Psychological Well-Being and Regional Brain Amyloid and Tau in Mild Cognitive Impairment

Stephen T. Chen, M.D., Prabha Siddarth, Ph.D., Nathan Y. Saito, B.S., Flori Rueda, B.S., Taylor Haight, B.A., Linda M. Ercoli, Ph.D., Karen J. Miller, Ph.D., Helen Lavretsky, M.D., Jorge R. Barrio, Ph.D., Susan Y. Bookheimer, Ph.D., Gary W. Small, M.D., David A. Merrill, M.D., Ph.D.

Objectives: *To determine whether psychological well-being in people with mild cognitive impairment (MCI), a risk state for Alzheimer disease (AD), is associated with in vivo measures of brain pathology.* **Methods:** *Cross-sectional clinical assessments and positron emission tomography (PET) scans after intravenous injections of 2-(1-{6-[(2-[F18]fluoroethyl)(methyl)amino]-2-naphthyl}ethylidene) malononitrile (FDDNP), a molecule that binds to plaques and tangles, were performed on middle-aged and older adults at a university research institute. Volunteers were aged 40–85 years with MCI (N = 35) or normal cognition (N = 29) without depression or anxiety. Statistical analyses included general linear models, using regional FDDNP-PET binding values as dependent variables and the Vigor-Activity subscale of the Profile of Mood States (POMS) as the independent variable, covarying for age. The POMS is a self-rated inventory of 65 adjectives that describe positive and negative feelings.* **Results:** *Scores on the POMS Vigor-Activity subscale were inversely associated with degree of FDDNP binding in the posterior cingulate cortex ($r = -0.35$, $p = 0.04$) in the MCI group but not in the control group.* **Conclusion:** *Psychological well-being, as indicated by self-reports of greater vigor and activity, is associated with lower FDDNP-PET binding in the posterior cingulate cortex, a region involved in emotional regulation, in individuals with MCI but not in those with normal cognition. These findings are consistent with previous work indicating that deposition of brain amyloid plaques and tau tangles may result in noncognitive and cognitive symptoms in persons at risk for AD.* (Am J Geriatr Psychiatry 2014; 22:362–369)

Key Words: Aging, FDDNP, positron emission tomography, POMS, well-being

Received April 17, 2012; revised August 17, 2012; accepted September 26, 2012. From the Department of Psychiatry and Biobehavioral Sciences and Semel Institute for Neuroscience and Human Behavior (STC, PS, NYS, FR, TH, LME, KJM, HL, SYB, GWS, DAM), Department of Molecular and Medical Pharmacology (JRB), Alzheimer's Disease Research Center (GWS), and UCLA Longevity Center (LME, KJM, GWS, DAM), University of California, Los Angeles, CA. Presented at the 2012 annual meeting of the American Association for Geriatric Psychiatry, Washington, DC, March 15–19, 2012. Send correspondence and reprint requests to Stephen T. Chen, M.D., 300 UCLA Medical Plaza, Room 2236, Los Angeles, CA, 90095-6968. e-mail: stephenchen@mednet.ucla.edu

http://dx.doi.org/10.1016/j.jagp.2012.09.002

INTRODUCTION

Although psychopathology associated with cognitive disorders has been studied extensively, self-perception of health and well-being is receiving greater attention, particularly in individuals who are at risk for Alzheimer disease (AD) and other dementias. Depression and anxiety are known risk factors for AD and are associated with neuropsychological deficits, higher rates of progression to dementia, and neuropathologic changes found in AD.[1–4] However, clinically significant depressive or anxiety symptoms are not present in most individuals who are at risk for AD[5] and are common exclusion criteria in studies on cognitive impairment. Psychological well-being, which can be reported by nearly all individuals, may be a more applicable measure in such nondemented populations.

Perhaps the most well-studied cohort at risk for developing AD is composed of individuals with mild cognitive impairment (MCI), which is characterized by cognitive decline intermediate between normal aging and dementia.[6,7] Approximately 14%–18% of individuals aged 70 years and older have MCI, 10%–15% of whom will progress to dementia each year.[8]

In subjects with MCI, our group found self-reported depression, anxiety, and memory complaints are associated with a biomarker for MCI and AD,[9,10] specifically the small molecule 2-(1-{6-[(2-[F18]fluoroethyl)(methyl)amino]-2-naphthyl}ethylidene)malononitrile (FDDNP), an in vivo probe that binds to cerebral aggregates of amyloid-beta plaques and tau neurofibrillary tangles,[11] the neuropathologic hallmarks of AD. FDDNP visualized via positron emission tomography (PET) differentiates individuals with MCI, AD, and normal cognition, wherein global FDDNP-PET binding is highest in patients with AD, intermediate in those with MCI, and lowest in normal comparison subjects.[11]

Previous studies have demonstrated the predictive value of positive self-perception of health and emotions in stroke, dementia, and delirium.[12–14] Such measures may provide insight and predictive value in patients with MCI who are at risk for dementia. Furthermore, one's sense of well-being may reflect and even influence neurobiologic changes in memory disorders. In this cross-sectional study, we hypothesized that psychological well-being in MCI patients is associated with decreased FDDNP-PET binding, a marker for amyloid and tau proteins and an early detection tool for MCI and AD.

METHODS

Participants

Volunteers were part of a larger longitudinal study of AD and age-associated cognitive decline[11] and were recruited through advertisements, media coverage, and referrals by physicians and families. Members of the research staff screened potential volunteers via telephone interviews. All participants provided written informed consent, in accordance with procedures of the Human Research Protection Program of the University of California, Los Angeles, and received clinical assessments, magnetic resonance imaging (MRI), and FDDNP-PET scans. Individuals with a diagnosis of dementia, major depressive disorder, or an anxiety disorder or radiographic evidence of stroke were excluded. Of the 1,617 individuals screened for the larger AD and memory study, 289 (17.9%) were excluded because of depression or anxiety. Cumulative radiation dosimetry for all scans was below the mandated maximum annual dose and in compliance with state and federal regulations.

Clinical Assessment

All volunteers received a psychiatric and medical history and mental status exam, comprehensive neuropsychological evaluation by a licensed neuropsychologist, and several self-rated and clinician-rated measurements of psychological symptoms. We used modified diagnostic criteria for MCI,[6,7] which included (1) patient awareness of memory decline, preferably confirmed by another person; (2) measurable, greater-than-normal cognitive impairment detected with standard assessment tests; (3) preservation of daily activities functioning; and (4) an absence of dementia.

Our clinical assessment included the Profile of Mood States (POMS), developed by McNair et al.[15] in 1971, that consists of 65 self-rated adjectives on a five-point scale from 0 (not at all) to 4 (extremely). Multiple-factor analytic studies have confirmed six