LETTER

Reply to Pomara et al: Spatially distributed patterns of cortical thinning likely constitute distinct brain-based biomarkers for disease

The hypothesis stated in the letter of Pomara et al.(1), that the pattern of cortical thinning detected in persons who are at increased familial risk for developing depression could also be a risk factor for developing Alzheimer's disease (AD), is interesting and testable. Whether the individuals in our study are at increased risk for developing AD is impossible to say at present. Nevertheless, if we continue to follow our cohort sufficiently far into the future, we will be able to test this hypothesis explicitly. We should note, however, that the pattern of cortical thinning detected in our sample differs markedly from the pattern of cortical thinning detected in persons with AD (2) or mild cognitive impairment (3). In the latter 2 groups, thinning was bilaterally symmetric, involving relatively small portions of the parietal cortex but spatially more extensive portions of the anterior temporal pole and superior frontal gyrus. Thinning in our sample, in contrast, was highly asymmetric, involving most of the lateral surface of the right hemisphere and mesial wall of the left hemisphere, but sparing the temporal pole bilaterally (4). These spatial patterns of thinning in familial depression and AD are sufficiently distinct, in fact, to suggest that they may represent diagnostic "signatures" or "biomarkers" for 2 distinct pathogenic processes. We also note that the characteristic pattern of thinning was present in the children in our sample. If the pattern of thinning in AD represents neurodegeneration, then its presence in children would seem unlikely, further suggesting that cortical thinning in depression and AD are distinct pathogenic processes.

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2. Dickerson BC, et al. (2009) The cortical signature of Alzheimer's disease: Regionally specific cortical thinning relates to symptom severity in very mild to mild AD dementia and is detectable in asymptomatic amyloid-positive individuals. *Cereb Cortex* 19:497–510.
3. Bakkour A, Morris JC, Dickerson BC (2009) The cortical signature of prodromal AD: Regional thinning predicts mild AD dementia. *Neurology* 72:1048–1055.
4. Peterson BS, *et al.* (2009) Cortical thinning in persons at increased familial risk for major depression. *Proc Natl Acad Sci USA* 106:6273–6278.

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The authors declare no conflict of interest.

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