after intervention (see images). All patients were tested using the Mini-Mental State Examination (MMSE) and symbol digit test and subtests of the CERAD battery. Cognitive speed was assessed with the modified trail making test (ZVT) and the Stroop colored word test.

Findings from the Beck Depression Inventory showed that none of the patients suffered from depression. Mean improvements in cognitive speed ranged from 3% on the ZVT number connection test to almost 7% on the Stroop colored word test.

"Stenting of the internal carotid artery seems to improve functions that involve cognitive speed, regardless of the patient's age, the side of stenosis and the degree of stenosis," Dr. Grunwald said. "Some patients showed [more] improvement after stent placement than others. The higher the degree of stenosis, the more marked was the perfusion deficit. Post-stenting perfusion increased in 17 of the 18 patients, though in 9 of them the increase was described as "slight." Increased brain perfusion correlated with increased memory function but did not quite reach statistical significance. ■



Perfusion and diffusion-weighted MRIs show impaired cerebral blood flow (red) in a carotid stenosis patient.



Placement of a carotid stent in the same patient restored cerebral blood flow to closer-to-normal (green) levels.

PHOTOS COURTESY DR. IRIS GRUNWALD

EVIDENCE-BASED PSYCHIATRIC MEDICINE

Donepezil for Traumatic Brain Injury

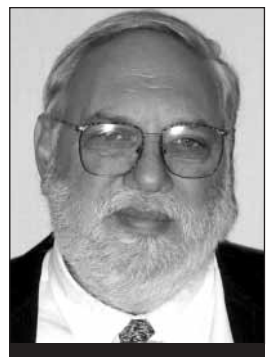
The Problem

You work in a forensic/correctional setting, and your newest patient has been judged incompetent to stand trial on the basis of cognitive problems secondary to traumatic brain injury.

The Question

Can donepezil (Aricept), which has some degree of efficacy in Alzheimer's, also benefit TBI patients?

BY JAN LEARD-HANSSON, M.D.



BY LAURENCE GUTTMACHER, M.D.

The Analysis

The Medline search we conducted combined "donepezil" and "brain injury."

The Evidence

Two of the earliest cases were reported in 1998 (Brain Inj. 1998;12:77-80). Patient A was a 21-year-old who had experienced a 3.5-month coma. Over 1 year later, donepezil 5 mg/day was initiated. Cognition was evaluated using the Rivermead Behavioral Memory Test (RBMT) and Ross Immediate Processing Assessment. After a 3-week trial the patient improved her score by 60% over the premedication score. Patient B, 46, had been in a coma for 2 weeks. After receiving 3 weeks of donepezil 5 mg/day, the patient seemed to require less verbal cuing for memory and cognitive tasks.

Other investigators conducted a review of 53 patients who had suffered a TBI or other neurological injury due to anoxia or vascular event (Ann. Clin. Psychiatry 2000;12:131-5). Patients had received donepezil 5-10 mg/day, vitamin E 800 IU/day and aspirin, plus antidepressants, mood stabilizers, anxiolytics, or antipsychotics. Medication regimens did not change (except dosage) throughout the study period. The mean treatment duration was 13.5 months. Outcomes were measured using the Wechsler Adult Intelligence Scale-Revised, which showed statistical improvement at $p = 0.02$ but not at 0.01, and Hooper Visual Organization Test, which showed improvement but did not reach statistical significance.

In an open-label study, investigators reported on four patients, aged 24-35 years, who had suffered a TBI with an initial Glasgow Coma Scale of 3-8 (Arch. Phys. Med. Rehabil. 2001;82:896-901). Patients received donepezil 5 mg/day for 8 weeks, then 10 mg/day for 4 weeks. Memory was evaluated, in part, using the Rey Auditory Verbal Learning Test (RAVLT) and the Complex Figure Test (CFT). On the RAVLT, mean scores for learning, short-term, and long-term recall improved by 0.4, 1.04, and 0.83 standard deviations above baseline, respectively. On the CFT, mean scores for short-term and long-term recall improved by 1.56 and 1.38 standard deviations above baseline.

Another open-label study involved seven patients, aged 19-51 years (mean 30.7), who were at least 1.5 years post-TBI (Brain Inj. 2003;17:809-15). Patients received donepezil 5 mg/day for 1 month, then 10 mg/day for 5 months, then no donepezil for 6 weeks, followed by donepezil 5 mg/day for 6 months. Patients were assessed, in part, using the Brief Visual Memory Test–Revised, which evaluates visual learning and memory. The investigators concluded that significant improvements were noted on immediate and delayed memory when patients took donepezil 10 mg/day.

A different group of researchers conducted a review matching 18 patients with a history of moderate to severe TBI who had received donepezil 10 mg/day to 18 patients with similar inclusion criteria who had received no donepezil (Brain Inj. 2004;18:739-50). No statistically significant differences in cognitive function were identified between the treatment and control groups.

In an open-label study of 111 patients with mild to "extremely severe" TBI, all of whom were at least 1 year removed from the trauma, patients were selected for the presence of at least one target symptom: fatigue, poor memory, diminished attention, or problems with initiation (Prog. Neuropsychopharmacol. Biol. Psychiatry 2005;29:61-7).

Of the 111 patients, 27 received donepezil (mean age 43 years) and the others received galantamine or rivastigmine. The maintenance dose averaged 7.2 mg/day. The assessment was based solely on subjective description. Response was graded as none, modest, good, or excellent. After an average of 18 months of treatment, 41% of patients experienced a good or excellent response, but the absence of a control group makes it impossible to know whether the improvement was associated with the medications, with a placebo effect, or with more time to recover from the TBI. Significant adverse effects were noted by a quarter of patients.

Dr. Lei Zhang and associates conducted a 24-week, randomized, placebo-controlled, double-blind crossover trial on 18 post-acute TBI patients (Arch. Phys. Med. Rehabil. 2004;85:1050-5). Patients ranged in age from 19 to 57 (mean 32 years) with a post-injury Glasgow Coma Scale score of approximately 9. Half of the patients received donepezil for the first 10 weeks (5 mg/day for 2 weeks; 10 mg/day for 8 weeks), followed by a 4-week washout period and 10 weeks of placebo; the other half reversed the order. Donepezil significantly increased cognitive functioning. Improved scores were sustained after the washout period and placebo phase in the group that had active medication first.

The Conclusion

Evidence for prescribing donepezil to enhance cognition in TBI patients is preliminary but positive, and is limited by small sample sizes and the lack of double-blind, placebo-controlled design. Dr. Zhang's study was small but very well designed. It is hoped that a longer and larger study can be conducted.

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