individual patient from those that are effective for her type of epilepsy.

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PLASMA MULTIANALYTE PROFILING IN MILD COGNITIVE IMPAIRMENT AND ALZHEIMER DISEASE

David A. Bennett, Chicago: In an elegant targeted proteomics study of 3 cohorts with more than 1,000 subjects, Hu et al.[1] nominated several peripheral proteins associated with Alzheimer disease (AD).

There has long been an interest in identifying peripheral biomarkers for AD.[2] Technological approaches to quantifying the proteome continue to improve, allowing the characterization of nearly 10,000 proteins from a single sample with about half of the proteins coded by the human genome.[3] However, hurdles remain. First, experiences with the genome suggest there will be many false-positives that are not consistently replicated. Second, common diseases (e.g., cerebrovascular disease, Lewy body pathology) and other factors—including proteins—that promote resilience track with clinically and pathologically diagnosed AD.[4,5]

Even the most carefully designed AD case-control studies will identify proteins associated with other diseases and resilience. Finally, determining whether proteins are resident in the human brain is essential for understanding their role in promoting cognitive impairment or maintaining cognition. Interestingly, one protein (interleukin-3) identified in the 2 discovery cohorts was identified in a targeted proteomics analysis of the human brain.[5]

Further study is needed but the human proteome is ripe for identifying novel therapeutic targets and biomarkers for AD and other neurologic diseases.

Author Response: William T. Hu, Atlanta; David Holtzman, St. Louis; Leslie Shaw, John Trojanowski, Philadelphia; Holly Soares, New London, CT: We agree with Dr. Bennett that determining the biological significance of CSF and blood biomarkers associated with AD represents the next logical step in developing these biomarkers further towards eventual clinical application. Along with interleukin-3, C-reactive protein (CRP) was found to be associated with plaques[6] and higher CRP levels in successful cognitive aging individuals were recently linked to lower risks of dementia among their relatives.[7] The connection to brain proteomic changes has also been observed. For example, altered CSF levels of fatty acid binding protein in 2 groups of patients with AD has been found[8,9] and fatty acid binding protein showed region-specific alterations in proteomic studies of AD brains.[10] While we do not expect all biomarker changes in the blood and CSF to directly reflect pathologic changes in the brain, a direct or indirect connection between brain pathology and biomarkers provides a window into detrimental and neuroprotective activities at the cellular and synaptic levels. As replication is a significant challenge in targeted proteomic analysis (such as the work we presented) as well as mass spectrometry-based unbiased proteomic studies, we hope a tandem discovery-validation design will accelerate the discovery of correlated brain, CSF, and blood biomarkers.

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CORRECTION

Levetiracetam in pregnancy: Results from the UK and Ireland epilepsy and pregnancy registers

In the article "Levetiracetam in pregnancy: Results from the UK and Ireland epilepsy and pregnancy registers" by E. Mawhinney et al. (*Neurology*® 2013;80:400–405), there is an error in the body of the abstract and in table 1. The polytherapy major congenital malformations (MCM) rate should read 5.56% (3.54%–8.56%) rather than 6.47% (4.31%–9.60%). The authors regret the errors.

Author disclosures are available upon request (journal@neurology.org).