

CHAPTER

1

Introduction



DEMENTIA

Dementia is one of the most common syndromes in late life. It was estimated that 24.3 million people were suffering from dementia worldwide in 2001.¹ The prevalence of dementia is rising exponentially with ageing. Because of increased life expectancies, the worldwide number of people with dementia will rise to an estimated number of 90.3 million people with dementia in 2040.²

Dementia is a syndrome characterized by progressive deterioration of cognitive functioning. It affects the ability to think, remember and behave normally. These deficits lead to another characteristic of dementia: it interferes with everyday functioning.³ As such, dementia causes a major burden on patients and caregivers.

DIAGNOSING DEMENTIA

Dementia is characterized by memory impairment and a combination of language, praxis, visuospatial and/or executive functioning impairments. These cognitive impairments interfere with a subjects' everyday functioning.³ The clinical criteria for dementia are shown in Table 1.

Table 1. DSM-IV criteria for dementia.³

Short- and long-term memory impairment
Impairment in abstract thinking, judgment, other higher cortical function or personality change
Cognitive disturbance interferes significantly with work, social activities or relationships with others
These cognitive changes do not occur exclusively in the setting of delirium

Once the presence of dementia is established, an attempt should be made to identify its etiology. Dementia can be caused by several neurodegenerative disorders. The cause of dementia is generally established by several investigations: a clinical history, clinical exam, neuropsychological assessment and, if possible, imaging and laboratory studies.

Alzheimer's disease

The most prevalent cause of dementia in the elderly is Alzheimer's disease (AD). This disease was first described more than one hundred years ago by the German neuropathologist and psychiatrist Alois Alzheimer. In its most typical form, patients present with memory problems. This impairment is followed by visuospatial disorientation, language dysfunction, apraxia or problems in executive functioning.

Occasionally, patients present with disruption of a single cognitive domain other than memory, such as executive dysfunction. This presentation is more common among patients with early-onset (referring to an onset below the age of 65 years) AD.⁴ It is estimated that about one third of the memory clinic dementia patients is below the age of 65.^{5,6}

During life, probable Alzheimer's disease is diagnosed according to the clinical criteria of the NINCDS-ARDRDA criteria.⁷ Recently, new diagnostic criteria made an attempt to enable a diagnosis of AD before the presence of dementia by included biomarker evidence of underlying AD pathology.⁸ The diagnosis of AD can be confirmed at post-mortem examination.

Mild cognitive impairment (MCI)

Dementia develops gradually and is in a certain number of patients preceded by a phase with cognitive impairment, usually memory deficits. When patients complain about forgetfulness in this stage, they cannot be classified as 'normal', but neither as 'demented' as they do not meet the criteria for dementia. This clinical condition is generally labeled as 'mild cognitive impairment' (MCI).⁹ MCI is defined by memory complaints of the patient in combination with an objective memory deficit, without interference with activities of daily living (see Table 2).^{9,10} Patients with MCI have an estimated chance of 10-12% of developing dementia within one year, with a majority of these dementia cases being AD.¹¹ Although MCI represents a heterogeneous group of disorders and is not necessarily progressive, it is commonly thought that these patients are already in the early stages of the disease, as depicted in Figure 1.¹²

ACTIVITIES OF DAILY LIVING

The interference of cognitive disorders with everyday functioning is mentioned in the criteria for both MCI and dementia. As it is difficult to ascertain this inference, instruments measuring 'activities of daily living' are commonly used.

Activities of daily living are typically divided into basic activities of daily living (BADL) and instrumental activities of daily living (IADL). BADL are basic self-care skills, such as washing, eating and toileting.^{13,14} Instrumental activities of daily living (IADL) are more complex activities, described as the activities necessary to function independently in society.¹⁵ These activities include, but are not limited to, cooking, doing finances and shopping.^{14,15}

Since IADL involves higher order activities, it is vulnerable to the early effects of cognitive decline. As a consequence, IADL activities are affected early in the disease course of dementia.¹⁵⁻¹⁷ It has been suggested that problems in complex everyday

Table 2. Criteria for mild cognitive impairment.¹²

Memory complaint, preferably corroborated by an informant
Objective memory impairment (memory test score below 1.5 standard deviation)
Normal general cognitive functioning
Intact activities of daily living
Not demented

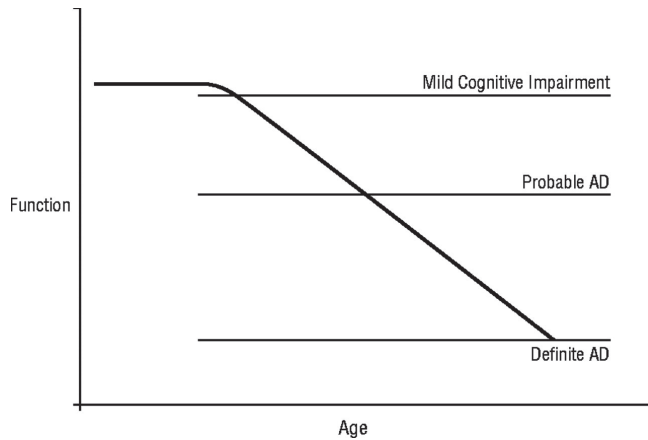


Figure 1. Theoretical progression of a subject with AD. The inflection point in the curve indicates the onset of mild cognitive impairment before the onset of clinically probable AD.¹² Reproduced from Petersen R.C. Aging, Mild cognitive impairment and Alzheimer's disease. *Neurologic Clinics* 2000;4:789-805 with permission of the author and W.B. Saunders Co. via Copyright Clearance Center.

activities might even be one of the first indications of the disease process to the patient or family members.¹⁸

IADL is thus important for the clinical diagnosis of dementia. According to the definition of MCI, IADL is also relevant for the distinction between dementia and MCI: patients with MCI have intact activities of daily living, whereas activities of daily living are affected in patients with dementia.^{3,9}

In spite of this definition, several recent studies have indicated that patients with MCI may already experience slight problems in complex activities of daily living.¹⁹⁻²² Longitudinal studies showed that patients with both MCI and IADL problems were at a higher risk of developing dementia than MCI patients without IADL impairment.^{23,24} The relationship between MCI, dementia and IADL might thus be more complex than generally assumed.

Background of IADL

Since the late 1960s, the BADL and IADL terminology provided by Lawton & Brody has been widely used.¹⁵ Theories that describe the general connection between pathological changes and everyday functioning are the 'disablement process' and

the ‘international classification of functioning, disability and health’ (ICF) of the world health organization (WHO).^{25,26} The ICF is based on a comprehensive biopsychosocial framework, including changes in body structures and body functions, the patient’s ability to participate in everyday life situations and the influence of environmental and personal factors. This framework is depicted in Figure 2.

In this framework, dementia is part of the health condition which determines the daily activities. These activities include both BADL and IADL, though some IADL activities are part of the ‘participation’ domain, such as traveling. Even though this model provides a concise framework of disability and general health, specific information on the relation between dementia, cognition and IADL tasks is lacking.

Several studies have investigated the link between cognitive functioning and daily functioning. Cognitive domains, such as memory, executive functioning, visuospatial function and object perception have all been found to correlate with IADL impairment in AD patients.²⁷⁻³³ However, part of the association between cognitive functioning and daily functioning remains unclear.^{28,34} It seems acceptable that most IADL tasks have multiple cognitive determinants, any one of which can diversely affect functional performance.^{14,35} Other determinants, such as behavioral disturbances or hallucinations were also found to contribute to everyday functioning.^{36,37}

Individual differences between dementia patients have been explained by the extent to which IADL activities rely on controlled versus automatic processing.³⁸ Controlled processing tasks require attention, are not entirely familiar or predictable and cannot

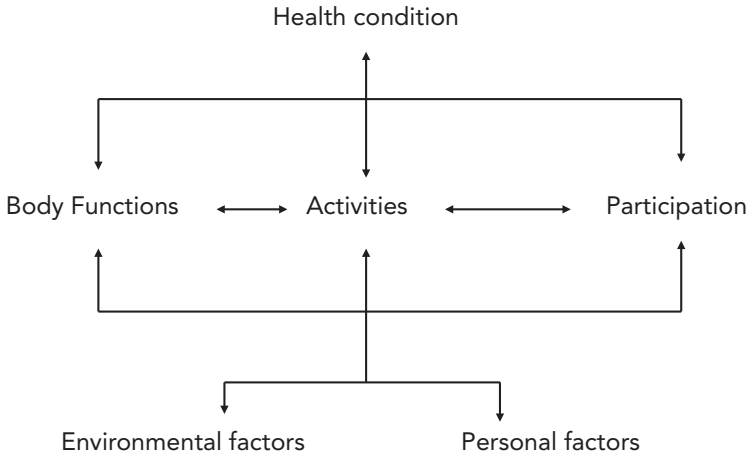


Figure 2. The ICF framework.²⁶ Reproduced from the ICF beginners guide (2002) with permission of the World Health Organization. <http://www.who.int/classifications/icf/training/icfbeginnersguide.pdf>

be carried out well in conjunction with other tasks. Automatic processing tasks on the other hand, demand little attentional capacity and are little affected by other processing demands³⁸. Practice can influence the extent to which activities rely on automatic or controlled processing. As with cognitive reserve, the amount of practice with complex tasks might result in functional reserve.¹⁴ These theories emphasize the complexity of everyday life, where coping with a rapidly changing multitude of tools and technologies is required. The factors involved in IADL functioning are depicted in Figure 3.

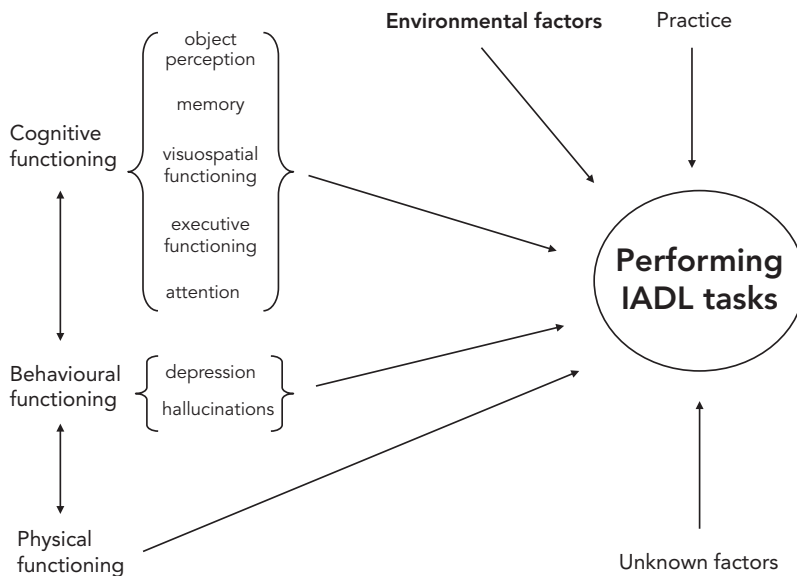


Figure 3. Underlying aspects of complex everyday tasks (IADL).

Methods of measuring IADL

There are three widespread assessment methods to assess an individual's ability to perform IADL: self-report by the individual, performance-based assessment and informant report.^{13,14,18,39} Each method of assessment has its own strengths and weaknesses.

Self-report is the easiest method, but in dementia patients, a limited disease insight might make reports invalid.^{18,40,41} Impaired awareness can be present in early stages and increases over time in dementia, evidenced by increasingly poor self and informant agreement.⁴² Performance-based assessment provides an objective behavioral evaluation of functional skills by a trained rater.¹⁴ However, patients performance has been shown to differ between settings, that is, in a clinical setting

versus at home.⁴³ Another limitation of the performance-based assessment is that only a limited number of activities can be evaluated and it is a time-consuming and costly assessment.^{18,39}

Informant reports are the most used IADL assessment method in dementia evaluation.¹⁴ An informant, or proxy, can be anyone who has had the opportunity to observe the patient in his real-world environment, such as a spouse, partner, sibling, child or a close friend. A limitation of informant reports is that informant characteristics such as anxiety, depression, caregiver burden and general perceived health may influence informant ratings.^{44,45} However, several important advantages include the ease of administration and the rating of real-world IADLs.

THE NEED FOR A NEW IADL QUESTIONNAIRE

The nurse specialists of the Alzheimer Center of the VU University Medical Center expressed the need for a new IADL questionnaire, as the instrument used until now was intended for patients with moderate dementia and had been developed over 40 years ago. The population of memory clinic patients had changed over time. Due to increased awareness in doctors and patients, patients come to a memory clinic in earlier stages of the disease. These patients will have only mild problems in everyday live.

The Alzheimer Center is specialized in diagnosing patients with early-onset dementia. Diagnosis in these patients is often missed as the presenting symptoms vary greatly and frequently include behavioral signs.⁴⁶

The existing IADL questionnaires had limited usefulness for early-onset patients, as they were aimed at elderly patients spending time in retirement. In addition, advances in technology changed our daily environment and made many existing IADL questionnaires out of date.⁴⁷ In spite of the presence of a large number of informant-based IADL questionnaires, the need for a reliable and valid new questionnaire was also expressed by numerous researchers.⁴⁸⁻⁵²

AIMS AND OUTLINE OF THIS THESIS

The main reason for this thesis was the need for a reliable and valid IADL measure. We aimed to extend the insight into the clinical applicability of IADL and to use this knowledge for the development of a new IADL questionnaire. We will address the following research questions and research aim:

- Does everyday cognitive functioning contribute to a diagnosis of AD?
- Does IADL contribute to a diagnosis of dementia at follow-up in non-demented patients?
- What is the psychometric quality of existing IADL measurement instruments?
- To develop a reliable and valid new informant-based IADL questionnaire

The first research question is addressed in **chapter 2** of this thesis. In **chapter 2.1** we explored the role of a general measure of everyday cognitive functioning in the distinction between AD, MCI and subjective memory complaints. We then investigated in **chapter 2.2** whether subgroups of items differed in their ability to distinguish between these patient groups.

We addressed the second research question in **chapter 3**. In this chapter we explored the role of an IADL assessment for the prediction of dementia at one and two year follow-up. This study was part of the Development of screening guideline and clinical criteria for predementia AD (DESCRIPA) study.⁵³

As many IADL instruments are available, we then investigated the quality of the informant-based IADL questionnaires in **chapter 4**. This chapter provides an overview of 12 informant-based IADL questionnaires. We rated the psychometric properties of these questionnaires to investigate the quality and to ensure that all relevant aspects of IADL in dementia are considered in the development of the new IADL instrument.

In **chapter 5** and **chapter 6** we addressed the last research aim. In **chapter 5** we describe the development of the new instrument: the Amsterdam IADL Questionnaire®. The construct of IADL is discussed in this chapter and we composed a new definition of IADL. We constructed new items, conducted a test-retest study and investigated the factor structure. In **chapter 6** we investigated the scoring and construct validity of the new questionnaire.

The final chapter summarized the main findings for this thesis, followed by a discussion of the results and conclusions. We conclude this thesis with recommendations for future research.

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