central venous catheter was introduced upward until the tip of the catheter was obstructed by the bone. Then, the catheter was drawn back 0.5 cm. The catheter tip location was verified by an antero-posterior X-ray taken in the recovery room. This technique was successfully applied for 48 patients. The mean length from the skin insertion to the tip of the catheter was 13 ± 0.2 cm (mean ± SD). It is recognized that the technique is very easy and no complication or dislocation of the catheter tip occurred.

Sincerely Yours,
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References

Flow and Neuronal Density in Tissue Surrounding Chronic Infarction

To The Editor

We should like to congratulate Dr. Mies and his colleagues on a most elegant study (Stroke 14: 22–27, 1983), and in particular for their lucid discussion of the potential role of diaschisis in electrophysiological suppression in areas where flow is reduced but remains above infarction thresholds. Using standard perfusion-fixation techniques we have examined the marginal (or anterolateral), suprasylvian and ectosylvian gyri in cats subjected to occlusion of the middle cerebral artery for two hours.1 Like Dr. Mies and his colleagues, we found a gradation of severity of change: ischaemic cell change of classical type was extensive and almost homogeneous on the ectosylvian gyri, more patchy but present in all experiments on the suprasylvian gyrus, and was also found on the marginal gyrus in five of six experiments after a careful search. On the marginal gyrus, the abnormalities were not always present on the convexity of the gyrus, but were sometimes found on the edge of the marginal sulcus facing the suprasylvian gyrus. We would anticipate that such changes would lead to visibly focal neuronal loss in long-surviving animals; small foci in which neurons are absent would be expected and we would also predict — although this would require experimental proof — that neurons would be lost more diffusely around these foci. Such a pattern of diffuse loss would explain the gradual decrease in neuron counts which would not be easily detected without the quantitative procedures adopted by Dr. Mies.

Our observations, therefore, suggest that there is patchy ischaemic cell change on the marginal (anterolateral) gyrus acutely following middle cerebral artery occlusion, and make it unnecessary to postulate retrograde degeneration due to white matter infarction, the mechanism proposed by Dr. Mies and his colleagues. Indeed we are not aware of any quantitative evidence that white matter infarction causes retrograde degeneration and loss of neurons in the cerebral cortex, and would be interested to know if such evidence actually exists. We would not however dispute that functional suppression of cortex could occur on this basis. Secondly, our findings serve to emphasise that ischaemic histopathological change should be classified broadly under two headings. First, homogeneous or uniform change resulting in a complete cystic infarct with loss of all neurons and glia: as demonstrated by Morawetz and his colleagues, the flow threshold for this change in the primate is approximately 12.5 ml/100 g/min,2 closely resembling that for massive potassium fluxes.3 Secondly, more restricted foci of ischaemic cell change may be associated with higher ischaemic flows, perhaps up to 25 ml/100 g/min. The pattern of histological change in such penumbral areas in our own studies was variable, but in one or two examples, there was a suggestion of neuronal loss in laminar distribution (layers 2 and 3) and it is possible that certain cortical layers are selectively vulnerable to penumbral cortical ischaemia in a fashion analogous to more well established instances of selective vulnerability, for example, hypoxic or epileptic damage in the hippocampus.

Dr. Mies and his colleagues make the further point that in ischaemic penumbra it is sometimes possible to restore physiological ion distribution by reperfusion, although electrophysiological function is less regularly restored. They interpret this finding as indicating ischaemic damage to deep white matter connections of the affected zone. However, there is evidence that certain synaptic mechanisms such as monoamine4 and acetylcholine5 synthesis may be sensitive to ischaemia, and recovery in these compartments may take longer than is required for recovery of normal extracellular cation concentrations. It should also be mentioned that normal or near-normal restoration of cation activity during reperfusion does not necessarily imply histological integrity; we have made some comparisons of histological appearance with the temporal profile and extent of loss of potassium homeostasis during the period of insult, and found that where potassium is restored almost to normal by reperfusion following increases above 10 mM, there is nevertheless considerable histological abnormality.

Dr. Mies and his colleagues state (p. 26) that "the decreased number of histologically intact nerve cells in the gyrus suprasylvius and gyrus ectosylvicus can be caused by retrograde degeneration due to white matter infarction and by transient impairment of blood supply severe and long enough to cause selective ischaemic cell necrosis." We would favour the latter explanation and our findings in the acutely ischaemic marginal gyrus support this: we doubt whether it is necessary to postulate any additional explanation.

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To the Editor:
The letter of Dr. Strong and colleagues refers to their recently published investigations on electrophysiological, hemodynamic, biochemical and histological changes occurring 2 hours after onset of focal ischemia. Although our data gave no indication of neuronal loss in the marginal gyrus 8 weeks after chronic brain infarction, it was of interest for us that indeed evidence exists for the acute histopathological changes of neurons in the marginal gyrus after shortlasting MCA occlusion concomitant with early diaschitic electrophysiological impairment. Discrete or even single neuronal cell loss, of course, will be very difficult to detect when assessed in several 0.2 x 0.2 mm areas at a magnification of 400. To correlate the histological appearance of tissue with regional autoradiographic blood flow measurements, this requires at least 1 mm² to be well above the autoradiographic resolution and certainly a compromise in our study. In the chronic stage of infarction, there are, however, variations of the neuron-flow relationship in the marginal gyrus (fig. 4) which may be related to disseminated neuronal changes already seen two hours after onset of MCA occlusion. It remains questionable, however, whether the single dark neurons present in the lateral gyrus are responsible for the reduction of spontaneous neuronal activity as Dr. Strong and colleagues suggest. The authors observe only mild reductions of blood flow within the marginal gyrus, thus, excluding the probability of hypoxic stress with subsequent effect on synaptic mechanisms. After prolonged complete ischemia of the brain for 30 min, the electrophysiological recovery as judged by the EEG is fully restored after 2 hours despite the presence of delayed hypoperfusion. Seemingly, additional mechanisms must be involved during the onset and persistence of electrophysiological diaschisis.

We are well aware of the fact that the stated axonal deafferentiation or degeneration or eventual neuronal loss contributing to chronic brain infarction must be considered hypothetical until proven. Different parts of the nervous system respond variably to axonal sectioning. Motoneurons of the spinal cord or cranial nerve nuclei undergo a typical chromatolytic reaction. In regions of the dorsal thalamus or in the inferior olive acute retrograde degeneration of neurons occurs after axotomy without typical alteration at the cellular site. Pyramidal cells of the cortex seem to be more resistant to axonal dissection when collateral branches exist proximal to the site of injury. Dissection of the optic nerve (eye enucleation) is known to lead to cessation of synaptic transmission in the lateral geniculate nucleus after 3-4 days concomitant with the degeneration of synaptic terminals. In chronic preparations the lateral geniculate body is reduced in volume and increased in cell density (gliosis) indicating neuronal loss with subsequent fiber degeneration. Thalamic lesions cause Wallerian degeneration which extends to the deep layer of the cortex. After entorhinal lesions involving the efferent axons of the CA1 pyramidal neurons delayed degeneration of the dorsal part occurs. On the other hand, after white matter lesions diaschistic impairment of the EEG was reported before. Functional deafferentiation between subcortical-cortical connections of whatever origin might very well influence the outcome of tissue surrounding chronic infarction. What we hypothesize is that white matter infarcts beneath the gray matter may contribute to the late neuronal loss when those axons are destroyed from neurons which do not collaterize or are vulnerable to axonal interruption. However, we also recognize that, for example, the development and delayed spread of brain edema within the white matter could also contribute to such changes apart from hemodynamic disturbances. The historical appearance of neuronal tissue around chronic infarctions, therefore, is likely to reflect the result of all damaging equivalents occurring during this period.

Careful studies of the interval between the acute and chronic stage of the brain infarctions are needed to supply the missing information on the pathophysiological sequelae after such an event.

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