with a neurological disorder therefore remains to be defined.

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Mononeuropathies in thyrotoxicosis

Recently Iguchi *et al*¹ reported two thyrotoxic patients with associated mononeuropathies and suggested a causal relationship. Other authors, such as, Beard *et al*² described the association between carpal tunnel syndrome (CTS) and Graves' disease. Also Siegler and Refetoff³ observed a bilateral peroneal palsy in a patient with thyrotoxicosis. Despite these observations the prevalence of neuropathies in thyrotoxicosis is unknown.

In a prospective study on 150 patients with CTS we found two patients with past history of thyrotoxicosis.⁴ This fact induced us to initiate a prospective study, presented in preliminary form at the XLI annual meeting of the Spanish Society of Neurology,⁵ to determine the frequency and course of CTS in thyrotoxic patients.

Sixty untreated thyrotoxic patients were studied clinically and by electroneurography (ENG): in 11, clinical symptoms of CTS were present (nocturnal paraesthesias or other symptoms that suggested median nerve damage). In eight of these 11 patients, ENG supported the clinical diagnosis (ENG diagnosis of CTS was accepted when sensory NCV across carpal tunnel was less than 45 m/s). Three patients had the simultaneous onset of symptoms of CTS and thyrotoxi-

cosis. All patients were followed clinically and by ENG for two years. The evolution of CTS and thyrotoxicosis was analogous and after two years all patients were free of symptoms. However, in one of them, with uncontrolled thyrotoxicosis, ENG studies deteriorated. The other patients, with remission of thyrotoxicosis, had normal ENG values in one case. Meanwhile in the other the ENG was unchanged. In another five patients of the series we also found ENG abnormalities supporting a subclinical CTS. The course of these cases was also parallel to thyroid status: two of them that developed, after 12 and 18 months respectively, typical CTS symptoms (with deteriorating ENG studies) were patients with uncontrolled thyrotoxicosis.

Another patient with thyrotoxicosis developed a right peroneal palsy due to nerve compression at the head of the fibula favoured, in our opinion, by the important muscular atrophy. After six months the recovery was complete.

Our results suggested that 5% of thyrotoxic patients developed a CTS as a consequence of thyrotoxicosis. In these cases we observed a good CTS evolution, always parallel to thyroid status. Excess thyroxine might play a role in the development of CTS. Other factors such as loss of weight, weakness, infiltration of the tendon sheaths with mucopolysaccharides² and infiltrative dermopathy³ can also contribute to generation of mononeuropathies in thyrotoxic patients.

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Mental representation and temporary recovery from unilateral neglect after vestibular stimulation

Vestibular stimulation temporarily reduces unilateral visual neglect.¹ Cappa *et al*² observed improvement of personal neglect and anosognosia for hemiplegia after vestibular stimulation. The effects on anosognosia and personal neglect suggest an influence of vestibular stimulation not only on the cerebral mechanism of attention to external stimuli, but also on deep cerebral structures involved in the mental representation of

space.³ Our study aimed to assess the effect of vestibular stimulation on mental visuospatial representation in subjects with unilateral neglect.

Five right handed subjects with clinical and CT evidence of right hemisphere damage (four ischaemic stroke and one spontaneous haematoma) were examined within one month of onset of illness. They all presented signs of left spatial neglect as revealed by a modified version of the Albert's line-crossing test.⁴ In this test the subject had to cross out 21 lines (2.5 cm in length), drawn in an apparently random manner on a sheet of paper, one line in the centre and 10 on each half of the paper. Personal neglect and anosognosia for motor deficits were evaluated by a four point rating scale.⁵ A visual representation task was carried out in the absence of stimuli from personal or extrapersonal space. The subject was asked to describe the cathedral square of Milan (Piazza del Duomo) from two opposing viewpoints;⁶ the results were evaluated by counting the number of landmarks unequivocally identified as belonging to the left and right sides of the piazza respectively according to the patients' (imagined) viewpoint. The battery of tests, taking less than 10 minutes, was applied immediately before vestibular stimulation (baseline assessment). Vestibular stimulation consisted in irrigating the left external auditory canal with approximately 30 cc of ice cold water. When a clinical reaction was manifest (nystagmus towards the right or possibly tonic displacement of the head or gaze to the left) the battery was repeated. The results are given in the table.

Vestibular stimulation improved patients' performance in the line-crossing test; four patients (cases 1, 3, 4 and 5) performed the task without error, while one (case 2) definitely improved. Case 2 had slight personal neglect and moderate anosognosia; under vestibular stimulation personal neglect temporarily disappeared but anosognosia was unchanged. In case 5 moderate anosognosia temporarily disappeared under vestibular stimulation. In another patient (case 3) vestibular stimulation produced a temporary amelioration of severe anosognosia.

In the visual representation task under vestibular stimulation, all subjects were able to report a greater number of "left side" landmarks of the cathedral square, while "right side" performance was unchanged. The differences between the number of "right side" and "left side" landmarks were computed for each patient and the paired Student *t* test showed a significantly different

Table Neuropsychological assessment before and after vestibular stimulation

Case	1	2	3	4	5
Line-crossing test*					
before	2	8	9	6	1
after	0	4	0	0	0
Anosognosia†					
before	0	2	3	0	2
after	0	2	1	0	0
Personal neglect‡					
before	0	1	0	0	0
after	0	0	0	0	0
Visual representation‡					
before (L-R)	1-3	1-3	1-5	0-2	3-6
after (L-R)	3-3	2-3	3-4	5-3	7-6

*Number of neglected lines on left side (max 10).

†Four-point scale: 0 = absent, 1 = mild, 2 = moderate, 3 = severe (for details see ref. 5).

‡Number of landmarks on left (L) and right (R) side.

performance after vestibular stimulation ($t = 4.8$, $df = 4$, $p = 0.009$). On repetition of the imagery task the day after vestibular stimulation performance was comparable to that at baseline.

One interpretation of the behavioural effect of vestibular stimulation on unilateral neglect is that it produces a non specific activation of the right hemisphere and decreases the imbalance caused by unilateral damage. We found, however, that more "left side" landmarks were registered after vestibular stimulation in all our patients in the visual imagery task, though the number of the "right side" landmarks did not decrease. This does not support the hypothesis that unilateral neglect is due to an imbalance in an opponent system that controls lateral orientation.

Our results suggest that the effects of vestibular stimulation on unilateral neglect are only partly caused by facilitation of visual exploration of the relevant sector of space as a result of displacement of gaze¹ or, more generally, by change in the relationship between outside stimuli and body coordinates: the results of the mental representation task suggest that the neuronal circuits underlying endogenous representation of egocentric space are modulated by vestibular projections.

The effects of vestibular stimulation on anosognosia support this supposition. One patient (case 3) had severe anosognosia at baseline evaluation: he denied his hemiplegia even after being asked to move the affected limbs: he grasped and raised his plegic upper left arm with the right hand. Under vestibular stimulation he acknowledged his motor deficit after being questioned specifically, but after about 30 minutes, when the effect of vestibular stimulation had disappeared the anosognosia worsened with respect to the baseline: on being asked to move his left upper limb he only raised the right one. In this patient high level cognitive processes, for example memory or reasoning, were not able to reverse the anosognosia after transitory amelioration following vestibular stimulation. This behaviour suggests that awareness of self is not founded on high level cognitive monitoring processes, but arises from neuronal integration of information about the present state of the body. The effects of vestibular stimulation on both visuospatial representation and anosognosia are consistent with the hypothesis that vestibular inputs exert a basic influence on the representation of self-centred space and the body.

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Ceftazidime encephalopathy: absence status and toxic hallucinations

We describe a case of absence status and non-epileptic hallucinations due to ceftazidime toxicity. Ceftazidime, a third generation cephalosporin, has structural similarities to penicillin.¹ The electro-clinical pattern in the patient closely resembled the generalised epilepsy model induced in cats by intramuscular penicillin.

A 34 year old man had chronic renal failure due to membranous glomerulonephritis. He was being treated with haemodialysis and was admitted for a parathyroidectomy. The operation was uneventful, and serum calcium was maintained postoperatively with supplements of calcium. On the second post-operative day he developed a left lower lobe pneumonia. Intravenous cefotaxime (1 g twelve hourly) and penicillin (1 million units six hourly) were administered. On the third post-operative day *Pseudomonas aeruginosa* was isolated from the sputum and cefotaxime was changed to intravenous ceftazidime (2 g twelve hourly). On the fifth post-operative day he was confused, incoherent, and had generalised myoclonic jerks as well as frequent eyelid fluttering. He reported vivid hallucinations at this time. On the sixth post-operative day uncontrolled sepsis was suspected and a further dose of ceftazidime was given. He then had a generalised tonic-clonic seizure. Serum calcium, magnesium, aluminium and glucose were normal. Blood cultures were negative.

An EEG showed continuous generalised three per second spike-and-wave activity that was abolished with 3 mg of intravenous clonazepam (figure). His confusional state immediately resolved and he was able to describe graphic visual and auditory hallucinations. They comprised vivid details of a man sitting in the room operating a complicated machine, the operation of which required the patient's utmost concentration. Other hallucinations were of brightly coloured balloons trying to come through the cracks in the wall, and of lights attached to a silver chain which broke when he averted his eyes. He also heard familiar voices outside his

room, and persistent knocking sounds. Ceftazidime and penicillin were ceased and tobramycin started. Hallucinations persisted for the subsequent two days during which dialysis was performed daily and his EEG did not show recurrence of the absence status. By the ninth post-operative day his mental state was normal. A cerebral CT scan was normal.

Serum ceftazidime levels were assessed using an anti-bacterial assay (*Bacillus subtilis*). Measurements on the fourth and fifth post-operative days yielded levels of 402, and 253 $\mu\text{g/ml}$ (normal peak level 55 $\mu\text{g/ml}$). The presence of penicillin would have interfered with the accuracy of the assay, but the levels of ceftazidime were still considered toxic. On day eight, after three days of dialysis, the serum level was 34.4 $\mu\text{g/ml}$.

The electro-clinical pattern in this patient, with impaired conscious state, fine myoclonic jerking, and generalised spike-and-wave discharges on the EEG was diagnostic of absence status.^{2,3} A similar clinical picture was described previously in a patient with renal failure given ceftazidime, but an EEG was not done and absence status was not diagnosed.⁴ The immediate reversal of the clinical and EEG abnormalities by intravenous clonazepam demonstrates that the drug caused a true epileptic encephalopathy. This must be distinguished from the usual pattern of toxic or metabolic encephalopathy where there is diffuse slow activity on the EEG, with little or no epileptiform activity, and the only treatment is withdrawal of the offending agent.

The electro-clinical features of this case were similar to those of the feline generalised penicillin epilepsy model, where there is strong evidence for the primary abnormality residing in the cerebral cortex.⁵ In humans, massive doses of systemic penicillin are required to cause convulsions, even in the presence of renal failure. It is unlikely that penicillin contributed significantly to the neurotoxicity, in the presence of an intact blood-brain barrier, with the doses used. Given the structural similarities of penicillin and ceftazidime,¹ we now suggest that the epileptic encephalopathy induced by ceftazi-

CEFTAZIDIME ENCEPHALOPATHY

Figure EEG performed on the sixth post-operative day. There was continuous generalised epileptiform activity associated with a confusional state and subtle generalised myoclonic jerks. Following the administration of intravenous clonazepam, the epileptiform activity disappeared and the confusional state and myoclonic jerks immediately resolved.