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CORRESPONDENCE

Transcranial Doppler sonography in acute stroke

We read with great interest Markus' overview of transcranial Doppler (TCD) ultrasonography.¹ Markus highlighted the new aspects of such clinical applications of this technology in cerebral haemodynamics and detection of emboli. Although the application of TCD in acute stroke was briefly discussed, we point out some of the recent and exciting findings in the acute stroke setting.

There is increasing evidence that intravenous tissue plasminogen activator (TPA) is an effective therapy for ischaemic stroke.² However, the impact of this therapy has been limited by several factors. Clearly TPA is not efficacious for all eligible patients, with about 50% of treated patients left dependent or dead. Explanations for this incomplete effect include poor recanalisation rate, completed infarction before reperfusion, no reflow phenomenon, and haemorrhagic complications. New strategies must be adopted to both improve our understanding of how and when thrombolysis treatment works to improve our approach to achieving benefit from these therapies. Vascular neuroimaging in the acute setting of ischaemic stroke is an important step in this direction. The technique of TCD is inexpensive, portable, and non-invasive, and is well suited to the acute stroke setting and readily accessible at many centres. Several recent studies have shown that TCD can define arterial obstruction in acute cerebral ischaemia with a high degree of sensitivity and specificity compared with magnetic resonance (MRA) or conventional angiography.³⁻⁴

It is able to confirm the presence of arterial occlusion, determine site and extent of obstruction, and uniquely monitor for signs of recanalisation.²⁻⁷ Previous studies have shown that early TCD studies can predict outcome. Arterial patency or early recanalisation predicts neurological improvement with TPA whereas persistent occlusion is associated with poorer outcome.⁵⁻⁶

Hence, TCD could become the ideal modality to assist the clinician in the emergency room with patient selection for intra-arterial therapy. If the middle cerebral artery stem occlusion can be confirmed or ruled out in a matter of minutes by bedside TCD, the need for angiography could be reduced to a minimum in this setting.³ Obtaining continuous information about the status of an arterial occlusion during intravenous thrombolysis has the potential to be very helpful in further

decision making. Dramatic clinical recovery can be achieved during TPA infusion if early complete recanalisation of the middle cerebral artery occurs.⁷ Microembolic signals have also been described during monitoring of thrombolysis or spontaneous recanalisation and may signify clot dissolution.⁷⁻⁸ On the other hand, persisting arterial occlusion may identify patients at high risk of worsening or recurrent stroke who may require aggressive measures of secondary stroke prevention.

Although TCD can offer a wealth of interesting information, its use is still limited due to many factors, including operator dependency and the need for in depth knowledge of cerebrovascular pathophysiology. Standardisation and prospective validation of TCD methodology is necessary to broaden its application for this exciting new setting. If TCD can be shown to be both valid and reliable for diagnosing occlusion among a group of clinicians we expect broader acceptance of this modality.

We view TCD as a neurological "stethoscope" of the brain (as Camilo Gomez described it) in the acute setting and utilise this technique to compliment our clinical findings in the emergency room. We encourage others to consider TCD for this application.

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Markus replies:

I agree with Barber and colleagues that transcranial Doppler (TCD) may well have important applications in selection of patients with acute stroke for thrombolysis. It is an appealing hypothesis that it may allow the identification of patients in whom recanalisation has already occurred, and in whom thrombolysis is not indicated, therefore sparing them treatment with thrombolysis and possible complications. This could increase the risk-benefit equation when giving thrombolysis. It is possible, however, that patients in whom the middle cerebral artery is patent may also benefit from thrombolysis. For

example, patients with middle cerebral artery branch occlusions, which are not detectable by TCD, may also benefit. In addition, it is unclear from the thrombolysis trials whether patients with lacunar stroke may also benefit. Stroke subtyping was not sufficiently rigorous to answer this question. Despite these provisos I would agree with Barber and colleagues that this hypothesis needs testing. I would strongly encourage any future thrombolysis trials to include assessment of middle cerebral artery patency by transcranial Doppler at the time of patient recruitment. The advent of new small easily portable TCD machines which are considerably cheaper than the previous PC based models, will greatly facilitate such a study.

Giant cell arteritis of the cervical radicular vessels presenting with diaphragmatic weakness

We were interested to read the paper by Burton *et al* reporting the association between giant cell arteritis and cervical radiculopathy. The evidence for giant cell arteritis seems incontrovertible, but the possibility remains that this patient might have had motor neuron disease coexisting with giant cell arteritis. Details of the clinical examination, investigations, and pathology point to this possibility. Furthermore, the neuropathological report does not include immunocytochemical studies that would be necessary to exclude the diagnosis of motor neuron disease.

The clinical picture is one of a lower motor neuron syndrome affecting all four limbs without objective sensory involvement. Denervation was confirmed in all four limbs, whereas the vascular inflammatory changes concentrated around the radicular arteries in the lower cervical roots. Pathological examination of the spinal cord demonstrated "diffuse pallor of myelin" with minor loss of anterior horn cells "and chromatolysis". In the differentiation of the syndrome from motor neuron disease, it must be confirmed that the classic pathological features are absent. In addition to myelin pallor in the corticospinal tracts, staining for the microglial marker CD68 and astrocyte marker GFAP should be performed. Furthermore, staining of the motor cortex, brain stem, and spinal cord sections for ubiquitin and neurofilament should be performed to exclude a primary motor neuron degeneration.

Lymphocyte cuffing and microglial infiltration are common in motor neuron disease, even in those cases attributable to mutant SOD1.¹ Ubiquitin staining is a very sensitive and specific marker for motor neuron disease, and should be searched for extensively before the diagnosis can be excluded with confidence.² It is well known that motor neuron disease may present with symptoms due to respiratory muscle weakness,³ and otherwise the clinical phenotype in this case is very suggestive of the flail arm variant of the disease,⁴ and we would hope that a comprehensive neuropathological search for this diagnosis was performed in a case such as this before it was ascribed to a vasculitis and recorded as such in the literature.

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Winer et al reply:

We are pleased that Leigh and Shaw found our report of interest and that the evidence that the patient had from giant cell arteritis is incontrovertible.

We also agree that the clinical features were very suggestive of motor neuron disease, which was in fact the antemortem clinical diagnosis. The only disagreement is whether the patient had two diseases or just giant cell arteritis.

Histological studies of the postmortem material, however, showed evidence of arteritis in the exact distribution of the clinical deficit—that is, the cervical roots associated with diaphragmatic function which we found convincing as the sole explanation for the clinical picture.

We agree that it is not possible to exclude the rare possibility of both motor neuron disease and arteritis and will undertake the suggested staining of sections of the brain stem, spinal cord and motor cortex with ubiquitin.

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Unidirectional dyslexia in a polyglot

We read with interest the short report by Leker and Biran,¹ describing unidirectional dyslexia in a polyglot, and would like to offer alternative hypotheses for the symptomatology.

The case describes alexia while reading Hebrew, but not when reading English. This is a recognised neuro-ophthalmic phenomenon, which we have encountered in our practice in patients reading the Urdu language, another script written right to left.

The extent of reading difficulties in patients with hemianopia is well described.² Patients with a right hemianopia cannot see letters following those already deciphered. Patients with a left hemianopia can read without difficulty, until they have to refixate the beginning of the next line which is in the hemianopic field, and their place in the text is then lost. It would be interesting to know if this was the case with this patient while reading English. Turning the page through 90° allows reading in the intact hemifield, and is standard advice to all patients with hemianopia.² Also by turning a page through 180° the Hebrew text would have been readable and comprehensible, as this would allow horizontal reading in a left to right direction.

The process of reading consists of repetitive small saccadic eye movements alternating with periods of fixation. Semantic identifica-

tion of word strings occurs during these pauses between the saccades. At the end of a line, a large saccade in the opposite direction, to the beginning of the next line occurs and the pattern of small saccades is repeated.³

Horizontal saccadic eye movements for reading are generated to peripheral visual stimuli (letters following those already interpreted). If the stimulus is in the hemianopic field, there is a primary inability to initiate the saccade (saccades can be generated without a target, but tend to be inaccurate). Also, the parietal eye fields are involved in horizontal saccadic eye movements, and may be implicated in the reported case given the anatomical location of the haematoma. Parietal eye field neurons discharge while executing visually guided saccades, and during learned saccadic tasks, which may be important during reading,⁴ and parietal lesions are known to cause saccadic defects. Vertical saccades are mediated via a separate system.

In true alexia, reading error results from an inability to interpret written material. The anatomical basis of alexia without agraphia is well described. This usually occurs in association with a right hemianopia, colour anomia, cerebral dyschromatopsia, and prosopagnosia, and is seen in left occipital lesions with damage to the contralateral visual association fibres which cross in the splenium of the corpus callosum.⁵ Reading pathways are well defined from visual cortex to auditory cortex via the dominant left angular gyrus, and such lesions have essentially isolated the angular gyrus from visual input. We think that the reported case describes "pseudoalexia" or "hemianopic dyslexia",¹ where a fixation splitting hemianopia causes difficulty reading by obscuring parts of words.

Visual hallucinations are common in patients with hemianopias despite being rarely mentioned,⁵ and in this case represent a release phenomenon, as ictal activity and pharmacological causes were excluded. They are a prognostically favourable sign.² Palinopsia is also seen in hemianopic fields. It would be interesting to know what palinoptic imagery was seen in this case, and under what circumstances. Was it perseveration of the hallucinations, or "blindsight" imagery of objects in motion being detected in the blind hemifield (the Riddoch phenomenon).

The "fluttering" described in the intact visual field of the reported case may reflect the "bilateral effect" seen from unilateral occipital lesions, which affect the primary visual and extrastriate cortex. Such damage is thought to alter interhemispheric connections along their presplenial course and cause disturbance of visual attention.² The effects are usually subtle relative to the hemianopia but often functionally significant.

We think that all the symptoms in the reported case can be accounted for within the realms of established knowledge, without postulating the existence of novel language associated neuronal networks in the right hemisphere.

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The authors reply:

We thank Mohamed, Elsherbiny, and Goulding for their insightful comments regarding our paper.¹ We also think that the essence of this case is the distinction between a peripheral and a central processing defect causing the lexical phenomenon encountered by our patient. Mohamed et al suggest saccadic dysfunction as a mechanism for explaining the unidirectional dyslexia in our patient. However, whereas such a mechanism can explain right to left dyslexia when reading sentences, our patient had the same language abnormalities when reading isolated words when such saccadic mechanisms are not as important. We agree with Mohamed et al that visual hallucinations in the hemianopic field represent a favourable sign as indeed exemplified by the favourable outcome in our patient. Furthermore, we concede that the fluttering motion probably contributed to our patient's lexical difficulties. As pointed out by Mohamed et al such motion results from alterations in interhemispheric (occipital) connections.² This favours a more central processing abnormality. Moreover, the persistence of the unidirectional dyslexia while the visual fields returned to normal, as well as the dissociation between reading Yiddish (written in Hebrew letters from right to left), which was preserved, to reading Hebrew which was abnormal both support a higher hierarchical disorder.

Last but not least, the role of the right hemisphere in language functions as suggested by our case is supported by recent observations on aphasia recovery after stroke.³

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Dyslexia in Hebrew

This letter concerns the very interesting short report about unidirectional dyslexia in a polyglot by Leker and Biran.¹ We wonder if the authors would offer an explanation for the fact that at a time the patient still had "minor deficits when reading Hebrew" (page 518) he made no mistakes when reading Yiddish?