

Malpetti M, Ballarini T, Presotto L, Garibotto V, Tettamanti, M., Perani D. Gender Differences in Healthy Aging and Alzheimer's Dementia: a 18F-FDG-PET Study of Brain and Cognitive Reserve. *Human Brain Mapping*, 2017.

Abstract: Cognitive reserve (CR) and brain reserve (BR) are protective factors against age associated cognitive decline and neurodegenerative disorders. Very limited evidence exists about gender effects on brain aging and on the effect of CR on brain modulation in healthy aging and Alzheimer's Dementia (AD). We investigated gender differences in brain metabolic activity and resting-state network connectivity, as measured by 18F-FDG-PET, in healthy aging and AD, also considering the effects of education and occupation. The clinical and imaging data were retrieved from large datasets of healthy elderly subjects (HE) (225) and AD patients (282). In HE, males showed more extended age-related reduction of brain metabolism than females in frontal medial cortex. We also found differences in brain modulation as metabolic increases induced by education and occupation, namely in posterior associative cortices in HE males and in the anterior limbic-affective and executive networks in HE females. In AD patients, the correlations between education and occupation levels and brain hypometabolism showed gender differences, namely a posterior temporo-parietal association in males and a frontal and limbic association in females, indicating the involvement of different networks. Finally, the metabolic connectivity in both HE and AD aligned with these results, suggesting greater efficiency in the posterior default mode network for males, and in the anterior frontal executive network for females. The basis of these brain gender differences in both aging and AD, obtained exploring cerebral metabolism, metabolic connectivity and the effects of education and occupation, is likely at the intersection between biological and sociodemographic factors.

Key words: gender; brain reserve; cognitive reserve; education; occupation; healthy aging; Alzheimer's Dementia; Fluorine-18-Fluorodeoxyglucose; positron emission tomography