Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Important advances in stroke research in 2020

Although 2020 has been marked by the evolution of the COVID-19 pandemic, important advances in medical research have been reported, particularly in stroke treatment and secondary prevention.

In 2006, the Stroke Prevention by Aggressive Reduction in Cholesterol Levels (SPARCL) trial[1] showed the benefit of intensive statin treatment (atorvastatin 80 mg daily) in secondary stroke prevention. Almost 15 years later, the effect of intensive reduction of LDL cholesterol after a recent ischaemic stroke or transient ischaemic attack in the setting of atherosclerotic disease was assessed in the Treat Stroke to Target trial,[2] a parallel group, single-blind, randomised trial done at 77 sites in France and South Korea. Almost 3000 patients were randomly assigned either an LDL target of less than 70 mg/dL (lower target group) or a target range of 90–110 mg/dL (higher target group). During follow-up of median 3·5 years (IQR 2·0–6·7), patients allocated to the lower target group had reduced risk for the composite primary endpoint of major cardiovascular events compared with patients in the higher target group. More than 65% of composite major cardiovascular events in both groups were ischaemic strokes or strokes of undetermined origin, highlighting the increased stroke risk in this population. The absolute risk of intracranial haemorrhage was small, and similar in the lower and the higher target group. These trial results corroborate those of SPARCL and emphasise intensive lipid management as a crucial therapeutic target in secondary atherosclerotic stroke prevention.

In a review of two independent randomised trials,[3] dual antiplatelet treatment with aspirin and clopidogrel was shown to be superior to aspirin monotherapy in patients after a minor acute ischaemic stroke or a transient ischaemic attack. A subsequent double-blind randomised trial—The Acute Stroke or Transient Ischaemic Attack Treated With Ticagrelor and ASA for Prevention of Stroke and Death (THALES)[4]—done at 414 sites in 28 countries compared the antiplatelet ticagrelor (180 mg loading dose followed by 90 mg twice daily) in addition to aspirin (300–325 mg on the first day followed by 75–100 mg daily) with aspirin alone within 24 h of onset of a minor non-cardioembolic acute ischaemic stroke or transient ischaemic attack. The combination of ticagrelor with aspirin was associated with lower rates of stroke or fatal events, a lower rate of ischaemic stroke events, and more severe bleeding episodes within 30 days of follow-up, compared with aspirin monotherapy. Although THALES reiterates the benefit of short-term dual antiplatelet treatment, any additional value from using ticagrelor instead of clopidogrel remains uncertain.

Although several observational cohort studies have investigated intravenous thrombolysis before endovascular thromboectomy,[5] the Endovascular Thrombectomy with or without Intravenous Alteplase in Acute Stroke trial[6] is the first to address the hypothesis that endovascular thrombectomy alone is non-inferior to the combination of endovascular thrombectomy preceded by intravenous alteplase in patients eligible for both treatments. After enrolling 656 patients at 41 academic centres in China, endovascular thrombectomy alone within 4·5 h of stroke onset was shown to be non-inferior to endovascular thrombectomy preceded by intravenous alteplase with respect to 3-month functional outcomes. Safety and efficacy outcomes did not differ between the two groups, except that successful reperfusion before endovascular thrombectomy occurred more frequently in the combined intravenous alteplase and endovascular thrombectomy group (2·4% *vs* 7·0%). Taking into account the 20% wide non-inferiority margin with respect to functional outcome, the difference between groups in the percentages of enrolled patients not receiving endovascular thrombectomy, and the many patients allocated combination treatment who did not receive the full dose of alteplase, in addition to the fact that alteplase is not reimbursed in China, this research question still remains open and will hopefully be answered soon by other ongoing randomised trials.[7]

Although endovascular thrombectomy has substantially improved functional outcomes of patients with acute ischaemic stroke, many treated individuals die or are left severely disabled. The Efficacy and Safety of Nerinetide for Treatment of Acute Ischaemic Stroke trial was the first randomised trial to assess the safety and efficacy of a neuroprotectant within the endovascular thrombectomy setting.[8] Around 1000 adult patients eligible for endovascular thrombectomy up to 12 h after symptom onset were randomly allocated either intravenous nerinetide (one dose of 2·6 mg/kg) or placebo. Nerinetide did not increase the likelihood of good

clinical outcome, defined as a modified Rankin Scale score of 0–2 at 3 months, compared with placebo; other safety or efficacy outcomes also did not differ between groups. In the prespecified subgroup analyses, there was evidence of a treatment effect modification by alteplase, which the investigators attributed to a presumed inhibitory action of alteplase to the study drug. Patients receiving either alteplase or tenecteplase before endovascular thrombectomy will, therefore, be excluded from the ongoing Efficacy and Safety of Nerinetide in Participants With Acute Ischaemic Stroke Undergoing Endovascular Thrombectomy Excluding Thrombolysis trial (NCT04462536).

We declare no competing interests.

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Dementia research in 2020: moving forward despite the COVID-19 pandemic

2020 has been the year of the COVID-19 pandemic, which has substantially affected our lives and interfered with clinical and research activities. However, there have been several major research findings and initiatives moving the dementia field forward. Important progress has been achieved in blood-based biomarkers, which are minimally invasive and more accessible compared with CSF-based and PET-based investigations. Blood-based biomarkers could, therefore, be applied to large populations for early and accurate detection of Alzheimer's disease across the clinical spectrum, from at-risk individuals with no cognitive symptoms to patients with dementia.

An ultrasensitive plasma immunoassay for tau phosphorylated at Thr181 (p-tau181), a highly specific biomarker of Alzheimer's disease pathology, has been developed and tested in four clinic-based prospective cohorts,[1] which overall consisted of 1131 individuals, including elderly patients at different stages of the Alzheimer's disease clinical continuum, age-matched controls, patients with other neurodegenerative disorders or vascular dementia, and healthy young adults. The study findings suggested that blood-based p-tau181 can predict tau and amyloid β neuropathology, differentiate Alzheimer's disease from other neurodegenerative disorders, and identify Alzheimer's disease across the clinical continuum.[1]

Encouraging findings have also been reported for a blood-based assay measuring tau phosphorylated at Thr217 (p-tau217), which has been tested in three cross-sectional cohorts consisting of 1402 individuals,[2] including elderly patients at different stages of the Alzheimer's disease clinical continuum, age-matched controls, and patients with other neurodegenerative disorders. The study also included an autosomal-dominant Alzheimer's disease kindred of carriers (and age-matched non-carriers) of the PSEN1 Glu280Ala mutation. The p-tau217 assay showed good ability to differentiate clinically diagnosed Alzheimer's disease from other neurodegenerative conditions, and it differentiated individuals with Alzheimer's disease neuropathology from those without diagnostic levels of Alzheimer's disease neuropathology, either by post-mortem analysis or by neuroimaging and CSF analysis. In the same study, the diagnostic accuracy of p-tau217 was superior to that of other Alzheimer's disease biomarkers, including plasma p-tau181, plasma neurofilament light chain, and structural neuroimaging