

## Editorial

# Overactive Bladder as a Brain Disease

Ryuji Sakakibara\*

Neurology, Internal Medicine, Sakura Medical Center, Toho University, Sakura, Japan

## EDITORIAL

Small-vessel disease of the brain affecting the deep white matter characteristically manifests with neurological syndromes of (1) vascular dementia and (2) vascular parkinsonism. There is, however, compelling evidence to suggest that cerebral white matter disease (WMD) can cause (3) 'vascular incontinence' (overactive bladder [OAB] and incontinence) and in some patients these may be the initial manifestation. Since WMD increases significantly with age and preferentially affects the prefrontal deep white matter, WMD becomes an anatomical substrate in the brain etiology of OAB. Treatment may entail the management of small-vessel disease risk factors and anticholinergic drugs that do not easily penetrate the blood-brain barrier, to improve bladder control. Here we discuss these briefly.

Urinary incontinence is a major concern in geriatric populations, which have grown rapidly in recent decades. In addition, the incidence of OAB is high in the general population over 40 years old, [1-3] and it increases significantly with age. It is widely acknowledged that urinary frequency and poor bladder control have a negative impact on the quality of life, [4] that bladder dysfunction in elderly person adds to their caregivers' burden, and that bladder dysfunction is an important factor leading to institutionalization [4]. The mechanisms underlying OAB and urinary incontinence in the frail elderly are multifactorial; the factors may include age-related changes in the bladder itself [4] or central nervous system changes innervating the bladder [5]. Atherosclerosis/lifestyle disease clearly has an impact on the generation of OAB. This is because ischemia of the bladder occurs in patients with pelvic arterial insufficiency and perhaps peripheral vascular disease, which causes reduced blood flow and neuronal death [5]. Bladder ischemia and reperfusion injures nerves, leading to smooth muscle damage and impaired contractility as well as detrusor overactivity [6-8]. Atherosclerosis is a systemic condition which inevitably affects cerebral arteries supplying the brain. Cerebral WMD progresses insidiously, leading to three different geriatric syndromes; vascular dementia, vascular parkinsonism, and 'vascular incontinence' [9,10]. Since the likelihood of WMD increases significantly with age, WMD might become an anatomical substrate in the brain etiology of OAB.

Until recently, WMD, variously described as white matter hyperintensities, multiple cerebral infarctions of the white matter type, etc., had been thought to be only an incidental phenomenon.

## Corresponding author

Ryuji Sakakibara, Department of Neurology, Internal Medicine, Sakura Medical Center, Toho University, 564-1 Shimoshizu, Sakura, 285-8741 Japan, Tel: +81-43-462-8811 ext. 2323; Fax: +81-43-487-4246; E-mail: sakakibara@sakura.med.toho-u.ac.jp

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The first pathological description of WMD in the aged brain dates back to Durand-Fardel in 1854, who named the condition 'atrophie interstitielle du cerveau' (interstitial atrophy of the brain) [11]. Binswanger in 1894 described it pathologically as 'Arteriosklerotische Hirnerkrankung/ Hirnatrophie' (arteriosclerotic brain atrophy) [12]. In 1987, Hachinski coined the name leukoaraiosis, which he derived from the Greek word leukos ("white") and araios ("rarefied"), to describe the radiological images of loss of density of the periventricular white matter observed by CT [13]. More recently, MRI enabled the early recognition of WMD corresponding pathologically to white matter rarefaction [14,15]. Recent population-based MRI studies suggest that the incidence of moderate WMD (periventricular WMD grade > 4/9 and subcortical white matter volume > 1.5 mL) is approx. 10% (7.6%–24%) in the general population of individuals over 55 years of age, [16] comparable to that of OAB at 10%–16% [1-3].

What is the cause of bladder dysfunction in subjects with WMD? Detrusor overactivity (DO) is the major underlying pathophysiology of vascular incontinence. The incidence of detrusor overactivity in WMD cases is reported as 70%–91% of patients, [9,10] and is more common than following hemispheric stroke [17]. DO is a urodynamic observation characterized by involuntary contractions during the filling phase which may be spontaneous or provoked [18]. The frontal cortex is now recognized as an important higher center for micturition: damage to the prefrontal cortex, medial superior/middle frontal gyri, anterior cingulate cortex, supplemental motor area and insula have been shown to result in marked lower urinary tract dysfunction in humans [17,19]. These clinical observations have been corroborated by functional neuroimaging in humans [20]. The connection between the prefrontal cortex and the micturition circuit is still uncertain, but it is known that the prefrontal cortex projects fibers to the hypothalamus-periaqueductal gray directly. The prefrontal-striatal pathway may also have a role [21]. DO is considered to be an exaggerated spinobulbospinal micturition reflex that normally promotes micturition in brain lesions [22]. Functional neuroimaging studies showed that the prefrontal cortex was deactivated in elderly subjects with urinary frequency/urgency compared to controls [23].

Cortical WMD in MRI looks diffuse. However, within the

brain, detailed pathology studies confirmed that the frontal lobe is most severely affected [24]. This is in line with the reports that MRI volumetry showed frontal lobe atrophy, [25] where glucose [26] and N-acetyl-aspartate [27] metabolism was most severely reduced. Corresponding to this, brain perfusion was most severely reduced in the frontal lobe of subjects with WMD, [28] a finding that remains to be fully explained. However, hypoxic-ischemic damage to oligodendrocytes was marked in the frontal lobe in such patients, thus impairing not only the frontal micturition pathway, but also the frontal gait and cognitive pathways. In very short, when caring for elderly OAB patients, we should look at both the brain and the bladder.

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