ELSEVIER

Journal of the Neurological Sciences 229–230 (2005) 89–93

Journal of the Neurological Sciences

www.elsevier.com/locate/jns

# Gait slowing as a predictor of incident dementia: 6-year longitudinal data from the Sydney Older Persons Study

L.M. Waite[a,*], D.A. Grayson[b], O. Piguet[c], H. Creasey[a], H.P. Bennett[c], G.A. Broe[c,d]

[a]*Centre for Education and Research on Ageing, C25, Concord Hospital, University of Sydney, Concord NSW 2139, Australia*
[b]*School of Psychology, University of Sydney, Australia*
[c]*Prince of Wales Medical Research Institute and the University of New South Wales, Australia*
[d]*Prince of Wales Hospital, Randwick, Australia*

Available online 8 December 2004

**Abstract**

Current definitions for the preclinical phase of dementia focus predominantly on cognitive measures, with particular emphasis on memory and the prediction of Alzheimer's disease. Incorporation of non-cognitive, clinical markers into preclinical definitions may improve their predictive power. The Sydney Older Persons Study examined 6-year outcomes of 630 community-dwelling participants aged 75 or over at recruitment. At baseline, participants were defined as demented, cognitively intact or having a syndrome possibly representing the preclinical phase of Alzheimer's disease, vascular dementia, an extrapyramidal dementia or various combinations of the three. Those with cognitive impairment in combination with gait and motor slowing were the most likely to dement over the 6-year period (OR 5.6; 95% CI 2.5–12.6). This group was also the most likely to die (OR 3.3; 95% CI 1.6–6.9). White matter indices on MRI scanning were not consistently correlated with gait abnormalities. Simple measures of gait may provide useful clinical tools, assisting in the prediction of dementia. However, the underlying nature of these deficits is not yet known.


*Keywords:* Dementia; Gait; Parkinsonism; Mortality; Cognitive decline; Vascular risk

## 1. Introduction

Identifying states that will predict the subsequent development of dementia has important implications for future therapeutic interventions. Much current focus is upon the entity of Mild Cognitive Impairment (MCI) [1,2]. However, it is argued that MCI may be a heterogeneous entity, with possible subtypes existing for the non-Alzheimer dementias [2,3]. Furthermore, there may be non-cognitive markers that predict the progression of MCI to dementia. Extrapyramidal signs in non-demented subjects are associated with higher mortality, increased functional impairment and the subsequent development of dementia [4–10]. Gait abnormalities have been found to precede the onset of dementia by many years. In the Bronx Aging Study of community living participants aged 75 and over, abnormalities of gait including unsteadiness, frontal gait disorders and hemiparetic gaits predicted the development of non-Alzheimer dementias over a median period of 6.6 years [11]. Over a 6-year period, the Oregon Brain Ageing study of initially well participants aged 65 and over, found that a longer time to complete a 30-ft walk was an independent predictor of persistent cognitive deficits [12].

Therefore, signs of extrapyramidalism and slowing of gait may act as clinical markers for the increased likelihood of progressing to dementia. This study aims to examine the predictive role of extrapyramidalism and slowing of gait in the development of incident dementia and mortality in a sample of individuals who were community dwellers and aged 75 and over at baseline. It was hypothesised that gait abnormalities would prove to be a useful adjunct in predicting those participants who would subsequently dement or die within the 6-year study period.

* Corresponding author. Tel.: +61 2 9767 7278; fax: +61 2 9767 5419.
*E-mail address:* lwaite@medicine.usyd.edu.au (L.M. Waite).

0022-510X/$ - see front matter © 2004 Elsevier B.V. All rights reserved.
doi:10.1016/j.jns.2004.11.009

## 2. Materials and methods

A sample of 630 non-institutionalised men and women aged 75 years or older residing in the Central Sydney Area Health Service participated in the Sydney Older Persons Study from 1991 to 1993 [13–15]. Participants were assessed at baseline and on a further three occasions—at 3 years, at 5 years for collection of blood samples including DNA and at 6 years for further reassessment. Data from baseline, 3- and 6-year follow-ups are presented in these analyses. By the 6-year follow-up, 226 (35.9%) participants had died, 33 (5.2%) were lost to follow-up and a further 64 (10.2%) refused to be interviewed. An additional 8 (1.3%) participants were alive but due to ill-health or distance were not seen. Those who died were older, more likely to be male and more likely to be cognitively impaired at baseline. Refusals and non-contacts did not differ in age or Mini-Mental State Examination (MMSE) score at baseline [16]. At all assessments, participants gave written informed consent and the study had institutional ethics approval.

Of the 630 participants at baseline, 522 participated in a medical assessment which included; a standardised medical history examining past and current health and medication usage; a neuropsychological battery and physical examination. Diagnoses of dementia using this baseline information were assigned by the clinician using DSM-III-R criteria [17]. As this study aims to examine the predictors of dementia, only participants not demented at baseline are included in analyses. Diagnoses of dementia at 3- and 6-year follow-ups fulfilled the general DSM-IV criteria (criteria A and B) [18]. Regular meetings were held reviewing dementia diagnoses over the course of the study to ensure consistency. In those participants at 3- and 6-year follow-ups where no assessment was possible or where participants had died, an informant questionnaire [19] which examined the six domains of the Clinical Dementia Rating (CDR) was used to identify incident dementia cases in order to achieve more complete case ascertainment (sensitivity 80%, specificity 98%). Participants assessed by the informant questionnaire were diagnosed as demented if they were rated as mildly, moderately or severely demented according to the informant CDR. Thus, in using both the clinical and informant data, we were able to include 394 (91.6%) of the 430 participants not demented at baseline in analyses examining incident dementia at 3 and 6 years. For mortality analyses, 428 participants not demented at baseline are included at 3 years and 417 at 6 years.

Preclinical syndromes for the three main dementias, Alzheimer's disease (AD), Vascular dementia (VaD) and the extrapyramidal dementias (EPD) were defined [9]. It was also necessary to define multi-pathology preclinical syndromes as 34% of dementia cases were found to be multi-aetiological at baseline [14]. As vascular and extrapyramidal features may be present initially without evidence of cognitive deficits, distinct sets of preclinical syndromes for VaD and EPD with or without cognitive deficits were defined.

Participants were hypothesised to have preclinical AD if they showed cognitive impairment without vascular or extrapyramidal features, termed here CI. Participants were clinically defined as having cognitive impairment if they displayed mild to moderate deficits in one or more areas of cognition (memory, language, visuospatial or executive function) but did not reach DSM-III-R criteria for dementia.

VaD is characterised by dementia with historical or clinical evidence of stroke in association with other vascular disease and the presence of vascular risk factors. At a pre-dementia syndromal stage, any of these characteristics may be expected. Participants met the pre-vascular criterion if they had experienced either a transient ischaemic attack or stroke or they had three or more vascular risks (atrial fibrillation, diabetes, hypertension, heart disease, claudication, self-reported hypercholesterolaemia or smoking). TIA and stroke were diagnosed according to history and clinical evaluation. Neuroimaging was not available at baseline assessment. Diabetes and hypertension were diagnosed from medical history, including review of relevant medications for treatment of these conditions. Heart disease was inclusive of all types of heart disease including both ischaemic and valvular. The pre-vascular group, termed preVasc, included participants with vascular features exclusively. Another group, CI+preVasc, included participants with additional cognitive impairment.

The extrapyramidal (EP) features associated with EPD include bradykinesia, rigidity and tremor. At a pre-dementia stage, such features, of lesser severity, would be expected to occur in association with varying levels of cognitive deficits. Two components comprised the EP measure. The first component was an EP score This EP score included severity graded measures of tone (rigidity, cogwheeling, nuchal rigidity), bradykinesia (slowed fine finger movements, reduced arm swing and an overall clinical assessment of the presence of bradykinesia), resting tremor, postural flexion and the glabella tap. A cutoff of one or more in the EP score was used corresponding to either one severe sign, one moderate and one mild sign or three mild signs. The second component was an objective measure of extrapyramidal gait changes as assessed by the time to complete the 5-m returned walk, controlled for causes of mechanical slowing such as arthritis. Participants who had either a slowed 5-m returned walk or scored one or more in the EP score were included in the EP prodromal group. The EP groups were termed preEP and CI+ preEP when occurring without or with cognitive deficits, respectively.

As both vascular and extrapyramidal features may co-exist, two groups termed preVasc+preEP and CI+preVasc+preEP were also created. Thus, a total of seven preclinical groups were created: three denoting a single underlying pathology: CI, preVasc and preEP; and four denoting multiple underlying pathologies: CI+preVasc, CI+preEP, preVasc+preEP and CI+preVasc+preEP.