Early uncontrolled studies of this application had small centromedial nucleus of the thalamus have also been 1990s, used the electrodes in the brain’s cerebellar re- controlled studies and case reports, which included about 115 people worldwide.

Now, data from three new or upcoming studies might help shed light on some of these questions, said Dr. Boon of University Hospital Ghent (Belgium), where he and his colleagues are leaders in researching an epilepsy application for DBS.

Some of the earliest studies, in the 1980s and early 1990s, used the electrodes in the brain’s cerebellar re- gions, but with very little effect, so the cerebellum is no longer considered a target. The caudate nucleus and centromedial nucleus of the thalamus have also been examined as possible targets, but in very small numbers of patients and with varying results, said Dr. Boon. The most promising approach to date is bilateral stimulation of the anterior thalamic nucleus, he said. Early uncontrolled studies of this application had small patient numbers, but their success led to the Stimula- tion of the Anterior Nucleus of the Thalamus for Epilepsy trial of 110 patients with medically refracto- ry partial-onset seizures. All of the patients received the implants; for the first 3 months, only half of the patient had the stimulators turned on. After this blinded treatment phase, all of the patients received neurostimulation. By way of detail- ing financial conflicts of interest, Dr. Boon said in an interview that Medtronic Inc., the company that makes DBS hardware, has been and is providing devices and electrodes in support of the pilot trial, and has pro- vided an educational grant. The medial temporal lobe and the hippocampus are other potential targets. Last year, Dr. Boon and his col- leagues published a study of 12 patients with refracto- ry temporal lobe epilepsy, who were also candidates for surgery. Instead of implanting recording electrodes during the presurgical period, they implanted DBS electrodes in the medial temporal lobe.

“We aimed to adjust the simulation parameters to get a 50% reduction in spikes for 7 consecutive days,” he said. “If the patient achieved that, then we went to chronic stimulation, and if they did not achieve that, then we adjusted the parameters until we met those cri- teria. If the patient still didn’t achieve the reduction, then we removed the electrodes and proceeded to surgery.” Of the 12 patients, 10 underwent long-term DBS and 2 had the resection. After a mean follow-up of 31 months, both of the surgical patients were seizure free. One of the DBS patients had a seizure reduction of more than 90%; five had a reduction of at least 50%, and two had a reduction of 30%-40% (Epilepsia 2007;48:1551-60).

Antiepileptic Age, Polytherapy Linked to More Adverse Effects

MADRID — Adverse events are more common in patients who take older antiepileptic drugs or who take more than one antiepileptic, compared with those on monotherapy or newer agents.

The adverse effect profiles of anti- epileptic drugs are often determining fac- tors in drug selection, and yet adverse ef- fects may be overlooked in everyday clinical practice,” Joyce A. Cramer wrote in a paper presented at the annual con- gress of the European Federation of Neu- rological Societies.

Ms. Cramer, a research scientist at Yale University, New Haven, Conn., conducted a population surveillance study in six Eu- ropean countries to evaluate the adverse effects of both newer and older antiepilep- tic drugs (AEDs). The study population comprised 1,019 patients (mean age, 31 years) who had been on a stable dosing regimen for a me- dian of 13 months. Of those, 57% were on monotherapy, and 43% were on polyther- apy. Most of the patients (71%) were tak- ing at least one older AED (carbamazepine, clonazepam, clonazepam, phenobarbitol, phenytoin, or valproate). The rest were taking at least one newer AED (gaba- pentin, lamotrigine, levetiracetam, ocar- bazepine, pregabalin, tiagabine, topira- mate, and zonisamide).

At least one adverse effect occurred in 68% of the patients. Newer AEDs were asso- ciated with fewer reports of adverse ef- fects than were older drugs (61% vs. 71%, respectively), and monotherapy was asso- ciated with fewer reports of adverse effects than was polytherapy (66% vs. 71%). Neurologic adverse effects were also more common in those taking older AEDs than in those taking newer AEDs (60% vs. 54%, respectively), as were systemic adverse effects (42% vs. 33%). Neurologic adverse effects were also more common in patients on polytherapy than in those on monotherapy (64% vs. 53%), although the percentage of patients reporting systemic adverse effects was equal in these two groups (40%). Adverse effects that were significantly more common in those taking the older drugs, compared with newer drugs, were cognitive slowing (30% vs. 22%), sedation (30% vs. 23%), and tremor (18% vs. 10%). Adverse effects that were significantly more common in those taking polythera- py, compared with monotherapy, were cog- nitive slowing (36% vs. 22%), psychologic problems (31% vs. 22%), tremor (21% vs. 11%), and gait disturbances (12% vs. 7%). A logistic regression analysis concluded that patients on newer AEDs were 36% less likely than were those on the older drugs to report at least one adverse effect. Treatment modifications were 52% more likely in those reporting adverse effects. The study was sponsored by UCB Phar- ma Inc., which makes levetiracetam. Ms. Cramer is a consultant for the company.

Lacosamide Bring Control to Treatment-Resistant Epilepsy

MADRID — The investigational antiepileptic lacosamide is well toler- ated and reduced seizures by more than 50% in almost half of patients who took it as adjunctive therapy for medication-refractory partial seizures.

“This study, with more than 5 years of follow-up, showed that lacosamide controls these seizures very well,” Dr. William Rosenfeld said at the annual congress of the European Federation of Neurological Societies. Lacosamide is also being investi- gated for neuropathic pain, said Dr. Rosenfeld, medical director of the Comprehensive Epilepsy Care Center for Children and Adults in St. Louis. The drugmaker, UCB Inc. of Brussels, received a not approvable letter from the Food and Drug Administration for this indication in late July, al- though the agency is still considering the drug’s use as an add-on therapy for partial-onset seizures.

The phase III trial was an open-label extension study that comprised 370 adults (mean age 40 years) who had previously participated in placebo-con- trolled studies of the drug. The mean follow-up time was 5.9 years. At base- line, all patients had partial seizures that remained uncontrollable despite numerous medication trials; more than half of the cohort had tried sev- eral or more drugs during their lifetime. Study protocol allowed titration of up to 800 mg/day; lacosamide could be used as either add-on therapy or monotherapy at the clinicians’ disc- retion. The most commonly used dosage was 400 mg/day (24%).

Overall, 46% of patients taking the drug experienced a reduction in seizures of at least 50%. This response rate was apparent by 6 months and continued to improve, with 65% re- sponding by 12 months.

“This doesn’t mean, however, that the drug was getting more effective as time went on,” Dr. Rosenfeld said. “It’s a function of adjusting the dose and having nonresponders drop out.”

Adverse events included dizziness (37%), which was transient and usu- ally ceased as patients adjusted to the medication; headache (18%), fatigue, and nasopharyngitis (14% each); and diplopia, abnormal vision, and upper respiratory tract infection (13% each). There were no significant cognitive side effects, Dr. Rosenfeld said.

According to the company Web site, lacosamide has a novel dual mechanism of action, selectively enhancing slow in- activation of voltage-gated sodium channels and modulating collapsin re- response mediator protein 2 (CRMP-2). Dr. Rosenfeld has been a principal investigator in several of the compa- ny-sponsored lacosamide studies.