Subjective Cognitive Complaints, Personality and Brain Amyloid-beta in Cognitively Normal Older Adults

Beth E. Snitz, Ph.D., Lisa A. Weissfeld, Ph.D., Ann D. Cohen, Ph.D., Oscar L. Lopez, M.D., Robert D. Nebes, Ph.D., Howard J. Aizenstein, M.D., Ph.D., Eric McDade, D.O., Julie C. Price, Ph.D., Chester A. Mathis, Ph.D., William E. Klunk, M.D., Ph.D.

Objective: *Subjective cognitive complaints in otherwise normal aging are common but may be associated with preclinical Alzheimer disease in some individuals. Little is known about who is mostly likely to show associations between cognitive complaints and preclinical Alzheimer pathology. We sought to demonstrate associations between subjective complaints and brain amyloid-β in cognitively normal older adults; and to explore personality factors as potential moderators of this association.* **Design:** *Cross-sectional observational study.* **Setting:** *Clinical neuroimaging research center.* **Participants:** *Community volunteer sample of 92 healthy older adults, screened for normal cognition with comprehensive neuropsychological evaluation.* **Measurements:** *Subjective cognitive self-report measures included the Memory Functioning Questionnaire (MFQ), Cognitive Failures Questionnaire, and the Subjective Cognitive Complaint Scale. Personality was measured with the NEO Five Factor Inventory. Brain amyloid-β deposition was assessed with Pittsburgh compound B (PiB)-PET imaging.* **Results:** *One of three cognitive complaint measures, the MFQ, was associated with global PiB retention (standardized beta = −0.230, p = 0.046, adjusting for age, sex and depressive symptoms). Neuroticism moderated this association such that only high neuroticism individuals showed the predicted pattern of high complaint−high amyloid-β association.* **Conclusion:** *Evidence for association between subjective cognition and brain amyloid-β deposition in healthy older adults is demonstrable but measure-specific. Neuroticism may moderate the MFQ−amyloid-β association such that it is observed in the context of higher trait neuroticism. Subjective cognitive complaints and neuroticism may reflect a common susceptibility toward psychological distress and negative affect, which are in turn risk factors for cognitive decline in aging and incident Alzheimer disease.* (Am J Geriatr Psychiatry 2015; ■:■−■)

Key Words: Amyloid imaging, cognition, personality, subjective memory

Received July 22, 2014; revised January 23, 2015; accepted January 31, 2015. From the Departments of Neurology (BES, OLL, EM), Psychiatry (ADC, RDN, HJA, WEK), and Radiology (JCP, CAM), University of Pittsburgh, Pittsburgh, PA; and Statistics Collaborative, Inc. (LAW), Washington, D.C. Send correspondence and reprint requests to Beth E. Snitz, Ph.D., Department of Neurology, University of Pittsburgh, 3501 Forbes Avenue, Suite 830, Pittsburgh, PA 15215. e-mail: snitzbe@upmc.edu

Supplemental digital content is available for this article in the HTML and PDF versions of this article on the journal's Web site (www.ajgponline.org).

http://dx.doi.org/10.1016/j.jagp.2015.01.008

Population studies indicate subjective cognitive complaints (SCCs) during aging are a risk factor for cognitive decline and dementia.[1–3] Neuroimaging studies have reported associations between SCCs and brain signatures of Alzheimer disease (AD) in otherwise cognitively normal adults, including medial temporal atrophy,[4,5] reduced glucose metabolism,[6,7] and amyloid-beta (Aβ) deposition,[8–10] although not all studies are positive.[11] This emerging literature has prompted interest in subjective cognitive impairment, especially in the absence of objective cognitive deficits, as a putative early neurodegenerative disease stage (i.e., pre-mild cognitive impairment; pre-MCI) and a potential preclinical phase for intervention.[12–14] That is, the notion that some older individuals may first show insight regarding their own memory changes associated with very early AD-pathologic processes, before objectively assessed deficits, has gained recent traction.[14]

The reasons that older adults express or endorse subjective cognitive complaints are likely complex and multifactorial, however. In addition to AD/brain biomarkers and objective cognitive performance, SCCs are associated with individual differences in affective variables, including mood and personality.[3,15] In particular, two personality factors from the five-factor model, high neuroticism and low conscientiousness, are consistent correlates of subjective memory/cognitive complaints.[15–17] Some authors argue that mood and personality correlates underscore the importance of psychological factors, as opposed to underlying brain dysfunction, in accounting for SCCs in aging.[18,19] Indeed, in dementia evaluation settings, the term "worried well" connotes patients who are anxious about memory changes (and perhaps anxious in general) but show no objective findings on exam; the conceptualization reflects a ruling-out of disease by the clinician.[20] Interestingly, however, a separate line of research suggests that personality traits, especially neuroticism, are themselves consistent risk factors and/or disease markers for AD and cognitive decline.[21,22] Neuroticism is closely related to other negative affect–associated variables, such as risk for depression and vulnerability to stress, which are in turn associated with risk for AD and cognitive decline in aging.[23–26] To date, relationships among subjectively perceived cognition, personality, and AD biomarkers in otherwise healthy older adults are not understood.

The aims of the present study were twofold. First, we examined associations between SCCs and Aβ deposition in cognitively normal older adults. We expected to replicate two previous studies showing association between subjective cognition and presence/degree of Aβ on imaging in cognitively normal participants.[8,9] Secondly, we explored personality factors as potential moderating variables on associations between subjective cognition and Aβ. Regarding neuroticism, specifically, two competing hypotheses were formulated: 1) a "worried-well" hypothesis would predict SCCs in the context of high neuroticism to be associated with *lower* risk for biomarker abnormality (i.e., low Aβ). In contrast, 2) a "negative-affect-risk" hypothesis would predict SCCs in the context of high neuroticism to be associated with *higher* risk for biomarker abnormality (i.e., high Aβ).

METHODS

Participants

Research volunteers for the present study were recruited from two ongoing Pittsburgh compound B (PiB)–positron emission tomography (PET) imaging studies at the University of Pittsburgh, one of normal aging (N = 48) and amyloid and the other focused on vascular-amyloid interactions in oldest-old normal aging (N = 44). Cognitive classification in both parent studies was based upon a multidomain neuropsychological assessment and review by a clinical neuropsychologist and/or multidisciplinary consensus diagnostic procedures.[27,28] Inclusion criteria were normal cognition and age 65 years or older. Normal cognition criteria were defined as not more than 1–2 tests out of the multidomain battery performed significantly below expectations given an individual's age and educational background (i.e., scores falling more than 1 standard deviation [SD] below age-corrected means and taking into account level of education). Exclusion criteria for both parent studies included contraindications for neuroimaging, and history of neurologic, psychiatric, or other medical conditions or treatment associated