Cognitive Domains and Trajectories of Functional Independence in Nondemented Elderly Persons

Hiroko H. Dodge, Yangchun Du, Judith A. Saxton, and Mary Ganguli

1Department of Public Health, Oregon State University, Corvallis.
2Department of Epidemiology, University of Pittsburgh Graduate School of Public Health, Pennsylvania.
3Department of Biostatistics, Boston University School of Public Health, Massachusetts.
4Department of Neurology and 5Psychiatry, University of Pittsburgh School of Medicine, Pennsylvania.

Background. Cognitive impairment in general is known to predict functional disability, but it is not clear whether performance on specific cognitive domains predicts future disability trends among nondemented elderly persons.

Methods. In a representative elderly community-based cohort over up to 10 years of follow-up, we examined predictors of longitudinal trajectories in ability to perform Instrumental Activities of Daily Living (IADL) among nondemented elderly persons. We used trajectory analyses to identify homogeneous groups with respect to trends over time in the numbers of IADL disabilities and their association with baseline demographics, social engagement, depression, physical well-being, and general and domain-specific cognitive functions. We excluded from these analyses those individuals found to have dementia at baseline or at any time during follow-up.

Results. Trajectory analysis revealed three homogeneous latent groups which we characterized as No Decline (no decline in abilities to perform IADL tasks over the course of study), Moderate Decline (some functional decline), and Sharp Decline (steep functional decline followed by death). Compared to the Sharp Decline group, the No Decline group was associated with higher baseline functions in all cognitive domains, and the Moderate Decline group was associated with higher baseline functions in all cognitive domains except psychomotor speed and naming. The Moderate and No Decline groups did not differ on any cognitive measure.

Conclusion. Among community dwelling elderly persons who remained free from dementia throughout the study, poorer scores in all cognitive domains predicted sharp functional decline followed by death.

Cognitive impairment and dementia are strong predictors of incident disability (e.g., 1–3). It is unclear, however, which (if any) specific domains of cognitive functions are particularly important in predicting future disability trends. Thus far, studies focusing on multiple domains of cognition and disabilities in nonclinical samples have been cross-sectional in design (4–6), and longitudinal studies have been limited to the examination of a single cognitive domain (executive function) (7,8). Our main aim in this longitudinal study is to examine whether specific cognitive domains predict trajectories of disability in Instrumental Activities of Daily Living (IADL) among nondemented elderly persons, after controlling for known confounders including physical and psychological well-being, social engagement, and demographic factors. We identified latent groups (9) whose 8-year longitudinal trajectories varied in total numbers of IADL disabilities, and examined multiple cognitive functions as predictive factors for these trajectories.

Methods

The data reported here were collected as part of the Monongahela Valley Independent Elders Survey (MoVIES Project), a prospective epidemiological study of dementia in a largely rural, blue-collar community in Southwestern Pennsylvania. The background, cohort, and methods of the study have been reported in greater detail earlier (10,11). Briefly, 1422 individuals 65 years old or older living in the community were recruited by age-stratified random sampling of voter registration and other lists for the selected area, with a further 259 volunteers included from the same area at study entry (1987–1989). Surviving and consenting participants were reassessed in a series of biennial “waves” until 2002. The most frequent reason for attrition between successive waves was death (9%–14%), with less attrition for other reasons such as dropout and relocation (average 2.8%).

Data on several variables including IADL were first collected at Wave 2 (1989–1991), which therefore served as the baseline for the current analyses. The cohort at Wave 2 (baseline) consisted of 1341 adults, aged ≥66 years (mean 74.9 years, standard deviation [SD] = 5.5). We excluded 122 prevalent cases of dementia (defined later) at baseline. To minimize the potential for undetected subclinical dementia to influence the results, we also excluded 253 incident cases identified during follow-up. After excluding 13 individuals (1.4%) with missing data, the remaining 953 participants served as the basis of the current report. Informed consent was obtained according to procedures approved annually by the University of Pittsburgh Institutional Review Board.

Dementia Assessment

Diagnosis of dementia was based on a multistage case-ascertainment process. At baseline and each follow-up, all participants were screened with a cognitive test battery (described later in this article), incorporating the...
neuropsychological panel of the Consortium to Establish a Registry for Alzheimer Disease (CERAD) (12). Clinical (diagnostic) assessment, blind to the screening data, was offered to all participants who met operational definitions for “cognitive impairment” at any wave, and for “cognitive decline” between waves, and was also offered to a matched sample of “unimpaired” controls selected at baseline (11,13). Clinical assessment followed a standardized protocol to determine the presence or absence of dementia, according to the Diagnostic and Statistical Manual of Mental Disorders, Third Revision (DSM-III-R) (14), and stage of dementia, according to the Clinical Dementia Rating (CDR) (15) on which a rating of 0 indicates no dementia and ratings of $\geq 0.5$ reflect increasing severity of dementia. For the present analyses, prevalent and incident dementia cases (CDR $\geq 0.5$) any time during follow-up were excluded.

**Outcome Variables**

IADL was assessed using the Older Americans Resources and Services questionnaire (16), which asks about ability to perform seven activities: using the telephone, getting to places out of walking distance, shopping for groceries (assuming participant has transportation), preparing meals, doing housework, taking medications, and handling money. For each IADL item, participants were regarded as having disability if they were reported as requiring help or being completely unable to perform the task independently.

Information was obtained by self-report from study participants except when they could not answer the questions or could not understand the questions. Under these circumstances, informants were asked about the participants’ ability. In the present cohort, restricted to participants free from dementia throughout the study, only 8 of 953 participants had one or more IADL questions answered by their informants throughout the entire study follow-up. We reran models excluding these 8 participants and obtained virtually identical results. Therefore, we report the results including these 8 participants.

We summed the IADL disability items for which participants needed either partial or complete help; this summing yielded a scoring range of 0 (can do all tasks independently) to 7 (disabled in all tasks). We added a score of 8 to represent mortality during follow-up, thus extending the IADL scoring range from 0 through 8. Because we know that functional disability is the most powerful predictor of mortality besides age [e.g., (17)], we conceptualized disability as being on a continuum that ends with death. Rather than exclude participants who died during follow-up (which would have skewed the sample towards the less disabled), we treated mortality as if it were an additional, most severe level of disability. Alternatively, to examine the influence of death on disability trajectories and their associations with covariates, we also ran models excluding those who died during follow-up.

**Explanatory Variables**

Demographic variables included age at baseline, sex, education (less than high school education vs high school or more education), and recruitment status (random vs volunteer sample). Cognitive function tests included the Mini-Mental State Examination (MMSE) (18), Trail Making Tests A and B (19), Consortium to Establish a Registry for Alzheimer’s Disease (CERAD) 10-word Word List Learning and Delayed Recall (13), Story Immediate Retell and Delayed Recall (20), Initial Letter (P and S) and Category (Fruits and Animals) Fluency (21), 15-item CERAD version of the Boston Naming Test (12,22), CERAD Constructional Praxis (23), and Clock Drawing (24).

Some cognitive domains were assessed using composite scores, grouping selected tests together on conceptual grounds as well as on previous factor analysis (25); other domains were assessed by a single test. Composites were created by first $z$-transforming each individual test score based on the distribution at baseline (Wave 2), and then combining and averaging $z$-transformed tests. In addition to global cognitive function (MMSE), the domains examined in this study were: 1) Learning (composite of Word List Learning test and Story Immediate Retell), 2) Recall (composite of Word List Delayed Recall and Story Delayed Recall), 3) Visuospatial (composite of Clock Drawing and CERAD Constructional Praxis), 4) Fluency (composite of Verbal Fluency for categories and initial letters), 5) Psychomotor Speed (Trail Making A Test alone; correct connections per second), 6) Executive function (Trail Making B Test alone; correct connections per second), and 7) Naming (Boston Naming Test alone).

Social engagement was assessed by response to a question asking how often the participant attended meetings or activities related to, e.g., churches, lodges, societies, or volunteer groups. The answers were coded as: 0, did not belong to any organizations; 1, $<1$/mo; 2, 1/mo; 3, 2–4/mo; 4, 2–6 d/wk; or 5, daily.

Depression was examined using the modified Center for Epidemiologic Studies-Depression Scale (mCES-D) (26,27), in which higher scores reflect more depressive symptoms. As previously reported (26), we used a threshold of $\geq 5$ symptoms (capturing the most depressed 10% of the sample at baseline) to indicate depression.

The total number of prescription medications which the participant reported taking regularly was used as an objective measure of overall morbidity and medical burden (28). Baseline disability (IADL score 0–7) at baseline was also included as a covariate to adjust for physical well-being.

**Statistical Methods**

Trajectory modeling is a latent class analysis which identifies homogeneous groups within a population assumed to contain different trajectories. To examine patterns (trajectories) of the numbers of IADL disabilities over time and death, the SAS procedure PROC TRAJ (9) (http://www.andrew.cmu.edu/user/bjones) was used. This procedure basically combines two separate statistical models and estimates their parameters simultaneously using maximum likelihood estimates. The first model builds trajectories for the different latent groups as a function of time from baseline. The second model builds a multinomial regression model that examines the associations of covariates with the probability of membership in the homogeneous latent
groups. Here, the trajectory of the total number of IADL disabilities and death over time, reported at Waves 2–6, was modeled by a censored normal distribution. Because the models use data collected over varying lengths of follow-up, participants who drop out over the course of follow-up do not need to be excluded. Covariates included in the models were described earlier.

The Bayesian Information Criteria (BIC) (29) were used to identify the optimal number of homogenous groups. Domain-specific cognitive scores were each included in a separate model along with the above-mentioned covariates.

RESULTS

The trajectory analysis identified three homogeneous groups as the best model based on the BIC (Figure 1). The procedure calculates the probability of each participant belonging to each trajectory and identifies a participant as belonging to one trajectory based on the largest probability. Figure 1 shows both actual trajectory (solid line; using exact probabilities of belonging to each trajectory for each participant) and estimated trajectory (dotted line; using the model-assigned group identification for each participant) including all covariates except domain-specific cognitive scores. Although the BIC varied slightly depending on the specific cognitive measure included in the model, the three-trajectory model always provided the best fit to the data, with trajectories virtually identical to those in Figure 1. Based on the shapes of IADL trajectories, we named them No Decline (group 1: stable at disability state), Moderate Decline (group 2: numbers of IADL disabilities increased somewhat over time), and Sharp Decline (group 3: number of IADL disabilities increased sharply followed by death).

In this community-dwelling cohort of 953 adults free of dementia, the majority entered the study with either no IADL disabilities (78.2%) or only one disability (14.1%). Table 1 shows the baseline characteristics of the overall cohort and of the three latent trajectory-defined groups described above.

Table 2 shows the association of the baseline cognitive score and other covariates with the three trajectories, using the Sharp Decline trajectory as a reference group. Each column of Table 2 represents the result of a model with all covariates including MMSE. The basic model (Model 1) includes no specific cognitive domains; Models 2–8 each include one of seven cognitive domains. As an example, a 1 SD increase in the Learning composite at baseline score is associated with a 95% increase in odds of being in the No Decline group (i.e., odds ratio [OR] = 1.95) and a 71% increase in odds of being in the Moderate Decline group (i.e., OR = 1.71), compared with the Sharp Decline group.

Compared with the Sharp Decline group, the No Decline group was associated with higher baseline scores on all cognitive domains as well as with fewer total prescription medications and higher frequency of social engagement, but not with depression. MMSE was not significant in any models.

Compared with the Sharp Decline group, the Moderate Decline group was associated with higher baseline scores on all cognitive domains except psychomotor speed and naming. Total prescription medications and higher frequency of social engagement were also significantly associated. Neither depression nor MMSE was significant.

We also examined the difference between the Moderate and the No Decline groups by making the reference group the No Decline Group. None of the cognitive functions distinguished the two trajectory groups, but number of...
prescription drugs was significantly associated with the Moderate Decline group. As a reference for interested clinician readers, Table 3 shows the actual mean (SD) baseline cognitive test scores for each of three trajectory groups and the overall sample.

**Effect of Death on the Association Between Trajectories and Covariates**

Table 4 shows the proportion of participants who died during the follow-up among each of the three trajectories and follow-up waves during which the death occurred. Only one participant died among the No Decline group. Death occurred during later waves (3rd and 4th follow-up) among the Moderate Decline group, whereas it occurred during earlier waves (1st through 3rd follow-up) among the Sharp Decline Group.

Figure 2 shows the IADL trajectories after excluding participants who died during follow-up from the sample. The three-trajectory model was still found to be the best model. However, none of the cognitive functions distinguished the trajectory groups; the total numbers of prescription medications and social engagement remained significant as previously found.

In post hoc analyses we repeated the analyses limiting them to participants free from any disabilities at baseline. The results remained the same comparing the No Decline and Sharp Decline groups, except social engagement was no longer significant. In the comparison of the Moderate Decline and Sharp Decline groups, visuospatial composite, psychomotor speed, executive function, and naming were all nonsignificant. The total number of prescription medications remained significant, but, as with the No Decline group, social engagement no longer distinguished the Moderate Decline group from the Sharp Decline group.

In post hoc cross-sectional analysis, executive function, indicated by Trails B, was the only significant variable (OR = 0.28; 95% confidence interval, 0.10–0.79) in the model where the outcome was disability in 3 or more IADL tasks. However, in the model where the outcome was disability in 2 or more IADL tasks, none of the cognitive domains was significant.

**Discussion**

In this 10-year study of a community-based aging cohort free from dementia, all cognitive domains assessed at baseline predicted subsequent trajectories of functional decline. Previous cross-sectional studies of cognitive and functional ability have shown strong associations between executive function and ability to perform IADLs (4–6,30,31), as did our own post hoc cross-sectional analysis restricting the definition of disability to ≥3 IADLs. Our longitudinal analyses, however, showed that the group that experienced virtually no functional decline over the next 8 years had subtle yet significantly higher functioning in all cognitive domains at baseline, even after controlling for demographics, baseline IADL status, depression, general morbidity, and social engagement. The group which declined moderately over 8 years also had higher baseline cognitive functions, compared with the sharply declining group, in all domains except psychomotor speed and naming. However, these significant associations between cognitive functions and IADL trajectories disappeared after excluding participants who died during follow-up, suggesting that the IADL decline associated with cognition largely represented the declines experienced by participants who died during follow-up. Furthermore, among Moderate Decliners, death occurred mostly during later follow-up waves whereas, among the Sharp Decliners, death occurred during earlier follow-up waves. Thus, potentially, longer follow-up of the Moderate Decline group might reveal an eventual steep decline similar to that reported here for the
study’s 8-year duration, it seems unlikely that the link
cognitive functions were so significant in distinguishing the
among nondemented elderly persons, disability trajectories
in cognitive function occurs 6 years (32) or even more than
the literature on the terminal decline showing that a decline
Sharp Decline group. This finding is in line with the bulk of
the literature evidence that cognitive decline precedes
onset of clinical symptoms of dementia by years (33). It is
remarkable that even among nondemented elderly persons, disability trajectories
differed in relation to distance to death, and that baseline
cognitive functions were so significant in distinguishing the
disability trajectories. As our cohort was restricted to elderly
persons who remained free from dementia throughout the
study’s 8-year duration, it seems unlikely that the link
between cognition and disability trajectory was mediated by
a dementing disorder. However, it is possible that some
participants had subclinical dementia for longer than our
study duration.

According to Salthouse’s processing-speed theory (34),
cognitive performance is degraded when processing is slow
because the products of early processing may no longer be
available when later processing is complete (i.e., relevant
operations cannot be successfully executed). Thus, variability
in processing speed leads to age-related variance
observed across various cognitive domains. Our aim in this
study was to find the cognitive domains predictive of future

### Table 2. Results of Trajectory Model, Adjusting for Age, Sex, Education, Recruitment Status, and Numbers of IADL Disabilities at Baseline: Odds Ratio and 95% Confidence Interval

<table>
<thead>
<tr>
<th>Baseline Characteristics</th>
<th>No Decliner (Group 1) Compared to Sharp Decliner (Group 3)</th>
<th>Moderate Decliner (Group 2) Compared to Sharp Decliner (Group 3)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Model 1</td>
<td>Model 2</td>
</tr>
<tr>
<td>Total No. of Rx meds</td>
<td>0.67</td>
<td>0.67</td>
</tr>
<tr>
<td></td>
<td>(0.60–0.75)*</td>
<td>(0.60–0.75)*</td>
</tr>
<tr>
<td>Depression</td>
<td>0.8</td>
<td>0.90</td>
</tr>
<tr>
<td></td>
<td>(0.35–1.83)</td>
<td>(0.39–2.09)</td>
</tr>
<tr>
<td>Frequency of social engagement</td>
<td>1.26</td>
<td>1.26</td>
</tr>
<tr>
<td></td>
<td>(1.09–1.46)</td>
<td>(1.09–1.46)</td>
</tr>
<tr>
<td>MMSE</td>
<td>1.44</td>
<td>1.28</td>
</tr>
<tr>
<td></td>
<td>(0.99–2.09)</td>
<td>(0.87–1.89)</td>
</tr>
<tr>
<td>Learning/Immediate recall composite</td>
<td>1.95</td>
<td>—</td>
</tr>
<tr>
<td>Memory/delayed recall composite</td>
<td>1.59</td>
<td>—</td>
</tr>
<tr>
<td>Verbal fluency composite</td>
<td>1.70</td>
<td>—</td>
</tr>
<tr>
<td>Visuospatial composite</td>
<td>1.65</td>
<td>—</td>
</tr>
<tr>
<td>Motor speed</td>
<td>1.46</td>
<td>—</td>
</tr>
<tr>
<td>Executive function</td>
<td>1.53</td>
<td>—</td>
</tr>
<tr>
<td>Naming</td>
<td>1.50</td>
<td>—</td>
</tr>
</tbody>
</table>

**Notes:** *p < .001; †p < .01; ‡p < .05.

IADL = Instrumental Activities of Daily Living; MMSE = Mini-Mental State Examination; BIC = Bayesian Information Criteria.
disability trajectories, rather than to identify a hierarchy of declines among cognitive domains. Possibly, the Moderate Decline group at baseline was already starting to show evidence of “normal aging” to be followed by gradual IADL decline until death, with psychomotor speed and word retrieval being the domains to deteriorate the earliest.

Additionally, past research has shown that gait velocity is a strong predictor of adverse events (35) and slowing gait is an indicator of subclinical diseases and frailty (36,37). Although gait velocity involves more than psychomotor speed, the slowing in fine motor movements required for Trails A in our study might be a harbinger of slowing of gross motor movements and gait, which in turn might suggest the presence of disease, gradual disability, and death.

Social engagement, the extent to which individuals engage with their social environments, has previously been found to be associated with better physical health (38) and to predict fewer disabilities (39) and less cognitive decline (40) over time. Although our measurement of social engagement was limited in nature, it significantly distinguished the No Decline and Moderate Decline groups from the Sharp Decline group. However, it lost its ability to predict disability when we restricted the sample to participants with no baseline IADL disabilities. Our measure of social engagement might be as much a consequence of existing disability as it was a predictor of future disability.

Our data are based on the relatively rural and largely white communities of Southwestern Pennsylvania and may not generalize to other populations. Using the total number of IADL tasks which participants cannot perform by themselves ignores the qualitative differences involved in IADL tasks. Despite our relatively large sample size, we could not disaggregate participants by specific combinations of disabled IADL.

Conclusion

We have found that, among the elderly participants free from dementia throughout the study, specific (but not general) cognitive domains were important in predicting future disability pathways followed by death. Future studies should examine the mechanisms underlying the observed associations of cognitive domains, disabilities, and death. In the

<table>
<thead>
<tr>
<th>Trajectory Groups</th>
<th>Participants Who Died N (%)</th>
<th>Mean Duration to Death (Among Participants Who Died) (Years (SD))</th>
</tr>
</thead>
<tbody>
<tr>
<td>No Decline</td>
<td>1 (0.31)</td>
<td>8.22 (NA)</td>
</tr>
<tr>
<td>Moderate Decline</td>
<td>135 (41.8)</td>
<td>7.69 (1.20)</td>
</tr>
<tr>
<td>Sharp Decline</td>
<td>187 (57.9)</td>
<td>3.53 (1.58)</td>
</tr>
</tbody>
</table>

Note: SD = standard deviation; NA = not applicable.
meantime, clinicians may find cognitive assessments useful in anticipating their patients’ functional declines over time.

ACKNOWLEDGMENTS

This work was supported by K01AG023014, R01AG07562, and K24AG023014 from the National Institute on Aging. We thank Dr. Gerda Fillenbaum at Duke University for her helpful suggestions.

Address correspondence to Hiroko Dodge, PhD, 304 Waldo Hall, Department of Public Health, Oregon State University, Corvallis, OR 97331. E-mail: dodge@oregonstate.edu

REFERENCES


