Concentrations of total tau protein immunoreactivity (TTIR) in lumbar CSF of patients with Alzheimer's disease (AD), elderly depressed patients (DEPR), patients with other neurological diseases (OND), young controls (COY), and elderly controls (COE). Mean values are indicated by horizontal bars.

sent study. Our investigation showed a highly significant increase of CSF total tau protein in patients with probable Alzheimer's disease compared with elderly depressed patients, patients with other neurological disorders, and young and elderly controls. It seems plausible that these increases are the result of enhanced release of tau protein from damaged neurons into the extracellular space and, as a consequence, into CSF. Recent results suggested an arbitrary cut off value of 200 pg/ml, at which only a small percentage of healthy controls are positive.² Based on our data, we would propose a 10% higher cut off value, of about 225 pg/ml, to better distinguish the elderly depressive patients as well as young and elderly controls. The observed difference between patients with Alzheimer's disease and elderly depressive patients confirms a recent study and is of particular interest.¹ Depressive periods can be accompanied by a severe impairment of attention, receptivity, and concentration which may mimic a dementing process. Thus early neurochemical identification of a depressive syndrome is of great importance for appropriate therapeutic strategies. The reason for more tau protein in depressed patients than in young and elderly controls is unknown. On the other hand, the non-significant difference between young and elderly controls leads to the assumption that increased tau protein is not merely a marker of aging itself.

There are contradictory reports regarding the correlation between MMSE and total tau protein immunoreactivity in the CSF of patients with Alzheimer's disease.¹⁻³ From our data there was a significant correlation only when including the whole range of scores, which became non-significant when excluding the patients with severe dementia. These results corroborate neuropathological findings which showed a significant correlation between the number of neurofibrillary tangles and MMSE only when including severely demented patients.⁵ In conclusion, total tau protein concentration in CSF is an important candidate for discriminating patients with Alzheimer's disease from elderly depressed patients as well as from young and elderly controls without mental illness. Further studies on other neurodegenerative diseases are in progress. Moreover, different combinations of tau

protein antibodies to detect exclusively normal or hyperphosphorylated tau protein may help to further evaluate the diagnostic value of tau determinations in CSF.

NORBERT RÖSLER
ILDIKO WICHART
KURT A. JELLINGER

Ludwig Boltzmann Institute of Clinical Neurobiology,
Lainz Hospital, Vienna, Austria

Correspondence to: Dr Norbert Rösler,
Psychiatrische Universitätsklinik, Hauptstrasse 5,
D-79104 Freiburg, Germany.

- 1 Hock C, Golombowski S, Naser W, Müller-Spahn F. Increased levels of tau-protein in cerebrospinal fluid of patients with Alzheimer's disease—correlation with degree of cognitive impairment. *Ann Neurol* 1995; 37:414-5.
- 2 Van de Voorde A, Vanmechelen E, Vandermeeren M, Dessaint F, Beckman W, Cras P. Detection of tau in cerebrospinal fluid. In: Iqbal K, Mortimer JA, Winblad B, Wisniewski HM, eds. *Research advances in Alzheimer's disease and related disorders*. New York: John Wiley, 1995:189-95.
- 3 Vigo-Pelfrey C, Seubert P, Barbour R, Blomquist C, et al. Elevation of microtubule-associated tau in the cerebrospinal fluid of patients with Alzheimer's disease. *Neurology* 1995;45:788-93.
- 4 Folstein MF, Folstein SE, McHugh PR. "Mini-mental state": a practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res* 1975;12:189-98.
- 5 Jellinger KA, Bancher C, Fischer P, Lassmann H. Quantitative histopathologic validation of senile dementia of the Alzheimer type. *Eur J Gerontol* 1992;3:146-56.

Bilateral infarction of the rostral pontine tegmentum as a cause of isolated bilateral supranuclear sixth nerve palsy related to hypertension

The difficulty in locating in vivo the paramedian pontine reticular formation (PPRF), which is the immediate premotor centre for saccade generation, has been a major obstacle to a better clinical understanding of many neuro-ophthalmological syndromes.^{1,2} Lateral rectus weakness from a pontine lesion is usually associated with other neuro-

logical signs.³ We report a hypertensive man with an isolated gaze disorder consisting of a severe bilateral abduction palsy and a sub-clinical bilateral gaze palsy—that is, bilateral conjugate slowness of saccades—with no other identifiable aetiology, who had a bilateral pontine infarction involving the rostral PPRF, seen on MRI.

A 64 year old man with a history of mild hypertension and hyperlipidaemia was referred for evaluation of painless horizontal diplopia of sudden onset. There was no history of head trauma, diabetes mellitus, or any other systemic disorder. Blood pressure was 150/100 mm Hg. Neurological examination was normal except for a complex type of gaze defect—namely, mild bilateral conjugate slowness of saccades with an additional severe right lateral rectus weakness and pronounced esotropia of the left eye on straight gaze. No nystagmus or internuclear ophthalmoplegia was seen and the rest of the extraocular movements were full. "Doll's head" manoeuvre (vestibular ocular reflex) in the direction of the palsy was intact. Pupil sizes and light reflexes were normal in both eyes. Sensation in the first division of the trigeminal nerve was intact. Facial and masseter muscles were of normal strength and there were no signs of long tract involvement. Results of routine laboratory tests, including CSF analysis, were unremarkable. Brain MRI (0.5 T) showed only minor bilateral hyperintensities at the upper pontine tegmentum, without definite relevance. One week later he suddenly complained of dizziness and a more intense diplopia on horizontal gaze. His neurological examination showed a newly developed complete paralysis of abduction of the left eye. A second MRI disclosed bilateral hyperintensities at the rostral pontine tegmentum compatible with infarction (figure). The oculomotor dysfunction resolved two months later with only a persistent mild bilateral slowness of saccades and no lateral rectus weakness.

Our patient's brain MRI showed a bilateral infarction with involvement of the rostral pontine tegmentum containing the PPRF, the structure responsible for the gen-

Axial T2 weighted MRI obtained with a 0.5 Tesla unit shows bilateral hyperintensities at the rostral pontine tegmentum compatible with infarction.

eration of horizontal saccades.⁴ In animals, this is located in the nuclei reticularis pontis oralis (NRPO) at the level of the upper pons.⁵ The patient presented a clinically evident paralysis of abduction of both eyes with a subclinical bilateral gaze palsy. Lesions impinged only on the area of the NRPO, with no abnormal signals in other pontine sections affecting structures such as the low PPRF (nuclei reticularis pontis caudalis (NRPC)), abducens nucleus, or the abducens nerve fasciculus. Bronstein *et al*,^{1,2} in their extensive review of the abnormalities of horizontal gaze, reported three patients with a single brainstem episode of unilateral gaze palsy with an additional "mild" sixth nerve palsy to the side of the gaze palsy. They attributed weakness of the lateral rectus to involvement of the sixth nerve nucleus and concluded that the presence of this sign may be useful in identifying the site of the lesion in the mild gaze palsies. Cells lying in the PPRF project directly into the abducens nucleus. The connectivity of this

network has been investigated in great detail and shows that several different groups of saccade related premotor neurons exist, the most important of which are the excitatory burst neurons.⁶ We think that involvement of these burst neurons or their descending axons as they course towards the sixth nerve nucleus could have contributed to the findings in our patient. Selective lesions within the PPRF might affect horizontal gaze in different ways, including "sixth nerve palsies" as in the patient in this paper.

Pontine infarcts should always be considered in the differential diagnosis of isolated sixth nerve palsies and in more complex gaze disorders. So in these patients, precise examination including MRI is needed.

JOSÉ MAREY LOPEZ

ROBUSTIANO PEGO REIGOSA

GEMA ALONSO LOSADA

SOLEDAD LOPEZ FACAL

MIGUELA MARIN SANCHEZ

Service of Neurology

ANGEL MARTINEZ MUNIZ

Section of Neuroradiology,

Hospital Juan Canalejo, La Coruña, Spain

Correspondence to: Dr J Marey Lopez, Servicio de Neurología, Hospital Juan Canalejo, Xubias de Arriba, 84, 15006 La Coruña, Spain.

- 1 Bronstein AM, Morris J, Du Boulay G, Gresty MA, Rudge P. Abnormalities of horizontal gaze. Clinical, oculographic, and magnetic resonance imaging findings. I Abducens palsy. *J Neurol Neurosurg Psychiatry* 1990;53:194-9.
- 2 Bronstein AM, Rudge P, Gresty MA, Du Boulay G, Morris J. Abnormalities of horizontal gaze. Clinical, oculographic, and magnetic resonance imaging findings. II Gaze palsy and internuclear ophthalmoplegia. *J Neurol Neurosurg Psychiatry* 1990;53:200-7.
- 3 Donaldson D, Rosenberg NL. Infarction of abducens nerve fascicle as cause of isolated sixth nerve palsy related to hypertension. *Neurology* 1988;38:1654.
- 4 Baloh RW, Furman J, Yee RD. Eye movements in patients with absent voluntary horizontal gaze. *Ann Neurol* 1985;17:283-6.
- 5 Henn V, Lang W, Hepp K, Reisine H. Experimental gaze palsies in monkeys and their relation to human pathophysiology. *Brain* 1984;107:619-66.
- 6 Fuchs AF, Kaneko CRS, Scudder CA. Brainstem control of saccadic eye movements. *Ann Rev Neurosci* 1985;8:307-37.