Functional magnetic resonance imaging response as an early biomarker of cognitive decline in elderly patients with metabolic syndrome

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ABSTRACT

Objectives: We assessed whether potential changes in brain activation patterns of elderly individuals with metabolic syndrome (MetS) who were cognitively healthy (without mild cognitive impairment or dementia) were associated with cognitive decline in executive function in the short-term.

Method: We analyzed 43 individuals (23 MetS, 20 controls) using a global geriatric evaluation, a neuropsychological battery, and task-related (attention) fMRI exam. Correlation analysis between the fMRI signal at baseline and cognitive impairment after 1 year was based on the voxel-based Pearson coefficient, corrected for multiple comparisons.

Results: At baseline, MetS patients showed reduced brain response in frontal and parietal regions compared to controls. After one year, the MetS group also showed a decline in verbal fluency performance. fMRI response in the right dorsolateral prefrontal cortex and bilateral parietal lobes was negatively correlated with verbal fluency decline in the MetS group.

Discussion: Our results provide an early biomarker of the possible development of cognitive impairment, particularly in the executive function, of elderly individuals suffering from MetS. These findings also point to an up or down regulation which could be interpreted as compensatory mechanism for possible brain tissue burden caused by MetS.

1. Introduction

Metabolic Syndrome (MetS) involves a series of clinical and laboratory abnormalities that increase the risk of cardiovascular disease. MetS has been best described as a set of symptoms that, altogether, are associated with greater cardiovascular risk compared to the risk of each laboratory abnormalities that increase the risk of cardiovascular disease.

Although much research has evaluated the association of MetS with cellular and cerebrovascular accidents (CVA) (De Silva et al., 2009; Haley, Gonzales, Tarumi, & Tanaka, 2012; Park & Kwon, 2008; Zhang et al., 2010), there is growing interest in the potential impact of MetS on cognitive impairment. In fact, elderly individuals diagnosed with MetS have shown poorer scores on cognitive tests compared to matched adults without MetS (Collinson, Tong, Loh, Chionh, & Merchant, 2014; Rouch et al., 2014), especially MetS patients with higher inflammatory activity (Cavaliere et al., 2010; Dik et al., 2007; Roberts et al., 2010). Similar findings were obtained with longitudinal studies using screening tests, which have shown a gradual development from normal to mild cognitive impairment (MCI) or even direct evolution of MCI to dementia in elderly individuals with MetS followed from two to 16 years (Bruce et al., 2008; Creavin et al., 2012; Luchsinger, Tang, Stern, Shea, & Mayeux, 2001; McEvoy et al., 2012; McGuire, Ford, & Ajani, 2006; Niwa et al., 2006; Raffaelli et al., 2011).

However, the extent to which the risk of cognitive impairment in...
individuals with MetS is associated with functional changes in brain activity is not well established, and the impact of these changes on cognitive performance in the long-term is still unclear. To our knowledge, there have been only three studies that have explored this issue to date. A cross-sectional study concluded that MetS in elderly individuals without dementia or a history of stroke was associated with cognitive impairment, especially impairment of memory and executive function. Individuals with higher inflammatory activity also had higher chances in light of the higher risk of neurodegenerative disease in patients with MetS.

In this study we aimed to evaluate whether brain activation patterns in cognitively healthy (without MCI or dementia) elderly individuals with MetS differ from those of matched healthy controls. We also evaluated whether these potential differences in activation pattern could predict cognitive decline in the short term. By showing that the MetS group exhibited reduced brain activation at baseline while having the same neuropsychological performance as controls, our results should help in the early diagnosis of neurodegenerative pathologies in this population. Indeed, we show that reduced pre-frontal MRI signal at baseline is negatively associated with reduced verbal fluency performance after 1 year.

2. Methods

This was a cohort study with one-year follow-up of Brazilian elderly subjects from two sites: volunteers from the public health system attending the geriatrics and gerontology outpatient clinic of the Universidade Federal de Sao Paulo, and healthy elderly individuals from the Serviço Social do Comércio (Commerce Social Service Units), both in Sao Paulo. The assessments occurred between April 2010 and March 2013.

The inclusion criteria were: (1) age ≥ 65 years; (2) schooling level between one and four years; and (3) score on the Mini-Mental State Examination ≥ 22, as suggested by Brazilian validation (Brucki, Nitrini, Caramelli, Bertolucci, & Okamoto, 2003). Using this criteria, in both groups there are no subject with MCI. Exclusion criteria were: (1)
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