

# Are Gait Disturbances and White Matter Degeneration Early Indicators of Vascular Dementia?

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## Key Words

Gait disorders  
Vascular dementia  
White matter lesions  
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Subcortical infarction  
Hypertension

## Abstract

The objective of this study was to correlate clinical and brain imaging findings with walking disabilities in patients with possible vascular dementia. For 24 patients with suspected initial vascular dementia according to DSM-III-R, structured neurological, neuropsychological and neuroimaging (magnetic resonance tomography) examinations were evaluated alongside computerized gait analysis. All patients revealed an increased variability of gait lines of various degrees: mild (11%), moderate (32%) and severe (57%). Lateralization of gait patterns was present in 68% and bipedal instabilities of posture in 54%. These findings were significantly correlated with frontal periventricular white matter lesions (WMLs), which probably affect the thalamo-cortico-mediocapsular pathways. The association of gait abnormalities with WMLs of the frontocentral subcortical and periventricular territories in patients with possible vascular dementing illnesses may be used as an early indicator of the disease for follow-up and treatment trials. However, since the degree of gait impairment varies considerably relative to the common mild intellectual limitations, these structural lesions are unlikely to be directly related to the dementing process.

## Introduction

Gait abnormalities are common in the elderly and are most often due to a variety of musculoskeletal and neurological diseases. While many of the latter may well be identified on inspection and their causes easily recognized (e.g. spastic paraparesis, cerebellar and peripheral sensory ataxia, Parkinson's disease), the categories of 'frontal gait disorder', 'gait apraxia', 'lower-half parkinsonism' and 'arteriosclerotic parkinsonism' [1-3] have caused consid-

erable confusion. This type of gait impairment has frequently been associated with cerebrovascular diseases producing multiple hemispheric lesions, and in particular with subcortical ischemia [3], which often causes cognitive impairment, dysarthria, frontal release signs, paratonia and urinary incontinence. Because of the highly variable topography and extent of impairment due to brain ischemia in these patients and the frequent overlap with other diseases affecting neural structures controlling posture and gait in aging people, the distinction between

gait pattern characteristics and disease entities has been rather difficult. In an attempt to classify these gait abnormalities clinically, Nutt et al. [4] have recently suggested the description of abnormalities in balance and locomotion, the elaboration of the pathophysiological cause, and an appropriate classification of the type of walking disability (e.g. subcortical or frontal disequilibrium and frontal gait disorder). Whether or not clinical separation may be possible or appropriate remains an open question, since involvement of both subcortical and cortical brain territories usually cause secondary remote neuronal metabolic depression. Masdeu and Gorelick [5] reported a series of patients after acute thalamic infarction with an inability to walk and severe frontal disequilibrium despite markedly preserved strength and somatosensory control. Bruns [6], van Bogaert and Martin [7], and Bell [8] had already reported patients with similar disturbances of standing or walking without support due to frontal lobe mass lesions sometimes associated with dementia, incontinence, frontal release signs, and difficulties in performing bilateral movements. Other authors, like Critchley [1], Meyer and Barron [9] and Thompson and Marsden [3] reported patients after frontal lobe insults with multiple lacunar infarction or subcortical white matter involvement. Despite different neurological disease entities, all patients reported the same gait imbalance, abnormal postural responses and short shuffling steps as a result of lesions affecting the thalamo-basal ganglia-frontal cortex territory circuits.

Clinical inspection alone is, however, difficult and there may be considerable interobserver disagreement, in particular if such disequilibrium is less pronounced in the early stage of diffuse subcortical cerebrovascular diseases involving small penetrating vessels rather than large cerebral artery circulation. Since small vessel territory ischemia may possibly lead to vascular dementia with progressive brain involvement, which might be prevented if associated risk factors of atherosclerosis were reduced, the recognition of minute symptoms may be important. This challenging task should, however, be facilitated by the application of the more sensitive and objective tests now available for the analysis of posture and gait [10]. This report summarizes preliminary results from an on-going prospective trial evaluating the long-term follow-up of patients with either mild neuropsychological/neurological dysfunction and/or evidence of subcortical lacunar/white matter lesions (WMLs) on magnetic resonance tomography (MRT), with regard to the association between the incidence, extent and pattern of gait disturbance and MRT findings.

## Patients and Methods

Twenty-four patients (16 men and 8 women, mean age:  $70.3 \pm 7.5$  years, range 53–84 years) from the trial are included in this report. Patients underwent a structured medical and neurological history as well as neurological and neuropsychological examinations following the research protocol, with particular emphasis on the presence of gait disturbances, memory and attention disorders, urinary incontinence, frontal release signs, and spontaneous episodes, which often represent frontal lobe dysfunction. Although all patients summarized in this report had evidence of memory impairment with at least one deficit in cognitive domains (e.g. abstract thinking, language, orientation, flexibility in task changing) (64%), or isolated functional impairment (36%) unrelated to physical deficits, none had, as yet, a definite diagnosis of dementia; on the basis of combining information from subsequent studies, dementia would be diagnosed using the modified Diagnostic and Statistical Manual of Mental Disorders, third edition, revised criteria (DSM-III-R) [11].

Several standardized test procedures including SIDAM, BAI and NAP were used to rate the current severity of vascular dementia and to exclude patients with other psychopathological diseases, in particular significant mood disorders.

Vascular risk factors were documented and extra- and transcranial duplex sonography was performed to exclude patients with significant obstructive lesions. Patients with a history or evidence from clinical and MRT examinations interfering with the diagnosis of subcortical vascular encephalopathy (e.g. a recent cortical infarction, dementia of Alzheimer or mixed type, multisystem degenerative diseases, epilepsy, aphasia or other neuropsychological deficits interfering with the study protocol) were excluded. In this series, patients with marked arthrogenic disease and neuropathy severe enough to interfere with walking and standing were also excluded.

Informed consent was obtained from patients according to the suggestions of the ethics committee at Heidelberg/Mannheim University.

Stroke classification was based on methods of the Mannheim Schlaganfall Datenbank. Thirteen percent of the patients had a stroke syndrome (80% dominant vs. 20% nondominant with only mild dysfunction not affecting the study protocol; 80% hemispheric vs. 20% brainstem/cerebellum). MRT findings were rated for lacunar, periventricular, and diffuse WMLs separately for degree and topography. In addition, the presence or absence and degree of hydrocephalus or cortical atrophy with annotation of topography was noted (table 1).

MRT studies were performed with a 1.5 T superconductive unit using a circular polarizing head coil (Magnetom 63 SP, Siemens Medical Systems, Erlangen, FRG).  $T_1$ -,  $T_2$ -, and proton-density-weighted spin-echo images were obtained in the transverse plane to evaluate structural lesions. The diagnostic criterion for infarction was an increased intensity in  $T_2$ -weighted images corresponding to decreasing intensities in  $T_1$ -weighted images in typical vascular territories; WMLs were diagnosed in areas of increasing intensities in  $T_2$ -weighted images only.

MRT data were standardized by a planar elastic matching procedure on a stereotactic atlas [12]. Image presentation demonstrated the incidence of WMLs and lacunar infarctions using superimposed gray scale ratings.

Gait properties were recorded using the principle of force transduction as reported elsewhere [10]. In principle, 16 force transducers were distributed in the soles of a pair of shoes. Time record intervals

**Table 1.** Classification of MR images

Type of lesion	Degree	Location
Lacunes	0 none	a brainstem
	1 VR spaces	b basal ganglia, thalamus
	2 <2 lacunes	c subcortical white matter
	3 2-8 lacunes	
	4 >8 lacunes	
WMLs	0 none	a subcortical
	1 VR spaces	b periventricular
	2 <2 lesions	c cortical
	3 multiple lesions	d frontal
	4 confluent lesions	e parieto-occipital
Periventricular caps	0 no	a halo
	1 yes	b frontal
		c occipital
Hydrocephalus	0 no	
	1 yes	

VR = Virchow Robin's spaces.

for a single gait condition lasted 20 s with a sampling rate of 50 Hz. Records were stored off-line to keep the subject independent. Off-line analysis included the determination of the application point (e.g. the joint vector summarized for each foot), the gait line (e.g. the distribution of consecutive application points for each foot), the points of gravity (e.g. the weighted vectors summarized from both feet) and the cyclogram (e.g. the distribution of consecutive points of gravity). In addition, a series of spatial and temporal parameters such as length, variability and orientation of gait lines, monopodal and bipedal lines were numerically analyzed for statistical evaluation of related and invariant parameters. Distance of walk was standardized and, additionally, the lengths of right and left steps were measured.

## Results

### Clinical Observations

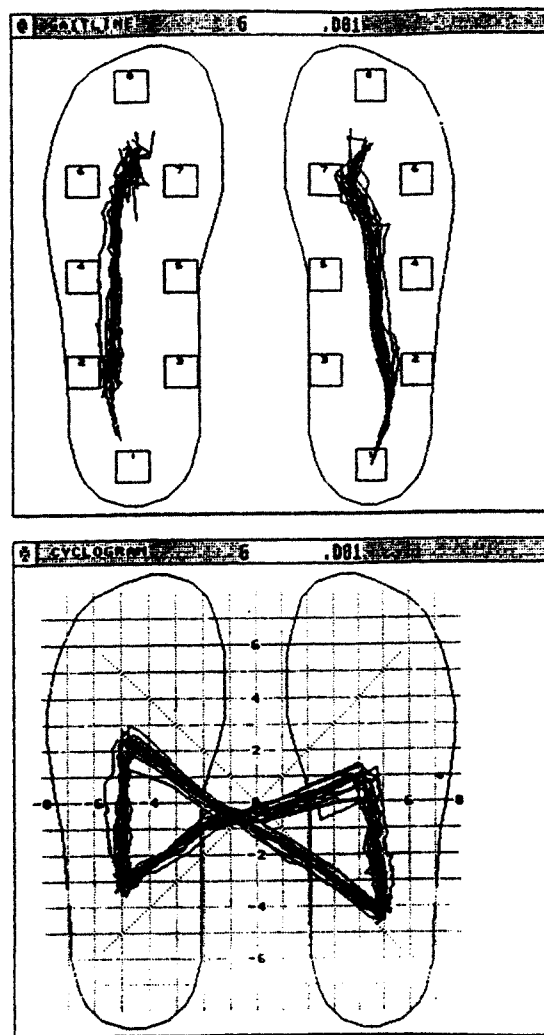
Seven patients on inspection revealed gait abnormalities with short and slow steps, specific difficulties in turning around with postural instability. Freezing, starting hesitation, hypokinesia, wide-based walking, rigidity and spasticity or tremor were absent: hand movements were normal in contrast to bilateral leg movements, which sometimes revealed impaired forward and backward bicycling apraxia. Pyramidal signs and primitive reflexes were present in 46%. Forty-four percent reported autonomic nervous system dysfunction with intermittent urinary incontinence.

### Objective Gait Analysis

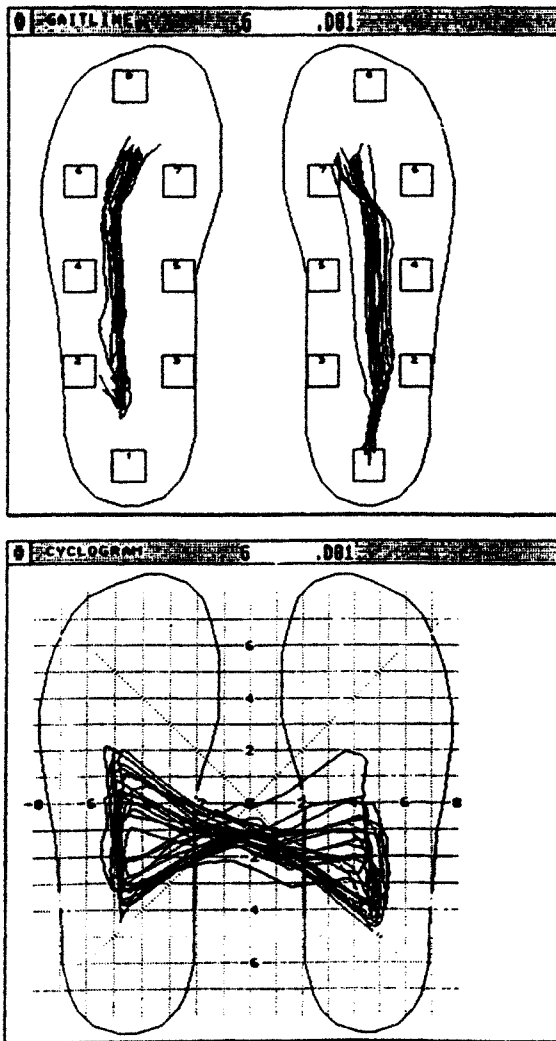
All patients revealed abnormal gait patterns with an increased variability of gait lines (100%), forward or backward bending or an increased variability or lateralization of the cyclogram (68%). The degree of impairment was mild (fig. 1) in 11%, moderate (fig. 2) in 32% and severe in 57%.

### MRT Findings

Abnormalities of gait correlated with a high prevalence of WMLs surrounding the frontal ventricular horns ('frontal caps') in 88% versus the occipital horns ('occi-



**Fig. 1.** Mild gait impairment with increased variability of gait lines (upper row) and mild left-right walking asymmetry in the cyclogram (lower row).



**Fig. 2.** Moderate gait impairment with increased variability of gait lines (upper row) and marked variability, asymmetry of walking and bending backwards for the gravity center (lower row).

tal caps') in only 50% (fig. 3, 4). Subcortical diffuse WMLs were found in frontal (96%) rather than parieto-occipital lobes (79%). In contrast, abnormalities of gait correlated less with lacunar lesions (26%).

#### *Associated Risk Factors*

Thirteen percent reported a history or revealed mild signs of a previous ischemic stroke, and 39% were admitted for a transient ischemic attack. Fifty-six percent had a history of hypertension and 22% of diabetes.

## Discussion

Impairment of gait and balance with preservation of strength and sensorimotor perception have long been said to be related to vascular brain lesions – these patients might, however, have been misdiagnosed as having cerebellar, spinal or metabolic diseases (e.g. Parkinson's disease) in particular if the initial walking disabilities were mild and the performance of proximal associated movements of arms and legs was not examined. As far back as 1907, Lhermitte [13] described the concept of 'cerebral paraplegia' in the elderly, and Critchley [1] later associated this type of gait disorder with arteriosclerosis of the cerebral vessels although the pathoanatomic substrate was unclear at this time.

With the advent of CT and MRT on the other hand, patients are seen with multiple subcortical WMLs and lacunar infarctions of subcortical nuclei and connecting pathways, but clinical descriptions of gait, balance and axial movements are often lacking or inadequate. This view is supported by the demonstration of gait disturbances in virtually all patients studied because of the suspected diagnosis of vascular dementia in our clinical and neuroimaging study protocol; this is not always the fault of clinicians, who, although instructed to report walking impairment even of a mild degree, did so in only 1/3 of the patients. The clinical diagnosis could be markedly improved by the additional use of an objective gait-measuring system.

The anatomic correlates most probably responsible for gait impairment are bilateral lesions of the suprathermal thalamo-cortico-capsular pathways, which link the supplementary motor area of the frontal cortex (area 6) with the efferent anterior part of the ventrolateral nucleus of the thalamus (VL<sub>a</sub>), and the efferent posterior portion (VL<sub>p</sub>) with the precentral cortex (area 4), with particular projection to the trunk and leg representation areas from its lateral part. These fibers are closely related to the lateral ventricles in the corona radiata and the posterior capsula interna.

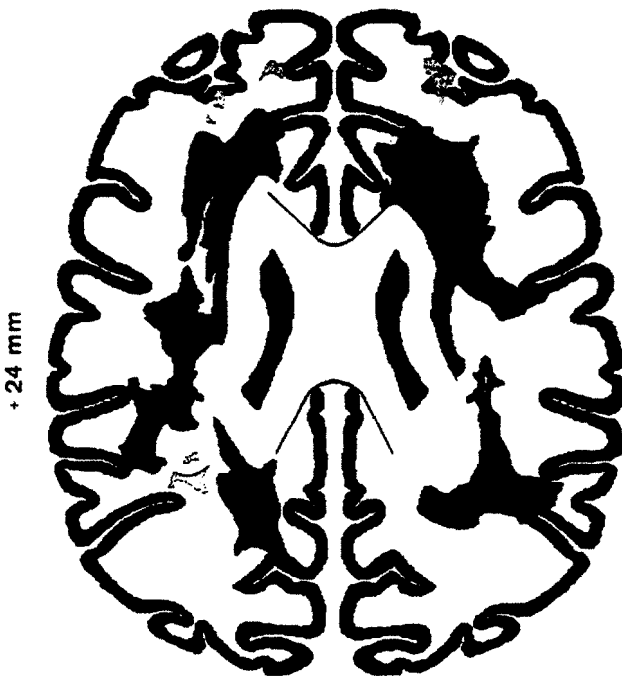
The pathoanatomic nature of this aspect in patients with possible dementia remains, however, a matter for future investigations. Few reports have addressed the possible correlation of WMLs, dementia and gait impairment [3, 14], although a large amount of work has been done to investigate the association of WMLs and dementia, with quite controversial results. George et al. [14] failed to find a significant correlation between WMLs and dementia but demonstrated a better correlation with gait disturbances and WMLs. Although the presence of gait abnormalities correlated with the observation of WMLs in the



3a

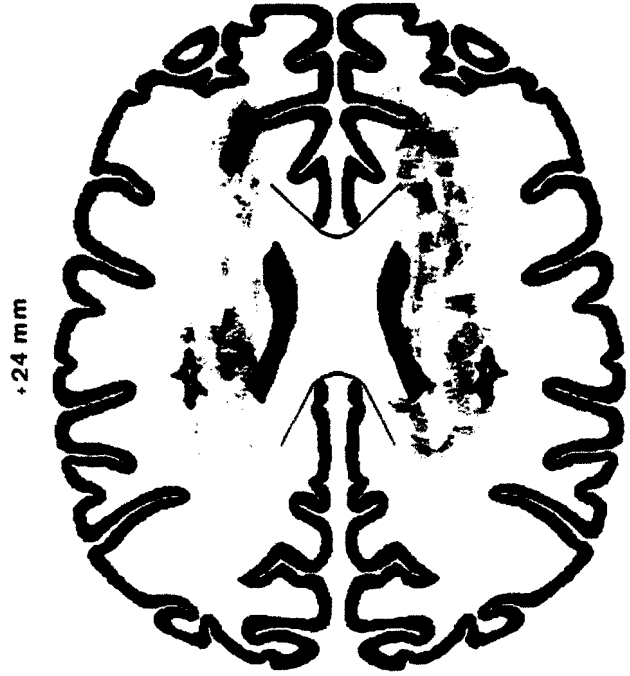


3b



3c

**Fig. 3.** a Original MRT. b Areas of WML marked in grey. c Standardization in a stereotactic atlas. Different regions of diffuse (dark) and circumscribed WMLs (grey) are coded in grey.



4

**Fig. 4.** Summary display of superimposed diffuse WMLs matched in a single MRT section from all the patients studied. Increasing gray tones indicate increasing numbers of patients with similar areas involved.

fronto-thalamo-capsular and periventricular areas in most of the patients studied, as yet there is no correlation established between this observation and the development of dementing illnesses. Furthermore, patients with similar MRT findings may well present without any evidence of gait dysfunction and postural imbalance – thus both items need careful further investigation.

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