months was striking. On the other hand, ataxia is also a prominent clinical feature of the Kuru-plaque variant found in this patient, which is linked to the MV genotype at codon 129 and PRP^{sc} type 2. However, we cannot elucidate whether CJD of this patient unmasked SCA12 at a subclinical stage or whether the 49 allele is a large and rare normal allele without any influence on the phenotype and, unfortunately, there are no other family members available for genetic evaluation. What remains is the coincidence of two very rare diseases, respectively genetic variations. The protein phophatase PP2A may play a part in tau phosphorylation and apoptosis. Therefore, the possibility that a large SCA12 repeat could influence the pathogenesis of sporadic CJD, especially the Kuru-plaques variant, should be further evaluated.

The role of the 40 and 41 CAG repeats in two sporadic late onset ataxia cases is also difficult to interpret and we cannot exclude a pathogenic influence, although an even larger allele was found in a young Indian healthy control. The findings of this study implicate a more sophisticated interpretation of SCA12 alleles and raise the question about the diagnostic threshold between normal and expanded alleles.

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References

1 **Holmes SE**, O'Hearn EE, McInnis MG, *et al*. Expansion of a novel CAG trinucleotide repeat in the 5′ region of PPP2R2B is associated with SCA12. *Nat Genet* 1999;**23**:391–2.
2 **O'Hearn E**, Holmes SE, Calvert PC, *et al*. SCA-12: Tremor with cerebellar and cortical atrophy is associated with a CAG repeat expansion. *Neurology* 2001;**56**:299–303.
3 **Parchi P**, Giese A, Capellari S, *et al*. Classification of sporadic Creutzfeldt-Jakob disease based on molecular and phenotypic analysis of 300 subjects. *Ann Neurol* 1999;**46**:224–33.
4 **Srivastava AK**, Choudhry S, Gopinath MS, *et al*. Molecular and clinical correlation in five Indian families with spinocerebellar ataxia 12. *Ann Neurol* 2001;**50**:796–800.
5 **Fujigasaki H**, Verma IC, Camuzat A, *et al*. SCA12 is a rare locus for autosomal dominant cerebellar ataxia: a study of an Indian family. *Ann Neurol* 2001;**49**:117–21.

Pre-treatment with corticosteroids and a single cycle of high dose albendazole for subarachnoidal cysticercosis

Cysticercosis is a common parasitic disease of the central nervous system and a pleomorphic neurological disorder. It is an endemic problem in developing countries and is now increasing in industrialised nations.[1] In Mexico neurocysticercosis is one of the main reasons for neurological consultation, and the first cause of epilepsy in adults.[2] The treatment of neurocysticercosis is controversial and depends on the clinical and neuroimaging features, as well as the extent and severity of the associated inflammatory reaction.[3] Basal subarachnoidal cysticercosis and racemose disease of sylvian fissure may behave aggressively producing intracranial hypertension, obstructive hydrocephalus, chronic arachnoiditis, vasculitis, and cerebral infarctions.[4] Subarachnoidal cysticercosis may have a chronic course and a poor prognosis, and is still treated surgically. In a recent open trial of 33 patients with subarachnoidal cysts of at least 50 mm in diameter, treatment with albendazole at a dose of 15 mg/kg/day during 28 days produced an adequate response in 12 patients (36%). The remaining 21 patients (64%) required repeated courses of albendazole and 10 treatments with praziquantel because of a partial or incomplete response to the first albendazole cycle.[5] Repeated treatments are not a minor problem in areas where cysticercosis is endemic and medical resources are limited. To explore a more effective regimen for subarachnoidal cysticercosis we started a pilot study in 1998 with corticosteroids pretreatment and a single course of a higher albendazole dose.

We included 12 patients with the diagnosis of subarachnoidal cysticercosis based in clinical data, imaging studies, and inflammatory cerebrospinal fluid with a positive enzyme linked immunosorbent assay (ELISA) test against cysticercal antigens. After written informed consent six hospitalised patients were pre-treated with intravenous dexamethasone at a dose of 8 mg every eight hours for five days. Four outpatients not receiving corticosteroids were given oral prednisone at dose of 1.5 mg/kg of body weight per day for five days. Two patients with severe arachnoiditis with incomplete response to prednisone, one of them with vasculitis proved by angiography were already receiving cyclophosphamide 100 mg per day, the drug was continued in both and one of them was also pre-treated with oral prednisone as above.

Albendazole was given at a dose of 30 mg/kg of body weight per day in three divided doses for 15 days. As soon as oral intake was tolerated patients taking dexamethasone were switched to prednisone at dose of 1 mg/kg of body weight a day. After four weeks, and depending on the clinical status prednisone dose was tapered individually. Magnetic resonance imaging (MRI) was performed before treatment and three to six months after treatment.

Four men and eight women with an average age of 32.8 years (range 20 to 47) were included. The mean hospital stay for inpatients was 17 days. Table 1 gives symptoms and signs before treatment and at the end of the 15 days of albendazole treatment. In five patients a ventriculoperitoneal shunt was placed before albendazole treatment. In seven patients, corticosteroids improved clinical manifestations within the first 24 hours.

On baseline MRI, the number of subarachnoid cysts varied from 1 to 24 cysts per patient; 10 patients had cysts in the basal cisterns and three had racemose cysts in Sylvian fissure. In three patients additional lobar and subcortical cysts were also present and ependymal or leptomeningeal enhancement was observed in five patients.

On MRI studies at six months of follow up a reduction of 86% of the number of the subarachnoidal vesicles was observed, decreasing from 73 to 10 cysts ($p = 0.02$; Mann-Whitney U test two tailed), with a

Table 1 Changes after treatment in neurological symptoms, signs, and cerebrospinal fluid (CSF) analysis

	Before treatment	After 15 days of corticosteroids and albendazole treatment	
Symptoms	**Number**	**Number**	**p Value***
Headache	11	7	0.115
Nausea	8	2	0.036
Vomiting	7	1	0.027
Blurred vision	3	1	0.590
Somnolence	3	0	0.217
Abnormal mental status	3	1	0.590
Seizures	3	1	0.590
Diplopia	3	0	0.478
Signs			
Intracranial hypertension	11	2	0.001
Papilloedema	10	3	0.012
Abnormal ocular movements	3	0	0.217
Incoordination	2	1	1.000
Motor deficit	1	0	1.000
CSF	**Before treatment**	**At six month follow up**	
Opening pressure mean (SD)	236 (130)	159 (37)	0.018†
Glucose mean (SD)	62 (39)	45 (15)	0.119†
Proteins mean (SD)	73 (94)	97 (117)	0.564†
Cells mean (SD)	70 (133)	59 (110)	0.998†
ELISA+cysticercus antigens	9	12	0.590

*Univariate analysis by Fisher's exact test. †Mann-Whitney U test, two tailed.

volume reduction of 80%. Eight patients had satisfactory clinical recovery and four patients presented minor neurological deficit with functional independence.

During treatment one patient required ventriculoperitoneal shunt revision for acute intracranial hypertension. In the remaining patients the observed adverse effects were headache and nausea in two who did not required drug withdrawal.

Significant changes after treatment were observed mainly in symptoms and signs of intracranial hypertension and these were attributable to corticosteroid effects or shunting, or both. No significant modifications of glucose cells and protein levels of CSF were observed during six months of follow up. This means that chronic aracnoiditis continues after cyst destruction, and for some patients corticosteroids are necessary for long term treatment. We base our dose reductions according to clinical parameters, CSF characteristics, and leptomeningeal enhancement (MRI). In this study ELISA test's sensitivity increased after treatment.

Pre-treatment with corticosteroids reduces the risk of complications secondary to destruction of cysticerci.[4–5] In our patients an immediate clinical improvement seemed to be an indicator of adequate tolerance to subsequent albendazole treatment. Because of the variability of albendazole pharmacokinetics, we considered that treatment with 30 mg/kg/day of albendazole will increase its concentration in plasma and CSF, improving the efficacy. This small series shows that a higher albendazole dose along with corticosteroid treatment was safe and useful in the treatment of subarachnoidal cysticercosis. Patients need to be carefully selected and require close observation and to be available for long term follow up. A randomised trial of standard compared with high albendazole dose is in progress at our centre.

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References

1 **Del Bruto O**, Sotelo J, Román GC, eds. *Neurocysticercosis: a clinical handbook*. Lisse, Netherlands: Swetz and Zeitlinger, 1998.
2 **Medina M**, Rosas E, Rubio-Donnadieu F, *et al*. Neurocysticercosis as the main cause of late-onset epilepsy in Mexico. *Arch Intern Med* 1990;**150**:325–7.
3 **Evans C**, García H, Gilman R, *et al*. Controversies in the management of cysticercosis. *Emerg Infect Dis* 1997;**3**:403–5.
4 **Bang OY**, Heo JH, Choi SA, *et al*. Large cerebral infarction during praziquantel therapy in neurocysticercosis. *Stroke* 1997;**28**:211–13.
5 **Proaño J**, Madrazo I, Avelar F, *et al*. Medical treatment for neurocysticercosis characterized by giant subarachnoid cysts. *N Engl J Med* 2001;**345**:879–85.

Short term benefit of battery depletion in vagus nerve stimulation for epilepsy

Interest in neurostimulation to treat epilepsy has rekindled over the past decade, with vagus nerve stimulation (VNS) now an accepted part of the algorithm for care of patients with medically refractory epilepsy.[1] More than 15 000 VNS devices have been surgically implanted in patients around the world. The reported improvements in seizure control are modest and the mechanism by which VNS may exert its effects is unclear, however, the benefits are presumed to be directly related somehow to the electrical stimulation applied to the nerve. A small number of relevant experimental studies have shown antiepileptic effects related to VNS, although the effects may be non-specific, for example, in rats heating of the tail is equally effective as stimulation of the vagus nerve in stopping seizures and decreasing interictal spikes.[2] In our own work with thalamic deep brain stimulation for epilepsy we found that the observed benefits in patients' seizure control bore no relation to whether the stimulators were actually turned on or not.[3] Because patients can sense active VNS in the form of laryngeal side effects, no similar sham stimulation placebo has been possible with VNS.

If stimulation of the vagus nerve is actually a necessary part of VNS for epilepsy, depletion of the stimulator battery would be expected to result in an increase in seizures. Indeed, status epilepticus was recently reported to have occurred in one patient after stopping VNS for an elective brain MRI scan.[4]

No study has been formally published describing the effects of battery depletion in a large group of patients treated with VNS for epilepsy, however, the data from just such a study have been published informally—in the Cyberonics *VNS Physician's Manual*.[5] It is of interest to examine these data. Over the course of follow up of patients in the E03 VNS trial,[6] a total of 72 battery depletions in 68 patients occurred. Seizure frequency after battery depletion was monitored for one to four weeks after stimulation was stopped, with the outcome results divided into three groups: patients having a greater than 25% increase in seizures, patients unchanged with a less than 25% increase or decrease in seizures, and patients with a greater than 25% decrease in seizures. Forty two of 72 cases (58%) were in the last group—that is, the large majority of patients *improved* after battery depletion. Nineteen of 72 cases (26%) were unchanged and 11 of 72 (15%) worsened.

A χ^2 analysis of the results comparing patients with a greater than 25% seizure reduction with patients with a greater than 25% increase in seizures after battery depletion shows a highly significant benefit to battery failure ($p<0.0001$; $\chi^2 = 18.14$, two tailed test). This is the most significant finding of any statistical analysis performed in all of the VNS studies used to support licensing of the device as a treatment for epilepsy.[5–7] As the research hypothesis here specifies the direction in which a change will occur—that is, "there will be an increase in seizures when VNS stops," the alternative hypothesis is actually one tailed, which makes the significance of the findings even greater ($p<0.00005$). This means that the probability that the observed findings of improvement with battery depletion in most patients could have occurred by chance is less than 1 in 20 000. It is possible that the findings do represent such a chance occurrence. It is equally possible, or perhaps more probable, that any sort of non-specific change in patients with epilepsy might provide a perturbation sufficient to effect improvements in seizure control, at least in the short term. Either way, benefits in seizure control with VNS in humans seem to have little specific to do with active stimulation of the vagus nerve.

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References

1 **Benbadis SR**, Tatum IV WO, Vale FL. When drugs don't work. An algorithmic approach to medically intractable epilepsy. *Neurology* 2000;**55**:1780–4.
2 **McLachlan R**. Suppression of interictal spikes and seizures by stimulation of the vagus nerve. *Epilepsia* 1993;**34**:918–23.
3 **Hodaie M**, Wennberg RA, Dostrovsky JO, *et al*. Chronic anterior thalamus stimulation for intractable epilepsy. *Epilepsia* 2002;**43**:603–8.
4 **Beitinjaneh F**, Guido M III, Andriola MR. Status epilepticus precipitated by turning off the vagus nerve stimulator for elective brain MRI. [Abstract]. *Epilepsia* 2002;**43**(suppl 7):337–8.
5 **Cyberonics**. *Physician's manual for the NeuroCybernetic prothesis system. NCP pulse generator*. Houston: Cyberonics, 2000.
6 **The Vagus Nerve Stimulation Study Group**. A randomized controlled trial of chronic vagus nerve stimulation for treatment of medically intractable seizures. *Neurology* 1995;**45**:224–30.
7 **Handforth A**, DeGiorgio CM, Schachter SC, *et al*. Vagus nerve stimulation therapy for partial-onset seizures. A randomized active-control trial. *Neurology* 1998;**51**:48–55.