A united approach to vascular disease and neurodegeneration

March, 2012, saw the first step in an ambitious international effort to create expert consensus on the terminology and definitions used to describe vascular pathology on neuroimaging. Supported by the Centres of Excellence in Neurodegeneration (CoEN) collaborative funding initiative, the project—Standards for Determining the Vascular Contribution to Neurodegeneration—should serve as a catalyst for research to establish the role of vascular factors in cognitive decline, dementia, and neurodegeneration.

Vascular pathology is highly prevalent in elderly people and vascular contributions to cognitive impairment and dementia in later life are now widely acknowledged. Evidence that vascular risk factors such as hypertension, diabetes, and hypercholesterolaemia increase the risk of Alzheimer’s disease (AD) has also led to a rethinking of the role of vascular factors in potentiating or even triggering neurodegenerative disease. Many people with dementia or clinically probable AD have mixed pathology—commonly AD and cerebral small vessel disease (SVD)—and there is evidence that vascular pathology can be additive with AD pathology in impairing cognitive function and increasing the likelihood of dementia. But vascular factors have been somewhat neglected in many areas of dementia research.

There are a number of reasons for this. There has been an intense focus on the amyloid hypothesis of AD in efforts to identify biomarkers for the various stages of the disease and in the development and testing of potential therapies. Uncertainty over the prevalence and relevance of vascular pathology in AD has hindered research, as has a lack of clarity over diagnosis. How much evidence of vascular pathology is required to give a diagnosis of vascular dementia? And how should this be assessed in life? This uncertainty stems in part from wide variation in the definition and description of vascular pathology on neuroimaging. For example, more than 20 different terms have been used in the literature to describe lacunes, including “lesion”, “small deep infarct”, “ischaemic stroke”, and “stroke”, many of which imply a cause that is not necessarily known rather than simply describing what is seen on neuroimaging.

The new project, led by Joanna Wardlaw (University of Edinburgh, UK), Martin Dichgans (Deutsches Zentrum für Neurodegenerative Erkrankungen, Germany), and Eric Smith (University of Calgary, Canada), is tackling the problem by bringing together experts on the imaging of cerebrosvascular disease and neurodegeneration to agree standard terminology and definitions for vascular pathology on MRI and CT (exemplars will be made available through a central website), and to suggest standards for image acquisition, analysis, and reporting. The initiative will include two workshops—a core group of experts attended the first workshop in Edinburgh, UK, on 8–10 March, 2012, and a larger, multidisciplinary group will meet in Munich, Germany, on 7–9 November, 2012—with a structured process for developing and agreeing standards in between.

The project will deal with the multiple manifestations on neuroimaging of SVD, in addition to other types of vascular pathology, and will relate imaging findings to relevant clinical, cognitive, and pathological variables. The focus on SVD is important because manifestations of the disease are prevalent in the elderly and are a common comorbidity in patients with neurodegenerative disease. But reaching a consensus is likely to be difficult. There is disagreement over terminology and definitions even among experts in vascular imaging, and the evidence base is unlikely to support rigid classifications for all features of SVD. A flexible system that acknowledges what we do not know but need to understand, with subsequent validation, might prove to be the preferred approach.

Standards agreed through this project should facilitate efforts to identify the causes and pathogenic mechanisms of lacunar stroke and SVD; to understand how vascular factors contribute to cognitive impairment, dementia, and neurodegeneration; and to develop interventions for the primary and secondary prevention of vascular disease. An early target for the use of standards could be the identification of biomarkers for monitoring disease progression. In future, prospective clinical–neuroimaging–pathological studies should allow a better understanding of the pathological basis of neuroimaging changes and further refinement of the terminology and definitions.

This impressive endeavour should strengthen links between the fields of cerebrovascular disease and neurodegeneration. A welcome consequence of this could be a stronger focus on concomitant vascular pathology in studies of AD and, potentially, new strategies for treatment and prevention. ■ The Lancet Neurology

For more on CoEN see http://www.coen.org
For more on vascular contributions to cognitive impairment and dementia see Stroke 2011; 42: 2672–713
For more on risk factors for Alzheimer’s disease see Review Lancet Neurol 2011; 10: 819–28
For more on cerebral small vessel disease see Review Lancet Neurol 2010; 9: 689–701
For more on variation in the definition, detection, and description of lacunes see Stroke 2010; 42: 359–66