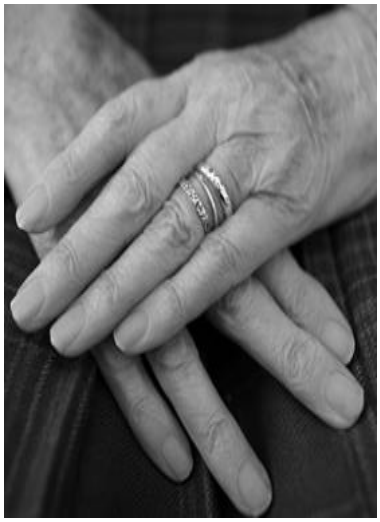
GAIT ABNORMALITIES AS EARLY SIGNS OF MCI

WITH AIM TO EVALUATE SPATIOTEMPORAL GAIT PARAMETERS AS PREDICTOR OF MILD COGNITIVE IMPAIRMENT (MCI) IN A POPULATION BASED COHORT OF 2600 MEN AND WOMEN

Gait disorders are frequent in individuals with cognitive disorders. However, the profile of spatio-temporal gait parameters in the different cognitive status in aging (from normal cognition to dementia) has been poorly studied. Determining this profile associated with the severity of cognitive disorders may be helpful to understand the complex interplay between gait and cognitive disorders and, thus, may have important implication for the diagnosis process of patients with and without dementia. For instance, defining a motor phenotype of the severity of cognitive disorders by using quantitative gait measurements could be used to improve the prediction and the diagnosis of dementia.



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MATERIAL & METHODS

STUDY POPULATION

This prospective observational study is part of the Healthy Ageing Initiative at Umea University, Sweden (www.healthyageinginitiative.com). The inclusion criteria for this study is 1) residence in the Umea municipal area and 2) age of exactly 70 years at the time of testing. Information from population registers is used to contact eligible individuals, who receives printed information about the research project. Telephone contact is made shortly thereafter, during which individuals accepts or decline the invitation to participate. As we aim to investigate a sample representing the general population, no eligible participant is excluded.

METHODS

Geriatric Depression Scale–Short form

Yesavage, et al. [1] originally developed the Geriatric Depression Scale (GDS) to screen for depression in persons aged > 60 years. It is the preferred instrument for depression screening in adults aged ≥ 65 years [2]. A short form (GDS-15) was later developed and validated [3]; this form was used in the current study. It consists of 15 yes/no questions, with one point given for each response pointing toward depression. A cutoff score of 5 points has been used as an indication of depression [4].

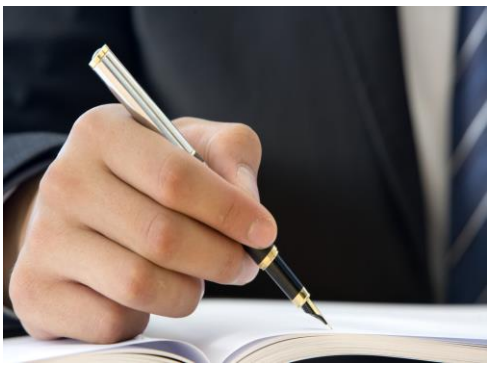
Mini–Mental State Examination

The Mini–Mental State Examination (MMSE) [5] is the most widely used screening instrument for cognitive functions. It has a maximum score of 30, divided into six domains: Orientation to time and place, Registration and learning, Attention, Memory, Language, and Visuospatial ability. It takes about 10–15 minutes to administer.

Integrated Visual and Auditory Continuous Performance Test

The IVA [6] is a computer-based test of sustained attention and response control. The participant is presented with a pseudo-randomly ordered series of visual and auditory 1s and 2s (total 500 trials), while asked to click the mouse every time he/she sees or hears the number 1. The main test lasts about 13 minutes; with warm-up, practice, and cool-down periods, the entire testing process requires about 20 minutes. In this study, the test administrator gave instructions in Swedish, with the computerized English instructions muted. The language option of the IVA is set to present auditory stimuli in Swedish.

The results of the IVA are presented in six primary



scales (three response control and three attention scales) in the auditory and visual domains. The response control scales are: Prudence, which measures response control through commission errors (i.e., proportion of clicks in response to 2s); Consistency, which measures the ability to stay on task using variability in response times, ignoring outliers; and Stamina, which measures sustained attention over time by comparing reaction times at the beginning and end of the test. The attention scales are: Vigilance, which measures inattention through errors of omission (i.e., proportion of 1s with no click response); Focus, which measures reliability of attention using variability in reaction times with sensitivity to outliers; and Speed, which measures reaction time using the mean reaction time for correct responses.

IVA results are also analyzed using six supplementary scales: Fine Motor Regulation, which measures small motor hyperactivity by recording clicks during instructions or multiple clicks during the test; Balance, which measures the relative speed of processing in the visual and auditory domains; Readiness, which measures the participant's relative attention in high- and low-demand conditions by comparing reaction times when 1s are frequent and rare; Comprehension, which measures carelessness, severe impulse control, or attention difficulties using the number of idiopathic errors; Persistence, which measures motor/mental fatigue or lack of motivation by comparing reaction times in the warm-up and cool-down periods; and the Sensory/Motor Scale, which measures simple reaction times during the warm-up and cool-down periods.

Gait Measurement

Gait measurements are obtained using the validated GAITRite system (CIR Systems, Sparta, NJ, USA), an 8.6-m-long and 0.88-m-wide electronic walkway containing sensors situated 1.27 cm apart.[7] The GAITRite system measures temporal and spatial gait parameters, with automatic initiation of the gait sequence from the first footfall contact and termination after the last. The sensors detect footfalls during ambulation, and raw data on gait parameters are subsequently transmitted to the application software for processing. [8]

Participants performs three progressively challenging gait trials. During the first trial, participants walks normally at a preferred pace. In the second trial, participants are asked to walk as rapidly as possible while maintaining control. During the third trial, we introduce dual tasking, where participants walks at a self-selected pace while counting backward from 100 in increments of 1. Participants removes footwear and are instructed to start each trial 1 meter ahead of the walkway to reduce acceleration effects.

The software calculates means and standard deviations (Ms ± SDs) of gait parameters for each trial. Combined Ms ± SDs for parameters with

SELECTED REFERENCES

1. Yesavage JA, et al. Development and validation of a geriatric depression screening scale: a preliminary report. *Journal of psychiatric research* 1982;**17**:37-49.

2. Bolla-Wilson K et. Absence of depression in elderly adults. *Journal of gerontology* 1989;**44**:P53-5.

3. Sheikh, J. I., & Yesavage, J. A. (1986). Geriatric depression scale (GDS): recent evidence and development of a shorter version. In T. L. Brink (Ed.), *Clinical gerontology: a guide to assessment and intervention.* (pp. 165-173). New York: Haworth.

4. Sharp LK Lipsky MS. Screening for depression across the lifespan: A review of measures for use in primary care settings. *Am Fam Physician* 2002;**66**:1001-1008.

5. Folstein MF, et al. "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. *Journal of psychiatric research* 1975;**12**:189-98.

6. Sandford JA Turner A. IVA+Plus - Integrated Visual and Auditory Continuous Performance Test - Interpretation Manual: BrainTrain Inc.; 2009.

7. Bilney B, et al. Concurrent related validity of the GAITRite (R) walkway system for quantification of the spatial and temporal parameters of gait. *Gait Posture* 2003;**17**:68-74.

8. Hollman JH, et al. Normative spatiotemporal gait parameters in older adults. *Gait Posture* 2011;**34**:111-118.

9. Burns A. Mini-Mental State: A practical method for grading the cognitive state of patients for the clinician. M. Folstein, S. Folstein and P. McHugh, Journal of Psychiatric Research (1975) 12, 189-198. Introduction. *Int J Geriatr Psych* 1998;**13**:285-

separate values for the left and right legs are calculated manually. Coefficients of variance (CVs; SD / M × 100) are then calculated for all gait parameters. The study cohort comprise all participants with complete gait measurements for the initial, normal-speed trial.

Covariables

Anthropometric variables is measured after participants had provided written consent. Height (m) is measured using a gauge (Holtain Limited, Crymych, Dyfed, Britain) and weight (kg) is measured with a scale (Avery Berkel HL 120, Fairmont, MN, USA). Body mass index (BMI) is then calculated as weight divided by height squared. Participants also reports smoking, as well as histories of cardiovascular disease and diabetes.

Highest achieved education, total income, and early disability pension at 40 years of age is obtained from the Statistics Sweden database.

Information on diagnosis from 1987-01-01 and onwards is obtained by record linkage with the National Hospital Discharge Register (HDR), covering all public inpatient care in Sweden, and the National Hospital Outpatients Register, covering all public outpatient specialist care in Sweden from 2003-01-01, administered the National Board of Health and Welfare in Sweden. Diagnosis were recorded using the International Classification of Diseases (ICD) version 9 (1987-1996) and version 10 (1997 and later). All diagnoses of dementia will be validated through patient journal records.

Prescribed drugs for every subject in the cohorts based on social security number is available from the National Prescription Database at the National Board of Health and Welfare from 2005-07 and onward. For each subject drug data is available concerning identity, amount, dose and date of delivery (for further information www.socialstyrelsen.se). Permission for merging data files has been obtained from the National Board of Health and Welfare. Socioeconomic data will be searched at Statistics Sweden (www.scb.se).

Ethics

The present study is approved by the local ethics committee of Umeå University and by the National Board of Health and Welfare in Sweden.

PRELIMINARY RESULTS

The present study is part of an ongoing study with the aim to include a total of 5000 men and women. The current study aim to evaluate gait in relation to cognitive function in a subsample of 2600 men and women. Permission for merging data files has been obtained from the National Board of Health and Welfare and Statistics Sweden. We will validate all diagnoses by retrieving all available journal records for all subjects with a diagnosed dementia.

BUDGET

The present project has part funding from the Swedish Research Council, VR, (I received funding from VR in 2012 young investigator grant (700 tkr in 3 years) and one year later for 50% research time and 850 tkr in 3 years for the present project. In 2013 I was co applicant to VR rambidrag 12.144 Mkr for 5 years (main applicant Prof Yngve Gustafson, Dpt. Community Medicine and Rehabilitation, Geriatrics Umeå University). The present project was one of 4 project in that application. In September 2015 I got an additional 5.5Mkr from VR for 3 more years of 50% research time and project funding (1 Mkr per year of the total sum).

The previous grants from VR do not cover the total project costs, and do not contain the present research focus i.e. detecting early gait deterioration as a marker for cognitive decline. Thus, the present application aims to secure further financing to analyse the collected data. Cost for post doc for three months for data analysing and manuscript preparation including overhead mounts to 189000.

IMPORTANCE

There is lack of studies that have evaluated gait deterioration as a marker for cognitive decline. To find such marker would be important to identify individuals at risk early, and such findings of a motor phenotype of decline in cognitive performance could be used to improve the prediction of cognitive decline.