LETTER

Reply to Pomara and Bruno: Need for prospective, randomized clinical trial

Thank you for giving us an opportunity to reply to the letter to the editor by Pomara and Bruno (1) requesting clarification about the APOE ε2 allele and family history status of the antidepressant-treated group vs. untreated group in our paper in PNAS (2). As pointed out in the letter, there is work describing protective effects of APOE ε2 allele status and higher risk with a family history of Alzheimer's disease. These indeed are potentially important covariates. We did not include APOE ε2 status in the paper because of the small number of individuals in our study sample with this allele ($n = 24$ out of the sample of 186 individuals). Nonetheless, we conducted post hoc analyses and found that the groups do not differ in APOE ε2 allele status but do differ in family history of Alzheimer's disease, with the untreated group having a higher rate of family history of Alzheimer's disease. Because the study was retrospective and constituted a sample of convenience, this is not surprising and supports the need to do a prospective, randomized clinical trial to assess the utility of antidepressants in protecting against increased amyloid-β levels.

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1. Pomara N, Bruno D (2011) Potential effects of APOE ε2 allele and of family history of Alzheimer's disease on brain amyloid-β in normal elderly. *Proc Natl Acad Sci USA* 108: E1007.
2. Cirrito JR, et al. (2011) Serotonin signaling is associated with lower amyloid-β levels and plaques in transgenic mice and humans. *Proc Natl Acad Sci USA* 108:14968–14973.

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The authors declare no conflict of interest.

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