Stroke research in 2018: extended time windows, refined benefit, and lifestyle prevention targets

2018 was a busy year for stroke research. Advances included extended time windows for recanalisation therapies in acute ischaemic stroke, development of ingenious devices to improve outcomes, refinement of the use of antiplatelet drugs in secondary prevention, and heightened awareness of the effects of adverse environmental and lifestyle exposures on brain health and of cerebrovascular disease on cognition.

Recanalisation therapy has finally broken the crucial 4·5 h time barrier, with successful outcomes achieved with treatment administered at 16 h[1] or 24 h after stroke,[2] or for patients with unknown time of onset,[3] using thrombectomy[1,2] or intravenous thrombolytic therapy.[3] These trials all used some form of imaging to select patients according to either perfusion imaging with a perfusion lesion-to-infarct core ratio of 1·8 or more,[1] or an acute ischaemic lesion visible on diffusion imaging but not on FLAIR MRI,[3] or a mismatch between the severity of the clinical neurological deficit and the infarct volume by CT perfusion or diffusion MRI.[2] However, these approaches vary in their applicability to the clinic. The trials were all stopped early and showed greater benefit of recanalisation therapy than of standard of care therapy, without excess hazard.[1–3] Attention should now turn to optimising treatment delivery. Delivering thrombectomy remains problematic in many settings and patients who undergo the procedure without general anaesthetic have better outcomes than those who have a general anaesthetic.[4] A change in licence criteria for intravenous alteplase treatment, the standard of care for acute ischaemic stroke, is long overdue. An individual patient data meta-analysis showed that removing the 80 years upper age limit (in Europe) and relaxing the time window from 3 to 4·5 h (in the USA) would allow substantially more patients to benefit from alteplase (about 17% more with the age limit increase and 36% with the time window increase) without additional harm.[5] Every acute stroke patient arriving at hospital should be considered for recanalisation therapy, unless contraindicated; "time every brain"[1] should be the new maxim.

Gadgets aimed at improving outcomes in various ingenious ways are achieving prominence and reaching the large trials sessions at international conferences. In patients requiring tracheostomy for impaired swallowing, 3 days of pharyngeal electrical stimulation increased the number of patients ready for decannulation.[6] The World Stroke Congress presentation of a trial of sphenopalatine ganglion stimulation to enhance collateral flow around the infarct suggests that this might become a new reperfusion approach.

In secondary prevention, the answer to the question of how many antiplatelet drugs should be used and for how long is becoming clearer. In the POINT trial,[7] 90 days of clopidogrel plus aspirin prevented 1·5% more recurrent ischaemic vascular events than aspirin alone (hazard ratio [HR] 0·75; 95% CI 0·59–0·95), but caused 0·5% more major haemorrhages (HR 2·32; 1·10–4·87) when given after transient ischaemic attack or minor ischaemic stroke. Even more intensive antiplatelet treatment was given in the TARDIS trial,[8] in which a 1-month regimen of three drugs was compared against guideline-based therapy in patients who had a transient ischaemic attack or minor ischaemic stroke; the three-drug regimen caused more major haemorrhages but no net hazard.[8] Reassuringly, the beneficial effects of randomised lipid-lowering and blood pressure-lowering drugs given for 3–6 years in the ASCOT trial[9] lasted beyond the 6 years of the trial: patients with hypertension who received amlodipine had fewer stroke-related deaths than those who received atenolol and patients with hyperlipidaemia who received a lipid-lowering drug had fewer cardiovascular deaths than those who received placebo.

For primary prevention of stroke and brain health in general, the focus is firmly on lifestyle, environment, and education.[10] The American Heart Association's *Life's Simple 7* campaign includes recommendations on diet, exercise, and weight control as well as blood pressure, blood sugar, cholesterol management, and smoking cessation, but estimates that only 0·5% of the US population meet the targets described in the campaign. Simple devices, such as mobile phone apps (eg, the World Stroke Organisation's Stroke Riskometer) that help individuals monitor their activities might help people adjust their lifestyles. These approaches are important; an analysis of more than 300 000 people in the UK identified that unhealthy lifestyle factors

For more on the **American Heart Association *Life's Simple 7* campaign** see https://www.heart.org/en/healthy-living/healthy-lifestyle/be-healthy-for-good-with-lifes-simple-7-infographic

increased the risk of stroke far more (66% increase *vs* people with healthy lifestyles) than genetic risk factors did (35% increase *vs* people without high genetic risk).[11]

Cognitive impairment and dementia are arguably the commonest manifestations of cerebrovascular disease. Regardless, vascular disease is still low priority among Alzheimer's disease researchers, even though vascular disease is preventable and treatable, whereas thus far Alzheimer's disease is not. Conversely, cognitive consequences of stroke still do not receive enough research or clinical attention. One factor that might help increase researchers' interest in stroke is that, as of 2018, stroke is no longer classed as a brain disease, but is officially a neurological disease according to WHO; however, arguably, given the diversity and size of its burden, stroke should be in a category of its own.

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Dementia research 2018: current and future population relevance

When asked to select the most important advances in dementia in 2018, as seen through a small number of papers (out of the tens of thousands published), I was presented with a challenge. Dementia research spans a huge range of subject areas, such as ageing, gerontology, developmental research, neuroscience, social science, ethics, law, engineering, architecture, and even environmental research. The academic literature reports on prevention, screening, early detection, treatment of symptoms, and end-of-life care. No one researcher can cover all these territories, and the meaning of best will vary hugely accordingly to an investigator's discipline and overall perspective. Given this complexity, I have chosen to reflect on changing approaches to dementia and have selected papers that use different methodologies and come from different disciplines.


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At present, the dominant approaches in dementia research include data science, imaging, and biomedicine (especially –omics). These approaches are being brought together as powerful methods to understand human disease, with neuroscience at the forefront. Artificial intelligence will be in the background, measuring, analysing, defining, and nudging our lives in directions that might or might not be transparent. Artificial intelligence techniques are being explored to incorporate the neglected area of small vessel disease into more accurate ways of linking brain imaging to clinical states.[1] However, major concerns remain about