Matters arising

The muscle specimens were obtained during surgery from the same part of the cranial portion of the palatalpharyngeal muscle in all patients and controls. The muscle was exposed after the tonsil had been removed. The same surgeon (HL) collected or supervised the collection of all specimens. We consider our finding of a neurogenic lesion in the palatalpharyngeal muscle in patients with obstructive sleep apnoea to be correct. The same type of lesions have been described by Woodson et al.4 in the uvular muscle of these patients. Recently we have published a study showing affected sensory pharyngeal nerve fibers in obstructive sleep apnoea patients.4

We believe the different findings in the study by Iannaccone et al.4 are due to a different biopsy site being examined and that the same type of lesions is seen from obstructive sleep apnoea. Whether the type of abnormalities described in the MRC muscle by Iannaccone et al. are present also in the palatalpharyngeal or uvular muscle of snorers remains to be studied.

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N-Methyl-D-Aspartate (NMDA) antagonists in Parkinson's disease

We would like to comment on the letter by Montastruc et al. in which negative results in Parkinson's disease (PD) with the NMDA antagonist ifenprodil were reported. Ifenprodil acts at the polyamine binding site of the NMDA receptor. The authors state "this drug is, as far as we know, the only NMDA antagonist currently available on the market", and "our study is the first to investigate the clinical effects of an NMDA antagonist in the treatment of PD.

The adamananitines amantadine and memantine have been used since 1969 in the treatment of PD.5,6 The weak dopamine agonism in experimental studies seems insufficient to account for their clinical effects.4 It has been recently shown that amantadine and memantine act at the PCP binding site of the NMDA receptor coupled ion-channel.4 It is therefore concluded that: 1) there are other NMDA antagonists clinically available besides ifenprodil and 2) NMDA antagonists have been used successfully for many years in the treatment of PD.

The disappointing results with ifenprodil do not therefore argue against the newly proposed "targeted amantadine" therapy.5,6,7,8,9 but may be related to: 1) the pharmacokinetic profile of the drug; 2) a rather weak influence of polyamine binding site antagonists compared with the channel blockers on NMDA receptor function or 3) a pathologically altered polyamine binding site in PD. These points have to be examined in future studies.

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Montastruc et al reply:

We acknowledge Drs Kornhuber and Riederer's comments concerning our trial on ifenprodil in Parkinson's disease.1 We are well aware that the adamananitines amantadine and memantine have anti-NMDA properties but amantadine is also known to release dopamine from striatal neurons, to inhibit the reuptake of dopamine and to have anticholinergic effects.2 Despite some experimental data, the respective role of these different pharmacological mechanisms remains unknown to explain the clinical anti-Parkinsonian properties of these drugs. Amantadine has only a weak and transient clinical anti-Parkinsonian efficacy which may be compatible with a weak dopamine effect. There are mainly speculative links between the anti-NMDA and the anti-Parkinsonian effects of amantadine. In our opinion, it is therefore still premature to support Kornhuber and Riederer, because of the amantadine and memantine data only, that "NMDA antagonists are used successfully for many years in the treatment of PD." This is why we were interested in investigating the clinical effects of another drug, such as, ifenprodil, which does not have dopamine effects.

It is perfectly clear, as we had already stated in our first letter,1 that "our work does not exclude a definite role for NMDA antagonists in PD" because of the negative ifenprodil data. We had also already written that other NMDA antagonists with better pharmacodynamic or pharmacokinetic profile may be effective.2 Since our results have been published, we know that another NMDA antagonist is available in clinical practice. A recent open study has suggested that dextromethorphan, an antitussive drug that is also a non competitive antagonist of the NMDA receptor, might have some efficacy in PD.3

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Risk of stroke in TIAs with a cerebral infarct on CT

I have read the article by Koudstaal et al.11 in which the authors find a relevant ischaemic lesion on CT in 13% of TIA's, 35% of RINDs and 49% of minor stroke. In their wide bibliographic review these authors present one comparative study on infarction characteristics between patients with transient and persisting signs.2 We reported four years ago similar results in 219 patients with reversible ischaemic attacks demonstrating that the frequency of brain infarction was related to the duration of the neurological deficit.3 Ischaemic lesions on CT closely correlated with abnormal transcranial Doppler ultrasound. A higher percentage of recurrence was found in those patients with infarctions, but the difference was not significant.

Koudstaal et al mentioned the possibility of an increased risk of major stroke in TIA's with cerebral infarct on CT.4 Using our pre-
vions, we have performed a Cox multivari-
ate analysis of the probability of survival with stroke in 92 TIA patients with normal CT scan and in 24 TIA patients with cerebral infarct, followed during an average period of 21 months. Age, carotid lesions detected by ultrasonographic exam-
ination or angiography, and glycaemia level higher than 100 mg/dl were used as covari-
ates. Since in a previous study we observed that these variables were related independ-
tently with the prognosis,9 Ninety nine per-
cent of the TIAS without infarct and 79% of the TIAS with infarct survived without suf-
ferring further strokes (Mantel-Cox test, p < 0.0001). The probability of survival, free of stroke, was related with the presence of carotid atherosclerosis (odds ratio = 3.07, 95% confidence interval 1.27–7.40). Ischaemic lesions in the CT scan, age, and glycaemia levels had no independent pre-
dictive value.

Our results suggest TIAS with cerebral infarct to have a poorer outcome than the patients with concomitant stroke due to a higher frequency of atherosclerosis of the neck arteries.

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3 Dávalos A, Codina A. Factors of risk and vascular events in the ataque isquémico transitorio and in the infarcts with residual mini.

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6 Dávalos A, Codina A. Factors of risk and vascular events in the ataque isquémico transitorio and in the infarcts with residual mini.

7 The Dutch TIA Study Group. Predictors of major vascular events in patients with a transient ischemic attack or minor ischemic stroke. Stroke (submitted for publication).

8 Kiers et al presented a prospective study on 176 stroke patients focused on stroke outcome in relation to hyperglycaemia and diabetes.1 The patients were divided into four groups: 1) normoglycemic patients with normal hemoglobin A1c (HbA1c) level, without history of diabetes; 2) hyperglycaemic patients with normal HbA1c, without histo-

Kiers, Davis, Larkin et al reply: We thank Drs Murros and Foghholm for their comments. The relationships between diabetes, stress hyperglycaemia and stroke outcome are indeed complex. In our study design, we attempted to examine separately the effects of diabetes and stress hypergly-caemia on stroke outcome, compared with the normoglycaemic non-diabetic group, using the four groups categorised on the basis of the history, fasting glucose and glycosylated haemoglobin.1 We acknowledge that stress hyperglycaemia was also likely to be present in the normoglycaemic, non-diabetic subjects, but we would agree that this adverse effect could have been due to stress hyperglycaemia in a proportion of the diabetic patients. We are aware that there have been ani-

mals studies of cerebral ischaemia which have suggested that hyperglycaemia may be protective,1,2 but there is also substantial evidence to the contrary, and this has been clearly shown by the results of our study, and previous human investigations,3 is that elevated blood glucose is associated with a worse outcome after stroke. This associa-
tion was even present within our eugly-
caemic group. As discussed in our paper, it is not possible to conclude whether this is a causal relationship or whether the degree of hyperglycaemia reflects the severity of the acute event. Until the pathogenesis of the association can be resolved, however, glu-
cose infusions should be avoided in acute stroke.

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