Editorial

Neurology in Practice and Practical Neurology

M Rossor

The last issue of *Neurology in Practice* was seen in 2005; it was a very successful educational review series that took us through the whole spectrum of neurology. The success was due to the commitment and creativity of Ian Bone and Geraint Fuller, the editors of the series, and our thanks go to them.

The value of the series demanded that we should continue in some guise or another and the solution has been the opportunity to marry up with *Practical Neurology*. *Practical Neurology* was the brainchild of Professor Charles Warlow who has edited the journal since the first issue in October 2001. It is a journal

of news, views and reviews, and previously was owned by Blackwell. When the title was acquired by BMJ Publishing Group there was an obvious opportunity for the *Neurology in Practice* cycle of reviews to be picked up by *Practical Neurology* and for it to continue as a bi-monthly companion to the *JNNP*, subscribers to *JNNP* will automatically also receive *Practical Neurology*. We are delighted that Professor Charles Warlow will continue as Editor and, as such, the Journal will maintain its own editorial policy and independence. We welcome *Practical Neurology* as our sister publication and look forward to the partnership with Professor Warlow.

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Periventricular white matter lesions

Is the whole brain periventricular?

F Barkhof, P Scheltens

The term periventricular is becoming meaningless and should be abandoned

The unique sensitivity of MRI to detect brain tissue alterations, especially white matter lesions (WML), has intrigued researchers ever since the introduction of this modality in the 1980s. Following early reports on the apparently meaningless nature of WML, and the naive labelling of WML as "unidentified bright objects" or UBOs,¹ a wealth of studies have examined the relevance of WML in normal and pathological ageing. This has yielded strong and converging evidence regarding risk factors for WML and, to a lesser extent, the clinical significance of WML for cognitive dysfunction. Contributing to the latter are factors such as study design (cross sectional *v* longitudinal), selection bias (population based *v* case-control), type of cognitive assessment (dementia screening tools *v* detailed neuropsychology), and MRI methodology (choice of scan acquisition and analysis technique).

In the quest for elucidation of the significance of WML for cognitive functioning, the issue of localisation of WML has gained considerable attention, since it is obvious that certain locations are more relevant than others, depending on the type of function probed. In the current issue, Van den Heuvel and colleagues (*see pages 149–53*)² report

an increase in periventricular, but not subcortical, WML in parallel with cognitive decline in a population based study on non-demented subjects. These longitudinal data are in agreement with results from the cross sectional Rotterdam Scan Study³ to the extent that they suggest that subcortical lesions may be less relevant (for certain cognitive functions). While one can certainly formulate a plausible hypothesis to support the specific clinical impact of periventricular lesions (disrupting important descending and association fibres traversing this area), such speculations depend very much on the definition of what constitutes a "periventricular" WML.

MRI-histopathological studies have revealed that a commonly encountered feature on scans of aged individuals, so called "caps" and "bands" of high T2 signal, reflect only mild pathology in the 5–10 mm zone directly adjacent to the ventricles.⁴ Since the associated histopathological changes (disruption of the ependymal lining, myelin pallor, and some subependymal astrogliosis) are relatively mild, these strictly periventricular changes (within 10 mm of the ventricular lining) are singled out in certain visual rating scales.^{5,6} Other studies, however,

apply the term periventricular much more loosely: van den Heuvel *et al* report that approximately 80% of WML are "periventricular", defined as any WML having contact with the ventricle; in the Rotterdam Scan Study, this percentage is around 60%.³ It is obvious that labelling such a high percentage of lesions as being periventricular deviates from the previously mentioned data on "caps" and "bands".

When WML grow, they have a tendency to become confluent, and in the end such confluent abnormalities are increasingly likely to be contiguous with the ventricles. In the most extreme case, with almost all white matter involved, up to 100% of WML would thus be labelled "periventricular", although extending almost to the cortex; it is clear that under such conditions the term periventricular becomes meaningless and might be better abandoned. Apart from questionable anatomical definitions, it is clear that this bias will preclude finding any clinico-radiological associations in the subcortical zone.

Since there is no radiologically meaningful definition on which part of the white matter is periventricular, and what constitute deep white matter, nor evidence for a distinct class of subjects with either type of lesion in isolation,⁷ it would make more sense to abandon this artificial classification and analyse WML in a more anatomically meaningful way. Using advances in computational neuroanatomy, this is now becoming feasible. One can either map a template (an atlas with known anatomical relationships) to the subject space to calculate a fractional volume of WML in a given tract, or study the relationship between a given cognitive measure and the probability of finding a WML across a group of subjects registered to standard space. On the other hand, the

apparent controversy detailed above marks the need for better radiological-pathological correlation studies, applying more sophisticated MRI and histopathological techniques.

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Authors' affiliations

F Barkhof, Department of Radiology, VU Medical Centre, PO Box 7057, 1007 MB Amsterdam, The Netherlands

P Scheltens, Department of Neurology, VU Medical Centre, PO Box 7057, 1007 MB Amsterdam, The Netherlands

Correspondence to: Frederik Barkhof, Department of Radiology, VU Medical Centre, PO Box 7057, 1007 MB Amsterdam, The Netherlands; f.barkhof@vumc.nl

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CADASIL

Cognitive profile in CADASIL patients

L Caeiro, J M Ferro

Age is an important predictor of clinical deterioration in CADASIL patients

Cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL) often starts with silent lacunar infarcts or white matter changes in the third decade of life and cognitive or other neurological signs become apparent within the next 10 years. In the following 20 years, dementia and psychiatric disturbances become more and more apparent and death frequently occurs in the sixth decade of life.^{1–3}

Age is an important predictor of clinical deterioration, with an odds ratio of 1.10^4 per year starting at the age of 24. Cognitive impairment affects about 60% of CADASIL patients, and psychiatric disturbances nearly 30%. Cognitive impairment initially manifests through mild executive and visuospatial deficits, psychomotor slowing, and apathy.⁵ Working and short term memory defects also appear insidiously⁶; later on, abulia and other executive dysfunctions are the main manifestations of CADASIL. Two thirds of CADASIL patients are dependent and have dementia by the time they die.¹ Dementia is more apparent if the patient has a lower educational level.⁶

In the paper by Buffon *et al* in this issue of the journal (*see pages 175–80*), the cognitive profile of 42 CADASIL patients is described. The authors conclude that executive dysfunction

dominates the pattern of cognitive impairment in CADASIL, followed by visuo-constructive memory impairment. With aging, other cognitive dysfunctions become more and more evident, denoting a diffuse cognitive impairment, except for the relative preservation of the encoding process in episodic memory.

This paper replicates the results of previous studies^{2–5} and confirms that the cognitive profile of CADASIL is similar to that presented by patients with subcortical ischaemic vascular dementia. In fact, CADASIL can be considered a pure form of subcortical ischaemic vascular dementia.

A limitation of the paper by Buffon *et al* is the design of the neuropsychological evaluation. Inferences concerning the role of age on cognitive impairment are drawn from a cross sectional evaluation of CADASIL patients of different age groups.

Much more robust conclusions would result from a longitudinal neuropsychological evaluation of CADASIL patients, starting in their third decade and repeated, in parallel with neuroimaging, for instance, every 5 or 10 years. To achieve adequate statistical power, such a longitudinal study would need to involve many centres and countries, because of the limited number of CADASIL patients available in

individual regions. The harmonisation of a neuropsychological battery to be used in different languages is a difficult but achievable task.⁷ This longitudinal study would elucidate the relative role of lacunes and white matter changes, their localisation and their influence on the development of cognitive impairment, mood changes, and movement performance in CADASIL patients.

As CADASIL is a pure subcortical ischaemic vascular dementia, it is a good model for pilot clinical trials for this type of dementia. Antiplatelets or statins to prevent progression of the disease are unlikely to be effective, as CADASIL is mainly a disease of the arterial media. Other candidate drugs to be tested with the aim of improving cognition are cholinergic agents, memantine, and antidepressants.

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Authors' affiliations

L Caeiro, J M Ferro, Stroke Unit, Department of Neurosciences and Mental Health, Serviço de Neurologia, Hospital de Santa Maria, Faculdade de Medicina de Lisboa, Portugal

Correspondence to: Lara Caeiro, Stroke Unit, Serviço de Neurologia (piso 6), Hospital de Santa Maria, Av. Professor Egas Moniz, 1649-035 Lisboa, Portugal; laracaeiro@fm.ul.pt

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