Notable in *Neurology* this week

This issue features an article that investigates whether arginine methylation is altered in patients with amyotrophic lateral sclerosis and its effect on disease severity, progression, and prognosis; another considers a plasma metabolomic biomarker signature for migraine. A featured article examines the predictors of 7- and 30-day readmissions for pediatric patients hospitalized with neurologic diagnoses.

**Articles**

**Effect of age at puberty on risk of multiple sclerosis: A mendelian randomization study**

Using mendelian randomization in 41,505 individuals, the authors demonstrated that genetic predisposition toward later puberty reduces risk of multiple sclerosis. Importantly, this effect was mediated by the association between pubertal timing and obesity. These findings suggest that strategies aimed at decreasing obesity rates may effectively reduce multiple sclerosis incidence.

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*From editorialists Goris & Dubois: “With increasing availability of sufficiently large datasets of individual-level genotypes and well-selected phenotypes and appropriate caution, MR is now starting to move beyond susceptibility toward heterogeneity.”*

Page 735

**Progressive parkinsonism in older adults is related to the burden of mixed brain pathologies**

In this study, the authors identified that progressive parkinsonism in older adults, with and without clinical Parkinson disease, is related to the burden of mixed brain pathologies. Parkinsonism in old age is not specific for Parkinson disease pathology but frequently indicates the presence of several age-related brain pathologies.

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**Top-down alteration of functional connectivity within the sensorimotor network in focal dystonia**

The development of diagnostic and therapeutic approaches for dystonia depends on understanding its causative pathophysiology. Dynamic causal modeling of brain activity in spasmodic dysphonia revealed top-down alterations of excitation and inhibition within premotor-parietal-putaminal circuitry. Dystonic network disruption occurs at the level of cortical sensorimotor preparation to movement execution, well before the dystonic behavior is output by motor cortex.

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Continued
Double-blind, randomized, placebo-controlled study of trofinetide in pediatric Rett syndrome

Rett syndrome is a neurodevelopmental disorder with debilitating symptoms but no approved therapy. In this trial, trofinetide demonstrated significant efficacy compared with placebo on 3 measures of core symptoms. These results provide evidence of the effectiveness of trofinetide as a potential treatment for Rett syndrome and support further trials.

From editorialists Hagerman & Tuchman: “This article is a positive light in a sea of negative studies for other neurodevelopmental disorders.”

Comparative effectiveness of teriflunomide and dimethyl fumarate: A nationwide cohort study (see p. 744)

1. Comparative effectiveness of teriflunomide and dimethyl fumarate: A nationwide cohort study
2. What’s Trending: The Rise of Pseudomedicine for Dementia and Brain Health

In the first segment, Dr. Stacey Clardy talks with Dr. Mathias Buron about his paper addressing the comparative effectiveness of teriflunomide and dimethyl fumarate. In the second part of the podcast, Dr. Jason Crowell focuses his interview with Dr. Joanna Hellmuth on the rise of pseudomedicine for dementia and brain health.

Disclosures can be found at Neurology.org.
Spotlight on the April 16 issue
Robert A. Gross
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