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Cognitive impairment and frontal-subcortical geriatric syndrome are associated with metabolic syndrome in a stroke-free population

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Abstract

Background: Metabolic syndrome (Met.S) consists of a conglomeration of obesity, hypertension, glucose intolerance, and dislipidemia. Frontal-subcortical geriatric syndrome (FSCS) is caused by ischemic disruption of the frontal-subcortical network. It is unknown if Met.S is associated with FSCS.

Methods: We evaluated 422 community-dwelling elderly (≥60) in Brazil. FSCS was defined as the presence of at least one frontal release sign (grasping, palmomental, snout, or glabellar) plus coexistence of ≥3 the following criteria: (1) cognitive impairment, (2) late-onset depression, (3) neuromotor dysfunction, and (4) urgency incontinence. All values were adjusted to age and gender.

Results: Met.S was present in 39.3% of all subjects. Cases without any of the FSCS components represented 37.2% ('successful neuroaging' group). People with 1–3 of the FSCS components ('borderline pathological neuroaging' group) were majority (52.6%), whereas those with 4–5 of these components (FSCS group) were minority (10.2%). Met.S was significantly associated with FSCS (OR = 5.9; CI: 1.5–23.4) and cognitive impairment (OR = 2.2; CI: 1.1–4.6) among stroke-free subjects. Number of Met.S components explained 30.7% of the variance on the number of FSCS criteria ($P < 0.001$). If Met.S were theoretically removed from this population, prevalence of FSCS would decline by 31.6% and that of cognitive impairment by 21.4%.

Conclusions: Met.S was significantly associated with a 5.9 and 2.2 times higher chance of FSCS and cognitive impairment, respectively. Met.S might be a major determinant of 'successful' or 'pathological' neuroaging in western societies.

Keywords: Frontal-subcortical; Metabolic syndrome; Successful aging; Cognitive impairment; Vascular depression; Executive dysfunction; Neuromotor dysfunction; Urgency-type incontinence; Elderly; Brazil

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1. Introduction

1.1. Metabolic syndrome and the frontal-subcortical syndrome

More than 100 years ago, Biswanger was the first to describe a syndrome of subcortical atherosclerotic encephalopathy (SAE) among the elderly, neuropathologically characterized by diffuse WML [76]. This was followed by the report of the 'lacunes of cerebral disintegration' syndrome by Marie [61] and Ferrand [27], when they described neuropathological findings in 50 patients who died in a nursing home. Clinical features included small-stepped gait ('marche à petits pas' of Dégerine), dysartria, psedobulbar palsy, dementia, incontinence and emotional lability; most of these symptoms denoting advanced frontal-subcortical network damage. Advanced cases evolved to the syndrome of apathia-akinesia and abulia, and terminal state was characterized by akinetic mutism. Multi-infarct dementia, a term coined by Hachinski [38], often coexists with SAE and represents an advanced state of cognitive deficit caused by such neuropathological lesions.

The clinical picture above described, though common in nursing homes, are rarely seen in the community [27,38,61,76]. Instead, a milder form characterized by cognitive impairment, late-onset depression, lower neuromotor dysfunction and urgency incontinence are often seen both in the geriatric outpatient clinic and in the community-dwelling elderly [54,82].

Just recently evidences accumulated that SAE disrupts the frontal network and promote frontal atrophy, leading to a 'frontal-subcortical syndrome' (FSCS) which is much more common among community-dwelling elderly than classical vascular dementia [54,82]. FSCS has been linked to a series of geriatric disorders, such as cognitive decline, late-onset depression, dysexecutive syndrome, gait disorders, falls, and urgency incontinence [54]. There is increasing evidence that these are manifestations of a single geriatric syndrome, namely, the FSCS [54,82]. FSCS is extremely common among otherwise neurologically normal elderly subjects, but it is usually underappreciated, and its prevalence in the community has not yet been investigated [82].

Several aspects of the FSCS have been independently linked to the metabolic syndrome (Met.S) or its individual components, yet no study has comprehensively evaluated the independent association between these two syndromes [5–9,16–19,53–57,81,82,84] as well as if these associations are dependent of clinical stroke.

Metabolic syndrome (Met.S) is defined as a cluster of obesity, glucose intolerance, hypertension, low HDL and/or high triglycerides [47]. Most of above items have been shown to be independent risk factors for stroke. Met.S itself was already evidenced to be an independent risk factor for cardiovascular disease, including stroke [6,63,71]. Met.S increases the risk of both clinical and asymptomatic stroke by 2–3 times [43,63]. Moreover, in patients with stroke the coexistence of Met.S is associated with a more advanced atherosclerotic process [71]. Met.S has also been previously shown to increase the risk of overall dementia [49], Alzheimer's disease (AD) [36], and cognitive decline [98].

Insulin resistance and hyperinsulinemia are usually considered to be the underlying common pathophysiological mechanism [30]. Prevalence of Met.S among the American elderly was shown to be around 24% [30].

Met.S, but not its conventional risk factors, was recently shown to be independently associated with intracranial atherosclerosis and lacunar stroke [6]. Hyperinsulinemia was also associated with cerebral small-vessel disease, with lesions in the white matter and basal ganglia [99]. Coexistence of DM and hypertension (a situation in which Met.S is often present) is associated with a three times higher chance of having silent infarct(s) in elective MRI, when compared with the group with HT but without DM [25].

Increasing evidences support a role for cerebral small-vessel lesions as a cause for dysfunction in frontal-subcortical systems [82]. It is unknown whether FSCS is associated with Met.S in a stroke-free population.

1.2. 'Successful', 'usual', and 'pathological' neural aging

'Successful' aging is defined as aging without major chronic-debilitating diseases and keeping independence for the activities of daily life (ADL) to a maximum extend before death [86].

Neural aging (here the term 'neuroaging' will be used) refer to the progressive deterioration of the nervous system capacity to promptly and adequately respond to a determined stimulus, be it cognitive, affective, motor or sensitive [11,65].

Recent evidences suggest that neural changes occurring during normal aging are more subtle and selective than once believed [11,65]. Among the brain regions affected by aging, the frontal-subcortical and hippocampus networks seem to be particularly vulnerable [11]. Nonetheless, even within these networks interindividual differences on the impact of chronological aging exist, with some individuals showing little age-related decline [42]. In fact, many healthy elderly, including those above 84 years, did not seem to experience measurable declines in cognitive functioning when followed for a period of 4 years [42].

Most individuals, however, usually show considerable age-related changes in cognitive, affective, and neuromotor functions; notably those functions which rely heavily on the medial-temporal and prefrontal networks, such as learning, memory, humor and executive function [11].

Cerebral small-vessel disease, a very common cause of pathological neuroaging, is associated with a steeper decline in information processing speed, executive function and memory [81].

Disruption of the frontal-subcortical network sufficient to cause concomitant cognitive deficit, vascular-type depression, executive/neuromotor dysfunction, and loss of urinary