

- 1 Ewers, M., Insel, P. S., Stern, Y., & Weiner, M. W. (2013). Cognitive reserve associated with FDG-PET in preclinical Alzheimer disease. *Neurology*, *80*, 1194-1201.  
Notes: OBJECTIVE: To examine the effect of education (a surrogate measure of cognitive reserve) on FDG-PET brain metabolism in elderly cognitively healthy (HC) subjects with preclinical Alzheimer disease (AD). METHODS: Fifty-two HC subjects (mean age 75 years) with FDG-PET and CSF measurement of Abeta1-42 were included from the prospective Alzheimer's Disease Neuroimaging Initiative biomarker study. HC subjects received a research classification of preclinical AD if CSF Abeta1-42 was <192 pg/mL (Abeta1-42 [+]) vs HC with normal Abeta (Abeta1-42 [-]). In regression analyses, we tested the interaction effect between education and CSF Abeta1-42 status (Abeta1-42 [+] vs Abeta1-42 [-]) on FDG-PET metabolism in regions of interest (ROIs) (posterior cingulate, angular gyrus, inferior/middle temporal gyrus) and the whole brain (voxel-based). RESULTS: An interaction between education and CSF Abeta1-42 status was observed for FDG-PET in the posterior cingulate ( $p < 0.001$ ) and angular gyrus ROIs ( $p = 0.03$ ), but was not significant for the inferior/middle temporal gyrus ROI ( $p = 0.06$ ), controlled for age, sex, and global cognitive ability (Alzheimer's Disease Assessment Scale-cognitive subscale). The interaction effect was such that higher education was associated with lower FDG-PET in the Abeta1-42 (+) group, but with higher FDG-PET in the Abeta1-42 (-) group. Voxel-based analysis showed that this interaction effect was primarily restricted to temporo-parietal and ventral prefrontal brain areas. CONCLUSIONS: Higher education was associated with lower FDG-PET in preclinical AD (Abeta1-42 [+]), suggesting that cognitive reserve had a compensatory function to sustain cognitive ability in presence of early AD pathology that alters FDG-PET metabolism
- 2 Stern, Y. (2012). Cognitive reserve in ageing and Alzheimer's disease. *Lancet Neurol.*, *11*, 1006-1012.  
Notes: The concept of cognitive reserve provides an explanation for differences between individuals in susceptibility to age-related brain changes or pathology related to Alzheimer's disease, whereby some people can tolerate more of these changes than others and maintain function. Epidemiological studies suggest that lifelong experiences, including educational and occupational attainment, and leisure activities in later life, can increase this reserve. For example, the risk of developing Alzheimer's disease is reduced in individuals with higher educational or occupational attainment. Reserve can conveniently be divided into two types: brain reserve, which refers to differences in the brain structure that may increase tolerance to pathology, and cognitive reserve, which refers to differences between individuals in how tasks are performed that might enable some people to be more resilient to brain changes than others. Greater understanding of the concept of cognitive reserve could lead to interventions to slow cognitive ageing or reduce the risk of dementia  
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- 3 Stern, Y. (2009). Cognitive reserve. *Neuropsychologia*, *47*, 2015-2028.  
Notes: The concept of reserve has been proposed to account for the disjunction between the degree of brain damage and its clinical outcome. This paper attempts to produce a coherent theoretical account the reserve in general and of cognitive reserve in particular. It reviews epidemiologic data supporting the concept of cognitive reserve, with a particular focus of its implications for aging and dementia. It then focuses on methodologic issues that are important when attempting to elucidate the neural underpinnings of cognitive reserve using imaging studies, and reviews some of our group's work in order to demonstrate these issues  
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- 4 Stern, Y. (2009). Cognitive reserve and aging. In W. Jagust & M. D'Esposito (Eds.), *Imaging the aging brain* (1 ed., pp. 92-104). Oxford University Press.

5 Stern, Y. (Ed.) *Cognitive reserve: Theory and applications* (2006). New York: Psychology Press.

Notes: 344pp; based on a special issue of JCEN, 2003, vol. 25, issue 5, but extended

6 Stern, Y., Alexander, G. E., Prohovnik, I., & Mayeux, R. (1992). Inverse relationship between education and parietotemporal perfusion deficit in Alzheimer's disease. *Annals of Neurology*, 32, 371-375.

Notes: Department of Neurology, Columbia University, College of Physicians and Surgeons, New York, NY A higher prevalence of dementia in individuals with fewer years of education has suggested that education may protect against Alzheimer's disease (AD). We tested whether individuals with more years of education have a more advanced AD before it is clinically evident. As a measure of pathophysiological severity, we quantified regional cerebral blood flow (rCBF), by the <sup>133</sup>Xenon inhalation technique; a specific pattern of flow reduction in the parietotemporal cortex corresponds to AD pathology. In 3 groups of patients with probable AD, matched for clinical measures of dementia severity but with varying levels of education, whole-cortex mean flows were comparable. However, the parietotemporal perfusion deficit was significantly greater in the group with the highest level of education, indicating that AD was more advanced in this group. We conclude that education or its covariates or both may provide a reserve that compensates for the neuropathological changes of AD and delays the onset of its clinical manifestations