

## Amyloid Burden: A Reason for Poor Antidepressant Response in Late-Life Depression?

*In cognitively intact individuals with late-life depression, cortical amyloid burden predicted poor antidepressant response.*

Accumulation of cortical amyloid- $\beta$  (A $\beta$ ) has been associated with greater depressive symptoms in cognitively intact older adults. Higher cortical A $\beta$  burden and late-life depression (LLD) are independently associated with risks for cognitive decline and Alzheimer disease. Also, our current antidepressants have poor efficacy for treating depression in people with dementia, although the influence that A $\beta$  burden has on treatment resistance is unknown. The present investigators hypothesized that cortical A $\beta$  burden in cognitively intact individuals with LLD would be associated with poorer antidepressant response.

The 27 individuals aged 60 or older had major depression but no evidence of dementia and were participating in a larger double-blind, controlled treatment trial involving randomization in a 2:1 ratio to escitalopram or placebo. For this ancillary study, participants underwent baseline florbetapir (18F) positron emission tomography for A $\beta$ ; five were amyloid-positive. At 8 weeks, depression did not remit in 80% of amyloid-positive participants versus 18% of amyloid-negative participants. In analyses adjusting for treatment arm, baseline depression severity, age, and sex, A $\beta$  positivity was associated significantly with a smaller decrease in depression severity and a lower likelihood of remission.

### COMMENT

This study highlights a key covariate not often measured in treatment trials for LLD, namely A $\beta$  positivity. With the growing availability of tests for A $\beta$  biomarkers, these study results can inform future development of LLD clinical trials. That said, as no targeted LLD treatment based on A $\beta$  positivity exists, this study cannot be used to justify collecting A $\beta$  biomarkers in clinical populations with LLD. In this era of precision medicine, a larger dedicated trial examining how A $\beta$  affects LLD antidepressant response would be warranted. — **Matthew E. Peters, MD**

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*Taylor WD et al. Preliminary evidence that cortical amyloid burden predicts poor response to antidepressant medication treatment in cognitively intact individuals with late-life depression. Am J Geriatr Psychiatry 2020 Sep 28; [e-pub]. (<https://doi.org/10.1016/j.jagp.2020.09.019>)*

At the time we reviewed this paper, its publisher noted that it was not in final form and that subsequent changes might be made.