**Research**

**Pioglitazone Therapy in Patients With Stroke and Prediabetes** 526
Insulin resistance should be treated in patients with stroke to prevent recurrent events, but quantification of such resistance in recent trials has been complex. In a post hoc subset analysis of the Insulin Resistance Intervention After Stroke (IRIS) randomized clinical trial of 2885 patients with prediabetes as defined by hemoglobin A1c level and/or fasting glucose level, 1456 patients were randomly assigned to receive pioglitazone and 1429 to placebo. Spence and coauthors found that there was a significant reduction of cardiovascular events and new-onset diabetes in patients with good adherence (at least 80% of the protocol dose taken), suggesting that insulin resistance screening and insulin-sensitizing agents as needed should be introduced into standard treatment of patients with stroke and prediabetes. Editorial perspective is provided by Pantoni.

*Editorial 521*

**Early Intensive Treatment vs Escalation for MS** 536
Uncertainty remains about how to optimally treat multiple sclerosis (MS): initially with high-efficacy disease-modifying therapies (DMTs) or a moderate-efficacy DMT approach with escalation as needed. In this cohort study of 592 patients, Harding and coauthors found that 5-year disability outcomes of patients who received high-efficacy DMT as first-line treatment had a smaller increase in disability vs those who received a monitored escalation approach to therapy, despite a more adverse prognostic profile at baseline. These findings suggest either that early high-efficacy treatment may confer a biological advantage that is unavailable in later disease or that real-world escalation algorithms may be inadequate to prevent unfavorable long-term outcomes. These data highlight the need for a prospective clinical trial comparing DMT algorithms.

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**Sex Differences in Global Amyloid and Regional Tau Deposition** 542
Although research suggests that there are sex differences in the progression of Alzheimer disease (AD), it is unclear why women show more rapid cognitive decline in the earliest stages of preclinical AD. Using data from β-amyloid and tau positron emission tomography scans from 2 cross-sectional cohorts of 296 clinically normal adults in the Alzheimer’s Disease Neuroimaging Initiative database and the Harvard Aging Brain Study, Buckley and coauthors found that women demonstrated higher levels of tau in neurofibrillary tangles than men in those with elevated levels of β-amyloid, particularly in the entorhinal cortex. It remains unclear why women might exhibit greater levels of tau overall, but it appears that there may be biological reasons for sex differences in AD risk.

**Swallowing Recovery and Enteral Tube Feeding After Stroke** 561
Around half of all patients who have a stroke are affected by swallowing difficulties and are at risk of malnutrition, dehydration, and aspiration pneumonia, but currently, there are only broad guidelines on who should receive enteral tube feeding. In a single-center derivation cohort of 153 patients and a multicenter validation study of 126 adults, Galovic and coauthors developed and prospectively validated in 4 Swiss tertiary centers the Predictive Swallowing Score (PRESS), a prognostic model of dysphagia recovery after stroke. Model predictions can inform the decision for nasogastric tube or percutaneous endoscopic gastrostomy feeding and can be calculated at bedside using a smartphone application for more individualized medical care.

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**Concussion Biomarkers: Deviating From the Garden Path** 515
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**Untethering Idea Generation From Protocol Execution in Neurorehabilitation Research**
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