

FOCUS ON RESEARCH

ANIMAL MODELS OF LACUNAR STROKE: ARE THERE ANY AND HOW RELEVANT ARE THEY? A SYSTEMATIC REVIEW

Researchers

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Aim

About a fifth of all strokes are quite small (less than 2 cm across) and specifically affect the deeper structures of the brain. These small "lacunar" strokes are caused by something going wrong in the small blood vessels that run deep into the brain, but the exact abnormality is unknown. Suggestions include blood clots or fatty plaque blocking the tiny vessels, or a malfunction of the vessel lining leading to failure of the mechanism that normally filters the blood before it reaches the brain. We aimed to find out as much as possible about experimental (animal) studies ("models") that were already published because this might enable us to understand what goes wrong in people when they have one of these small deep lacunar strokes

Project Outline/Methodology

We sought experimental models that could represent lacunar stroke, including those explicitly claiming to mimic lacunar stroke and those representing other diseases with similar features (e.g. vascular dementia). Studies were identified from online databases using a defined search strategy. We used a structured data extraction form based on prior systematic review experience, to extract key information (stroke induction method, brain lesion size, vessel and tissue changes, etc) to assess pertinence to lacunar stroke.

Key Results

We found 5670 references including 40 relevant studies (45 publications). Over 10 different ways of causing an experimental stroke were identified. Only 7 claimed to be relevant to lacunar stroke. Summarising the studies was difficult as important information such as the size of the stroke or number of animals used, was often missing. In general, the strokes produced were too large and too diverse to represent human lacunar stroke. The few studies that could be deemed relevant tended to focus on brain damage (not blood vessel abnormalities). However, we can say that blood clots and fatty plaque build up in the blood vessels are unlikely to be a common

mechanism for lacunar stroke. Only one experimental animal showed both brain and blood vessel abnormalities consistent with human lacunar stroke, but the mechanism appeared to involve failure of the small vessel lining and leak of substances into the vessel walls and brain, rather than blockage of vessels by blood clot.

Conclusions

Although there are models which produce small deep stroke lesions, in most cases the method of creating these abnormalities does not mimic what we know about what causes small deep strokes in humans. The model which is most similar to the human problem involves failure of the normal blood filters in the small deep vessel walls, and not sudden loss of blood supply due to a vessel blockage as with most larger strokes.

What does this study add to the field?

Blood vessel blockage by blood clots and fatty plaque are unlikely to be common mechanisms for lacunar stroke. Therefore, most animal models of small deep strokes that are available would have limitations for evaluating new treatments to reduce damage in humans due to small deep strokes. A model that more closely mimics the small deep strokes that occur in humans does exist, but the mechanism is quite different to the traditionally accepted causes of stroke.

Implications for Practice or Policy

The mechanism of small deep strokes may be different to that of most other strokes and so require different prevention and treatment approaches to other types of strokes.

Where to next?

Studies should look in more detail at what goes wrong in the small deep vessels in the models that most closely mimic human lacunar stroke.

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