

Is migraine a progressive disorder?

Considering the clinical implications of new research data on migraine and brain lesions

Migraine has received considerable attention in the past 15 years as it has come to be better understood as a brain disorder with new and efficient treatment strategies.¹ The World Health Organization considers a day with severe migraine to be in the highest category of disability, comparable to quadriplegia.² Migraine is classically described and defined as an episodic disturbance manifest primarily as head pain and sensitivity to afferent stimuli, such as light (photophobia), sound (phonophobia) and head movement.³ Against this background, new data have emerged that open the issue of whether migraine may be *progressive* in some way.

Kruit and colleagues recently published a cross-sectional, population-based study of Dutch adults aged 30–60 years. They compared the prevalence of brain infarctions and white-matter lesions between people with migraine and control subjects matched for age, sex, place of residence and potential risk factors for cerebrovascular disease.⁴ Overall, there was no difference between people with migraine and controls in prevalence of infarction. There was an increase in posterior circulation lesions in patients with migraine with aura, and more deep white-matter lesions in women with migraine. The authors concluded that some patients with migraine are at increased risk for subclinical lesions in certain brain areas.

These data come at a time when others have suggested a link between migraine and right-to-left cardiac shunts⁵ (which may predispose to stroke), and when there are known risks for stroke in women under 35 years with migraine.⁶ It has been suggested that these data may mark migraine as a progressive, rather than simply

episodic, disorder.⁷ This is not a trivial question for migraineurs or their physicians.

A progressive disorder is one where there is a continuous increase in severity or extent (*Oxford English Dictionary*). This may relate to symptoms or some objective measure, such as brain imaging. Migraine certainly does not, in general terms, increase in severity with time, as the natural history is to abate and disappear in later life.⁸ So, with very few exceptions, it could not be called progressive on the basis of increasing severity with time. This does not negate the fact that some migraine sufferers go through enormously disabling periods of frequent attacks — chronic migraine.⁹ This smaller group¹⁰ needs attention, but progression should not be ascribed to the vast majority of sufferers.

Whether migraine causes permanent, progressive brain lesions is also not established. The relationship between migraine and cardiac right-to-left shunts is at best cloudy. These shunts may arise from a patent foramen ovale (found in about a quarter of the population), atrial septal defects and arteriovenous malformations; they have been implicated in stroke and decompression illness as a result of paradoxical embolism. However, studies of the association with migraine were not population-based, and case definitions were very poor, mixing migraine with aura with isolated aura. The latter makes it impossible to be sure whether the events described were migrainous or ischaemic in nature.

Stroke risk is certainly increased for women under 35 with migraine with aura, but the increase is small, and one wonders if this highlights a prothrombotic or vasculopathic comorbidity in a particular subset, rather than a general pathophysiological princi-

ple for all patients. The new study by Kruit and colleagues⁴ gives pause for thought, but, as it is cross-sectional, it provides a hypothesis, not proof. It certainly does not provide evidence that lesions in the brain produce chronic migraine. Only a longitudinal study would give information on accumulation of lesion load that would provide evidence for a progressive course. While the authors of a recent meta-analysis of observational studies of ischaemic stroke risk in migraine conclude that there is an association,¹¹ their review, unfortunately, adds nothing to our understanding. Most studies show an association, and half of the 14 studies in the meta-analysis did not divide their patients with migraine into those with and without aura. Thus, the really interesting possibility suggested by Kruit and colleagues⁴ of patients with migraine with aura being at increased risk of subclinical brain lesions could not be explored.

What are the clinical implications of the new data? First, we can assure patients with migraine without aura that there seems little risk of any progressive or serious problem in terms of brain lesions. Unfortunately, we can also assure them that they will suffer, losing time from work and their personal life, year on year, unless we can help them manage their attacks properly by appropriate advice and use of acute attack and preventive medicines. For patients with migraine with aura, I explain that the risk of stroke is small. Indeed, it is smaller, even for those taking oral contraceptives, than the risk of stroke during pregnancy itself. The available data do not, in my view, justify antiplatelet agents in patients with migraine with aura, nor do they provide intellectual justification for paternalistic limitations on patient choice in, for example, contraceptive use. As a rule, I investigate the unusual: one might target those with prolonged aura (ie, over an hour³) with standard stroke investigations.

Migraine is a horrible, disabling, biologically determined, inherited brain disorder rendering life much less tolerable, but for the

moment there is no sustainable position that it is *progressive* for most patients. We can look forward to new data with which to qualify and quantify the issue.

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