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Original Research Article

Increasing the Sensitivity of Functional Status Assessment in the Preclinical Range (Normal to Mild Cognitive Impairment): Exploring the IADL-Extended Approach

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Abstract
Background/Aims: Dementia exhibits an insidious onset consisting of cognitive, behavioral, and functional impairment. We explored a functional continuum that extends assessment beyond the clinical instrumental activities of daily living (IADL) range and into advanced activities of daily living. ***Methods:*** We examined the predictive power (Cox regression; n = 2,471) of a unidimensional IADL-extended (IADL-x) scale for incident mild cognitive impairment (MCI). We also examined "time to MCI" as an outcome measure. ***Results:*** Each additional task endorsed on the IADL-x hierarchy (e.g., endorsing participation in 6 vs. 5 activities) resulted in a 10% reduction in MCI risk (HR 0.90, 95% CI 0.85–0.94, $p < 0.001$). For the fully adjusted model the risk reduction dropped to 6%. The odds of incident MCI within 2 years (for those below the median IADL-x total score) was 2.5 times higher (OR 2.60, 95% CI 1.52–4.4, $p < 0.001$) and 2 times higher for incident MCI within the next 5 years (OR 1.93, 95% CI 1.76–3.2, $p < 0.01$). ***Conclusion:*** The IADL-x metric appears to be a valid approach for determining the risk of MCI based on one's position along a formal hierarchy of function.

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Introduction

There is a higher risk of incident dementia for individuals with cognitive deficits and instrumental activities of daily living (IADL) difficulty than for those with cognitive deficits alone [1, 2]. More striking is the observation that IADL impairment alone can present with very similar trajectories toward dementia [3, 4], perhaps a reflection of neuropathology that has not compromised individuals in a global fashion. Cerebral Aβ deposition (an early pathologic hallmark of Alzheimer's disease) has been associated with functional status (IADL) in the prodromal stage of dementia [5]. What is less clear is whether the emergence of difficulties in traditional IADL tasks represents the limits of detectable functional change. It has been suggested that, like cognitive decline, functional status exists on a continuum from normal aging to dementia onset [6], with IADL impairment reflecting a relatively late stage in functional decline. Similarly, the NIA/Alzheimer's Association workgroup [7] noted the need to develop measures of very early functional changes (e.g., social interaction). The preclinical Alzheimer's disease stage is important for studies aimed at prevention of progression to the clinical state [8]. Detecting functional decrements at earlier stages of dementia may serve to improve risk assessment and widen the window of interventions or care planning; early intervention efforts may enable the use of treatments that are not effective at more severe levels of impairment, thus preventing or slowing progression [9].

Promising measures for functional assessment at very early stages of cognitive impairment include performance-based and observed IADL, e.g., medication [10] or financial management tasks [11]. Inquiries into compensatory strategies relating to IADL performance may also serve to improve sensitivity [12]. Additionally, extended activities of daily living (ADL) [13] and advanced or complex ADL [14, 15] have been proposed in an effort to broaden the range of functional assessment. Early proponents of incorporating advanced ADL into the assessment process considered the following tasks: visiting relatives or friends, participating in community activities, and taking care of other people [14], as well as reading newspapers or books, writing letters, going out socially, and managing a garden [15]. An example of a more contemporary effort to increase the complexity of functional status assessment is the addition of technology use among older adults [16]. Advanced ADL are volitional, with less automated skills and increased potential for "effortful processing," which requires greater attentional resources. Advanced ADL have been shown to predict incident dementia [17] and to differentiate between patients with mild cognitive impairment (MCI) and cognitively healthy subjects [18]. Doi et al. [18] demonstrated that using IADL assessment alone resulted in 87–94% of MCI subjects presenting with no detectable functional impairment, and more noteworthy, for those who exhibited functional impairment on IADL (after adjustments), this did not significantly differ from healthy subjects. In contrast to IADL (e.g., "organization" difficulty in personal finance, housework, meal preparation), advanced ADL were shown to better differentiate between severity of cognitive impairment to normal, single-domain amnestic MCI, multi-domain amnestic MCI, and Alzheimer's disease [19]. Furthermore, correlations between neuropsychological test performance on IADL can be relatively modest [20]. Perhaps not surprising, advanced ADL have been shown to exhibit stronger relationships with neuropsychological measures [21].

The aim of this paper was to examine the utility of an IADL-extended (IADL-x) instrument, which incorporates advanced or complex ADL into the more common IADL assessment. Here we consider the less common range of functional assessment, namely cognitively normal to MCI.

Table 1. Demographics/health status, incident MCI versus normal

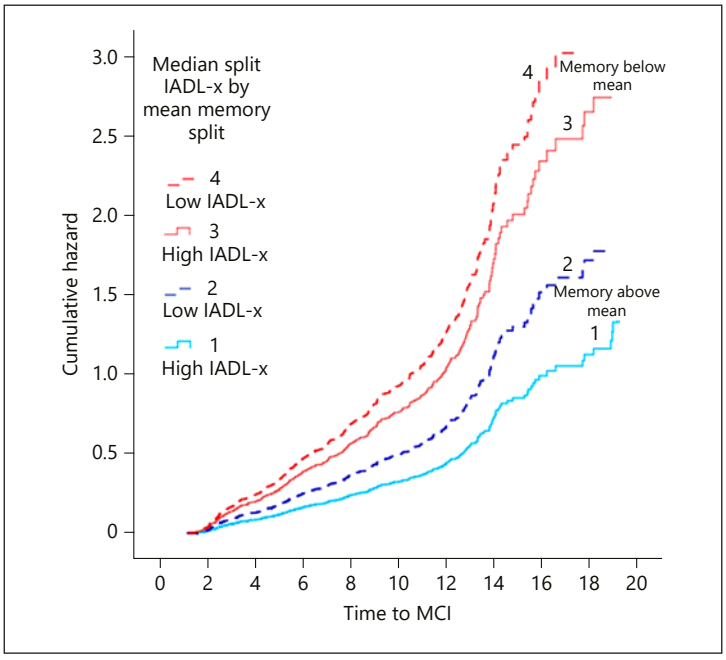
Demographics	Incident MCI	Normal	*p* value
Number of subjects	618	1,853	
Age, years (mean ± SD)	76.5±6.1	76.1±6.4	–
Education, years (mean ± SD)	9.9±4.8	10.5±4.7	<0.05
Race, white versus minority	73%	72%	–
IADL-x (mean ± SD)	5.8±1.7	5.9±1.8	–
Memory composite (mean ± SD)	0.24±0.62	0.45±0.64	<0.05
Female sex	71%	66%	<0.05
High occupation	18%	26%	<0.01
Stroke	21%	13%	<0.01
Hypertension	87%	77%	<0.01
Heart disease	46%	37%	<0.05
Heart failure	14%	12%	–
Diabetes	17%	19%	–
Depression	17%	18%	–

Occupation: low = housewife, unskilled or semiskilled, skilled trade, or craft, clerical, or office work; high = business/government manager, professional. IADL-x, instrumental activities of daily living-extended; MCI, mild cognitive impairment.

Methods

We examined cognitive impairment and functional status in the Washington Heights/Hamilton Heights Inwood Columbia Aging Project (WHICAP) cohort (community-dwelling sample), for subjects free of cognitive impairment at baseline (n = 2,471) who regressed toward MCI (n = 618). The average age of the sample at baseline was 76.2 years (SD = 6.3), and the mean duration of education was 10.4 years (SD = 4.7, median = 12). Additional demographic information is presented in Table 1. The average follow-up period was 5.1 years (SD = 2.4) and the median number of visits was 3. The average time between assessments was 2.2 years (SD = 1.0). The subjects were Medicare beneficiaries living within three adjoining census tracts in the northern Manhattan (New York City) communities of WHICAP. The sample included individuals from several countries of origin and three broadly defined ethnic categories: Caribbean Hispanic, black, and non-Hispanic white of European ancestry. The study included longitudinal data from two separate recruitment periods: 1992 and 1999. Follow-ups were ongoing and occurred at intervals of 18–24 months.

To assess functional status, we used an IADL-x scale. Details concerning construct validity, using the WHICAP sample, have previously been reported [21, 22]. Validation of this scale supported a continuum of function from traditional IADL tasks (e.g., medication management) to advanced ADL (e.g., volunteer work). Briefly, we employed item response theory (IRT) Mokken scaling [23] to establish monotone homogeneity (i.e., unidimensionality, local independence, and monotonicity). A final, rather stringent IRT assumption (double monotonicity) was employed to confirm a formal hierarchy of task difficulty. This resulted in the final 9-item ADL-extended scale meeting the IRT assumptions of unidimensionality, local independence, and double monotonicity, with a sufficient Mokken rho coefficient (comparable to Cronbach's alpha) of 0.73. Altogether, there were nine functional tasks assessed that were summed to derive a total IADL-x score. The items, in order of difficulty, include (1) taking classes, (2) volunteer work, (3) attending clubs, (4) going to the movies/restaurants/sporting events, (5) visiting friend or relatives, (6) shopping, (7) light housework, (8) finding one's way around the neighborhood, and (9) medication management. Response options were binary (yes/no) in terms of difficulty. The diagnosis of MCI was made retrospectively according to standard criteria [24]. Specifically, the MCI classification required: (1) memory complaint: endorsement of one or more of 11 items assessing perceived difficulty with memory on the Disability and Functional Limitations Scale and the Blessed Functional Activities Scale; (2) objective impairment in at least one cognitive domain: average score on neuropsychological measures within a domain 1.5 SD below normative level based on age, sex, race/ethnicity, and education; (3) essentially preserved ADL: endorsement by the patient or his/her



Color version available online

Fig. 1. Cox regression and incident MCI. Cumulative hazard of MCI, which contrasts IADL-x baseline status by memory performance. Low IADL-x is depicted with the dashed lines, composed of all IADL tasks, with one transitional advanced ADL "visit others." The solid curves represent high IADL-x "classes," "volunteering," "clubs," "movies/sporting events." ADL, activity of daily living; IADL, instrumental activities of daily living; IADL-x, instrumental activities of daily living-extended; MCI, mild cognitive impairment.

caregivers of two or fewer items from the Disability and Functional Limitations Scale assessing IADL; and (4) no consensus diagnosis of dementia.

We employed Cox regression to calculate the crude and adjusted HR of MCI in the WHICAP cohort according to continuous IADL-x scores. We also examined, using multinomial ordinal regression, the odds of "time to MCI" for only those subjects with confirmed MCI, thus bypassing data censoring (dead/lost to follow-up; n = 1,226).

Results

The mean IADL-x performance was 5.8, with a maximum value of 9 (higher scores equal more participation). The median value was 6, with an interquartile range of 2. A total of 21 subjects presented with incomplete IADL-x data and were removed from analysis. The mean values for each item were (i.e., frequency of endorsing tasks): (1) taking classes = 0.31, (2) volunteer work = 0.36, (3) attending clubs = 0.39, (4) going to the movies/restaurants/sporting events = 0.58, (5) visiting friend or relatives = 0.63, (6) shopping = 0.76, (7) light housework = 0.86, (8) finding one's way around the neighborhood = 0.94, and (9) medication management = 0.94. The most difficult task was "taking classes," with only 31% of the sample endorsing participation, and the least difficult task was "taking medication," with 94% of subjects endorsing no difficulty. During the course of the study, 618 subjects developed MCI. The Cox HR indicated that for each additional activity (total of 9 tasks) endorsed, the HR of MCI decreased by 10% (HR 0.90, 95% CI 0.85–0.94, $p < 0.001$). The fully adjusted model (gender, disease status, baseline memory performance, age, education, ethnic group, depression, and occupation), reduced the effect to 6% for each additional activity endorsed (HR 0.94, 95% CI 0.89–0.98, $p = 0.01$).

Figure 1 depicts the cumulative hazard of MCI for 2,471 subjects. The figure contrasts high and low IADL-x baseline status in participants with either high or low memory performance at baseline.

The reference group for all analyses were participants presenting with memory performance above the mean and an IADL-x score above the median. For those subjects below the mean memory performance and those who fell below the median IADL-x score, there was nearly three times greater odds of developing MCI (OR 2.9, 95% CI 4.5–1.63, $p < 0.001$). Participants with memory performance above the mean (well beyond the clinical criterion of 1.5 SD) and those who fell below the median IADL-x score demonstrated 50% greater odds of MCI (OR 1.53, 95% CI 2.4–1.10, $p < 0.01$).

Confirmed MCI

Limiting the analysis to participants who developed MCI ($n = 618$; thus excluding censored data relating to death or loss to follow-up), using "time to MCI" as the outcome in linear regression, we observed that baseline IADL-x score and baseline memory performance presented with the largest effect sizes in predicting time to MCI: Cohen's $d = 0.41$ and 0.49, respectively. In the fully adjusted model, both variables remained significant at $p < 0.001$.

Using multinomial logistic regression (reference group: avoiding MCI for a decade or more), we observed that, for subjects falling below the median of six IADL-x activities, the odds of developing MCI within 2 years of baseline assessment was more than 2.5 times higher (OR 2.60, 95% CI 1.52–4.4, $p < 0.001$), and nearly 2 times higher for developing MCI within the next 5 years (OR 1.93, 95% CI 1.76–3.2, $p < 0.01$). This relatively small reduction in the effect sizes for the odds of conversion to MCI from 2 to 5 years appears to be in the appropriate direction, indicating that assessment of risk is diminished the further a subject is from baseline status.

Discussion

These findings contribute to the identification of very early functional impairment in those at risk of cognitive impairment. The functional scale employed in this report proved sensitive to incident MCI, despite 91% of the total sample being free of any IADL difficulty at baseline; in a sample of subjects free of cognitive impairment at baseline, the HR of MCI decreased by 10% (HR 0.90, 95% CI 0.85–0.94, $p < 0.001$) for each additional activity endorsed. Detecting functional decrements at earlier stages may serve to improve risk assessment and widen the window of interventions or care planning. The functional hierarchy, advanced/complex ADL to IADL, examined in this report appears to be a valid tool for assessing the risk of development of cognitive impairment.

In the most recent criteria for prodromal AD proposed by the National Institute on Aging-Alzheimer's Association workgroups, it is recognized that individuals with MCI "commonly have mild problems performing complex functional tasks" [25, p. 271]. Examining cognitive IADL (e.g., financial management) measures represents a valid approach to targeting early functional change in the course of dementia. For example, Pérès et al. [4] found that IADL difficulty could be detected in incident dementia cases 10 years prior to diagnosis. However, 65% of the 104 subjects who developed dementia did not present with difficulty at baseline, and an additional 17% presented with minor difficulties that did not translate into risk 10 years later. Thus, risk in terms of function could not be evaluated for a large majority of subjects. This is a problem relating to content validity and a restriction in the measurement of functional status. In a review by Sikkes et al. [26], it was concluded that the psychometric properties of the commonly used IADL questionnaires either were unavailable or did not meet the standards of quality, citing large ceiling effects as one important example (content validity). A recent article reinforces this concern by asserting that currently available functional instruments "are capable of detecting functional impairment in the MCI and AD stages, few of them capture the earliest functional deficits seen in preclinical AD" [27, p. 859].

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Limitations

In its current format, this IADL-x scale is relatively crude (see online supplementary material for how increased response options may improve reliability and validity; for online supplementary material, see www.karger.com/doi/10.1159/000487632). The response options are a dichotomous yes/no format, which reduces the amount of information to be obtained from each subject. A revised scale would include a polytomous five-category response option.

It could be argued that advanced ADL are not a feature of disability, as they are nonessential functions, and thus should not be incorporated into the assessment of disability. We acknowledge this position, particularly as it relates to assessment at a single time point. However, when considering longitudinal trajectories and risk assessment, a functional continuum appears valid.

While the advanced social and cognitive leisure ADL are nonessential functions, they have previously been conceptualized as a dimension of disability, for example in the Nagi Disablement Model (elaborated on by Verbrugge and Jette [28]). These authors operationalized disability as a broad range of role behaviors that are relevant in most people's daily lives. Five commonly applied dimensions of disability evolved from this line of scientific inquiry: (1) basic ADL (e.g., basic personal care), (2) IADL (e.g., preparing meals and shopping), (3) paid and unpaid role activities (occupation and parenting), (4) social activities (attending clubs), and (5) leisure activities (attending museums and reading). This highly cited conceptualization of disability highlights the varied nature of role task behavior from basic ADL to advanced or complex social activities, work, and leisure activities.

Conclusion

A recent review of prodromal dementia indicated that functional decline, like cognitive decline, exists on a continuum from normal aging to dementia onset and is readily apparent by the MCI stage [6]. The IADL-x scale examined in this paper appears novel in its attempt to establish a functional continuum from a psychometric standpoint, targeting the early prodromal range of dementia and beyond. Including an IADL-x approach into dementia research may prove fruitful in several ways: (1) the establishment of a functional continuum; (2) a small number of findings suggest the possibility of bolstering daily functioning in MCI [6]; thus, observing the transition from the successful maintenance of advanced ADL to subtle IADL impairment (i.e., functional decrements at earlier stages) is likely to increase the window for the successful implementation of such interventions; (3) reduction of large ceiling effects observed in traditional IADL; (4) an additional metric for previously proposed multimodal functional assessment strategy; (5) as compared to IADL, higher correlations with neuropsychological tests; and (6) a low-burden, cost-effective screening tool which makes repeated assessments quite reasonable.

Statement of Ethics

All of the participants signed informed consent prior to inclusion in the study. This study was approved by the Ethical and Scientific Committee of the Columbia University Medical Center.

Disclosure Statement

The authors have no conflicts of interest to report.

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