Declining Executive Control in Normal Aging Predicts Change in Functional Status: The Freedom House Study

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OBJECTIVES: To assess the contribution of executive control function (ECF) to functional status.

DESIGN: Three-year longitudinal cohort study.

SETTING: A comprehensive-care retirement community.

PARTICIPANTS: Five hundred forty-seven noninstitutionalized septuagenarians.

MEASUREMENTS: The Mini-Mental State Examination (MMSE) and Executive Interview (EXIT25). Functional status was assessed using instrumental activities of daily living (IADLs). Latent growth curves of MMSE, EXIT25, and IADL were modeled. The rate of change in IADLs (ΔIADL), adjusted for baseline IADLs and cognition, was regressed on the rate of change in each cognitive measure (adjusted for baseline cognition). Models were also adjusted for baseline age, level of care, and comorbid illnesses.

RESULTS: Baseline test scores were within normal ranges, but mean EXIT25 scores reached the impaired range by the second follow-up. There was significant variability around the baseline means and slopes for all variables. The rate of change in EXIT25 was strongly correlated with ΔIADL (r = −0.57, P < .001). This remained significant after adjusting for baseline EXIT25 scores, IADLs, age, comorbid disease, and level of care. The effect of the EXIT25 on ΔIADL was stronger than those of age, baseline IADLs, comorbid disease, or level of care. The rate of change in MMSE scores was not significantly associated with ΔIADL.

CONCLUSION: ECF is a significant and independent correlate of functional status in normal aging. Traditional dementia case finding is likely to underestimate cognition-related disability. Neither a normal baseline MMSE score nor stable MMSE scores over time preclude functionally significant changes in ECF. J Am Geriatr Soc 52:346–352, 2004.

Key words: aging; disability; assessment; longitudinal; executive function

Age-related decline in executive control functions (ECFs) is one plausible explanation for the decline in functional status that accompanies old age. Executive functions are cognitive processes that orchestrate complex, goal-directed activities.1 The latter include functional activities such as cooking, dressing, and housework.

Traditionally, ECF has been associated with the prefrontal cortex, but it is also dependent on the integrity of frontal-subcortical systems.2 Thus, frontal lesions are sufficient, but not necessary, for ECF impairment. This greatly broadens the differential of conditions that affect executive control. ECF impairment has been associated with conditions as diverse as major depression, subcortical vascular disease, adult-onset diabetes mellitus, Alzheimer’s disease (AD), and even normal aging.3

The natural history of ECF during normal aging cannot be easily derived from the existing literature because familiar screening measures such as the Mini-Mental State Examination (MMSE)4,5 or its derivatives do not detect it well. The American Psychiatric Association added ECF impairment to its definition of dementia in 1994.6 Nonetheless, epidemiological studies seldom incorporate ECF measures into their case definitions. Moreover, many epidemiological studies are cross-sectional in nature. The conclusions about age-related cognitive decline that can be validly drawn from cross-sectional models may be severely limited.7

The authors have been studying longitudinal changes in ECF in residents of continuing-care retirement communities (CCRCs). CCRCs provide longitudinal access to large, stable elderly populations receiving care across a wide range of services. The Freedom House Study (FHS) examines the incidence of ECF impairment within a single CCRC, the Air Force Villages (AFV). This FHS report investigates the longitudinal effects of emergent cognitive impairment on functional status using two measures: the MMSE, a familiar measure of “global” cognitive ability, and the Executive

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Interview (EXIT25), a measure specifically designed to assess ECF.

METHODS

Participants

Five hundred forty-seven elderly retirees were recruited from a randomly ordered list of AFV residents aged 70 and older living at noninstitutionalized levels of care; these included garden apartments and congregate high-rises. Garden apartments were considered the lowest level of care. Each is a standard duplex apartment with a full kitchen/laundry, standard bath, and attached parking space. There is no special handicap access. In contrast, high-rise residents eat in common. There is handicap access and handicap-adapted bathroom facilities. Light housecleaning and laundry services are provided. Limited outpatient medical care, including medication supervision, is available on site. All AFV residents benefit from on-campus security and restricted public access.

The FHS subjects represented 57.3% of potentially eligible participants and did not differ significantly from nonrecruited residents with regard to age, sex, or baseline level of care. Informed consent was obtained before their evaluations. The University of Texas Health Science Center at San Antonio’s institutional review board approved this protocol.

Participants were evaluated at three separate points over 3 years (mean interval ± standard deviation = 18.2 ± 3.6 months). As functional status declined over time, frail subjects were interviewed in their own residences. collateral informants were used when available.

The attrition rate across the first two waves was 10.2% cases/y (4.0% to death, 5.5% to refusal, and 0.4% untestable at follow-up), but unforeseen budget restrictions limited Wave 3 data collection to a subset of the surviving cohort (n = 137 (25.0%)). These represented the surviving fraction (71.0%) of 193 FHS subjects who were randomly selected at baseline to receive a detailed formal neuropsychological test battery. Thus, the attrition was unrelated to clinical condition and should satisfy the “missing at random” constraint on the analyses (see below).

Clinical Variables

Functional status and comorbid medical conditions were assessed using the Older Adults Resources Scale (OARS). The OARS is a structured clinical interview that provides self-reported information on activities of daily living (ADLs), instrumental activities of daily living (IADLs), health history, healthcare usage, and current medications. The OARS IADL scale is scored inversely relative to disability, with lower scores indicating higher levels of disability. ADL and IADL are often highly skewed. Summing them into a single disability index following the method of a reported study can ameliorate this, but this did not appreciably affect the results, because ADLs had little variance in this sample. Moreover, IADL performance is more transparent than a combined disability index. Thus, only IADL data are reported here. The number of self-reported medical conditions was summed to create a proxy for comorbid disease.

Depressive symptoms were assessed using the short Geriatric Depression Scale (GDS). GDS scores range from 0 to 15. Higher scores are worse. A cutoff of 6 to 7 best discriminates clinically depressed from nondepressed elderly.

Predictor Variables

The Executive Interview

The Executive Interview (EXIT25) provides a standardized clinical ECF assessment. Items assess verbal fluency, design fluency, frontal release signs, motor/impulse control, imitation behavior, and other clinical signs associated with frontal system dysfunction. It takes 15 minutes and can be administered by nonmedical personnel. Interrater reliability is high (r = 0.90). It correlates well with other ECF measures including the Wisconsin Card Sorting Test (r = −0.54), Trail Making Part B (r = 0.64), Lezak’s Tinker Toy test (r = 0.57), and the Test of Sustained Attention (Time, r = 0.82; Errors, r = 0.83). EXIT25 scores range from 0 to 50. High scores indicate impairment. A score of 10 reflects the 5th percentile for young adults. Scores of 15 or higher suggest clinically significant ECF impairment.

The Mini-Mental State Examination

The Mini-Mental State Examination (MMSE) is a well-known and widely used test for screening cognitive impairment. Scores range from 0 to 30. A score of 28 is the median for normal octogenarians with more than 12 years of education. Scores below 24 reflect cognitive impairment. The MMSE has no items that are specifically addressed to ECF and may underestimate cognitive impairment in frontal system disorders. The MMSE was chosen for this study not only because it is a familiar and widely used measure, but also because it has been the starting point for many other widely used global cognitive measures, including those employed as dementia screening measures in epidemiological studies.

Analysis

Data in the third wave were available for approximately 30% of the eligible subjects. Rather than discarding information from the first two waves by limiting the analysis to cases with complete data, Full Information Maximum Likelihood (FIML) methods were used to address this problem. FIML uses the entire observed data matrix to estimate parameters with missing data. In contrast to list-wise or pair-wise deletion, FIML yields unbiased parameter estimates and preserves the overall power of the analysis. This analysis was performed using AMOS software (Small Waters Corp., Chicago, IL.).

FIML can accommodate significant data loss, provided the data are “missing at random.” Because the vast majority of missing data was from Wave 3, and because the subjects observed at Wave 3 represent the survivors from a random subset of the original sample, the missing data points should satisfy this constraint. As a test of this assumption, the baseline cross-sectional age, education, sex, EXIT25, GDS, and MMSE scores were examined for those with complete data at Wave 3 versus those lost to follow-up. Attrition had no significant effects on these variables (by analysis of variance: df (1), P = ns).
The survival rates (mean observation time = 60.9 ± 15.3 months) to the outcomes of death, next transition in level of care, and nursing home placement were also retrospectively tested for those with complete data versus those lost to follow-up at Wave 3. Attrition did not affect survival to any of these outcomes (by log rank test, all P = ns).

Latent-Growth-Curve Analysis

Data were submitted to latent-growth-curve (LGC) modeling. In contrast to multiwave auto-regressive models, which estimate interindividual rates of change across measurements, LGC models estimate the full trajectory of change across each individual’s measurement points.21 This is a well-documented strategy for assessing longitudinal rates of change in the elderly.22 The first and second factor loadings on the latent-growth parameter were fixed to 0 and 1, respectively. The last time-point loading was freely estimated from the data.

LGC Variables of Interest

To test the hypothesis that the rate of change in cognition is associated with the rate of change in disability, associative models were assembled in which two fully adjusted LGCs were estimated simultaneously. The latent growth variables (e.g., rate of change in IADLs (ΔIADL) and rate of change in the predictor measure) reflect the mean rates of change in functional status and cognition, respectively. The variances about these means are also of interest because they indicate whether there is heterogeneity among the individual growth curves within the sample. Significant variation in the rate of change in a latent growth variable indicates that there are statistically significant interindividual differences in the rates of change. Nonsignificant variation would indicate that all subjects were following the same change trajectory.

ΔIADL was regressed on the rate of change in each cognitive measure separately, while adjusting for baseline IADLs and baseline cognition. This association was further adjusted for baseline age, level of care, and comorbid illnesses. The covariances between the latent variables and covariates were also estimated.

Figure 1 depicts the final, fully adjusted model using the rate of change in EXIT25 scores (ΔEXIT25) to predict the rate of change in functional status. (The MMSE was tested separately in an identical model.) To the left are latent variables (IADL and EXIT25) representing the mean and variance of the observed data at baseline. To the right are the latent growth variables (ΔIADL and ΔEXIT25). A unidirectional arrow represents the association between ΔIADL and ΔEXIT25. This implies that the rate of change in ECF causes the rate of change in functional status, rather than vice versa.

Goodness of Fit

The fit of each individual growth model was compared with a competing model of “no growth.” The validity of structural models was assessed using three common test statistics. A nonsignificant chi-square signifies that the data are consistent with the model.23 A root mean square error of approximation (RMSEA) of 0.05 or less indicates a close fit to the data, with models up to 0.10 viewed as acceptable fit.24 The comparative fit index (CFI) compares the specified model with a model of no change.25 With values ranging between 0 and 1, values below 0.95 would suggest model misspecification. Values of 0.95 or greater indicate adequate to excellent fit. All three fit statistics should be simultaneously considered to assess the adequacy of the models to the data.

RESULTS

Cross-Sectional Analysis

Baseline EXIT25, MMSE, and GDS scores were within their normal ranges (Tables 1 and 2). The EXIT25 and MMSE were moderately inversely correlated (r = −0.36, P < .001), but the EXIT25 was more sensitive to the cognitive impairments in this sample. One hundred seventy-five participants (32.0%) failed the EXIT25 with a score of 15 or higher. In contrast, only n = 36 (6.6% of the sample) failed the MMSE with a score less than 24. One hundred forty-nine (85.1%) of those who failed the EXIT25 passed the MMSE. The mean GDS score was well below its clinical threshold. Only 12 individuals scored higher than 6 out of 15 on the GDS. Four hundred fifty-five (83.2%) subjects estimated their health as good or excellent.

Baseline EXIT25 and MMSE scores were significantly correlated with baseline functional status (IADLs scores) (EXIT25×IADL: r = −0.48, P < .001; MMSE×IADL: r = 0.50, P < .01). Both associations remained significant after adjusting for age, comorbid illness, and level of care (both P < .01).

Longitudinal Analysis

Table 2 shows the descriptive statistics for the EXIT25 and MMSE. The observed mean values for the EXIT25 increased (deteriorated). The means for the MMSE and IADLs showed small decreases (deterioration). Clinically significant ECF impairment (mean EXIT25 > 15/50) appeared by the second follow-up. In contrast, clinically
significant MMSE impairment (mean <24/30) never appeared during the 3 years of observation. Nonetheless, the sample as a whole suffered a slight decrease (deterioration) in mean IADL scores over the course of the study.

Tables 3 and 4 present adjusted LGC models of \( \Delta \)EXIT25, the rate of change in MMSE scores (\( \Delta \)MMSE), and \( \Delta \)IADL. The first row of Table 3 presents the fit estimates, and the second row presents the corresponding parameter estimates for three separate longitudinal growth curve models. Each model demonstrated acceptable to excellent fit to the data and was significantly different from a corresponding model of “no change.” Model loadings suggested a linear trend in EXIT25 scores, an accelerated trend in MMSE scores, and an approximate log or leveling trend in IADL ratings over time.

The mean baseline and rate-of-change estimates are shown at the bottom of the table. The average baseline scores estimated by the models were practically identical to the observed baseline values shown in Table 2. There was also significant variability around these means. Similarly, there was significant rate of change in all three variables and significant variation around their respective rates of change. EXIT25 averaged 0.89 per year. This can be interpreted as an average increase of 0.89 EXIT25 points per year of follow-up. The MMSE decreased 0.13 points per year. IADLs decreased (deteriorated) by 0.50 points per year.

Next, LGC models of change in the cognitive measures were regressed onto the LGC model of change in IADLs. Both models show acceptable to excellent fit (EXIT25: \( \chi^2 = 22.3, df = 14, P = .07, \text{CFI} = 0.999, \text{RMSEA} = 0.03; \) MMSE: \( \chi^2 = 11.9, df = 14, P = .62, \text{CFI} = 0.999, \text{RMSEA} <0.01 \)). \( \Delta \)EXIT25 scores were significantly associated with IADL (\( \beta = -0.36, \text{standard error (SE)} = 0.16, P<.001 \)). This association remained significant after adjusting for age, baseline comorbid disease, level of care, baseline disability, and baseline EXIT25 (\( \beta = -0.37, \text{SE} = 0.18, P<.001 \)). The relative effects of \( \Delta \)EXIT25 and its covariates on the rate of change in functional status can be estimated.
by examining their standardized coefficients in Figure 1. The effect of ΔEXIT25 on ΔIADL was stronger than that of age and more important than that of comorbid disease, baseline physical function, or level of care. In contrast, ΔMMSE was significantly associated with ΔIADL only in an unadjusted model (β = 2.33, SE = 1.05, P < .05).

To test the assumption of causality, ΔIADL was regressed on baseline EXIT25 (β = −0.04, SE = 0.006, P = .001) and ΔEXIT25 on baseline IADL (β = −0.24, SE = 0.15, P = .09) in separate post hoc models. The fact that the former model is significant, whereas the latter is not, is consistent with the hypothesized direction of causality (that ΔEXIT25 causes observed changes in disability).

DISCUSSION

A high prevalence of ECF impairment has previously been reported in affluent, well-educated, noninstitutionalized elderly retirees with normal MMSE scores. Moreover, in the AFV, the EXIT25 is a significant independent correlate of level of care. The current analysis goes beyond previous work to demonstrate that the deterioration in ECF during normal aging is also independently associated with longitudinal declines in functional status. In this study, the effect of EXIT25 on ΔIADL was the strongest of the variables modeled.

There are several potential limitations to the results. First, there was considerable loss of data in the third observation. This was due to administrative reasons, not simple attrition, and satisfies the “missing at random” constraint for valid FIML applications. As a check to these findings, ΔEXIT25 and ΔMMSE were also modeled as predictors of change in functional status under a variety of alternative conditions, including as a simple change score (IADL at T3 − IADL at T1) and cross-lag regression (IADL at T1 > IADL at T2 > IADL at T3). Each of these models was performed with FIML and case-wise deletion (data not shown). Under all four conditions, the ΔEXIT25 was a significant independent predictor of change in functional status; ΔMMSE was not. Although these results are qualitatively similar to those presented in this paper, the current model takes full advantage of the information available in the data set. This allowed for the modeling of changes in cognition and disability as LGCs. The resulting model provides a better goodness of fit and explains more variance in ΔIADL than any of the four models described above. Nonetheless, the findings should be considered provisional until they can be replicated in future longitudinal samples.

Second, the MMSE is known to exhibit ceiling effects in cross-sectional studies, and the IADL and MMSE exhibited skewed distributions in this data set. Log and square root transformations of these variables were tried, but this had no appreciable effects on the results and would be much more difficult to interpret than the untransformed models reported here. In addition, it is not known that ΔMMSE suffers from ceiling effects. Several studies (reviewed below) find significant group effects on ΔMMSE in longitudinal studies of community-dwelling older adults. The rates of 3-year change in MMSE scores in this sample ranged from −23 to +7 points.

Third, the IADL variable is a convenient but meager substitute for the direct measurement of functional status. The clinical significance associated with the mean rate of change in IADL ratings observed (−0.5 points/y) is not clear. It would roughly translate into the loss of one self-reported IADL every 2 years. Although self-reported clinical symptoms might be considered suspect when obtained from executively impaired subjects, the EXIT25 has also been shown to be a significant cross-sectional correlate of objective and performance-based functional measures.

Nevertheless, it is important to distinguish between fixed and random effects when interpreting LGC models. Traditional regression examines only the fixed effects on group means. Nonetheless, there is significant variability about the mean baseline IADL in this sample and ΔIADL (Table 3). These random effects represent interindividual differences within the FHS sample with regard to baseline IADL performance and individual ΔIADLs. Table 2 demonstrates a broad range of observed IADL scores at baseline, despite the high mean performance. The strong significant associations between EXIT25, IADL, ΔEXIT25, and ΔIADL in an adjusted random effects model suggests that the associations between these variables should be valid across a broad range of individual functional capacities and rates of change in these capacities.

The rate of change in ECF observed in this study is likely to have substantial clinical implications. For example, ECF as measured with the EXIT25 is strongly associated with forensic capacities, such as the ability to execute an advance directive or give informed consent for medical care. These abilities may also suffer as a consequence of the decline in ECF observed.

Similarly, the EXIT25 has previously been shown to distinguish each level of care in comparable CCRCs.
The average separation between levels of care is about 7.0 EXIT25 points. By the third observation, mean EXIT25 scores had increased by almost 3.0 points and were already in the impaired range. The linear deterioration in ECF observed suggests that these subjects will eventually succumb to increases in their levels of care.

Nevertheless, the significant variability about the ΔEXIT25 parameter in Table 3 suggests that there is heterogeneity across the individual ΔEXIT25. Subsets of AFV residents may be deteriorating at faster or slower rates. For example, after age 80, ΔEXIT25 is faster than reported here for the entire FHS sample. Moreover, Figure 1 suggests that ECF may substantially mediate the association between age and functional status. Baseline IADL and ΔIADL are more strongly associated with baseline EXIT25 and ΔEXIT25, respectively, than with age. Moreover, age itself is more strongly related to baseline EXIT25 and ΔEXIT25 than to baseline IADL or ΔIADL. Age is more strongly associated with baseline IADL, but neither age nor baseline IADL is strongly associated with ΔIADL independently of its association with the EXIT25. Thus, it appears that ECF mediates a significant fraction of age’s total effect on change in IADL.

A growing literature suggests that the cognitive deficits associated with normal aging are related to frontal systems impairment. Aging has been associated with disproportionate frontal atrophy, fronto-thalamo-cortical hypometabolism by single photon emission computed tomography, and dysexecutive pattern of cognitive test performance. The frontal atrophy associated with normal aging may be regionally specific. Mesiofrontal regions are affected more than dorsolateral frontal. Orbitofrontal regions seem relatively spared. The EXIT25 has been associated with mesiofrontal system pathology, particularly left-sided lesions. Similar lesions are associated with impaired performance on verbal fluency measures, apathy, and depression, all of which are increasingly common in advanced old age.

These data do not address the mechanisms by which increasing age leads to a decline in ECF and hence functional status, but two recent longitudinal studies have applied LGC models to cognitive test scores in aging twins. As in this study, cognitive measures showed significant variability with regard to baseline distributions and interindividual rates of change, but the variability in cross-sectional baseline cognitive test performance appeared to be much more heritable than the rates of change in those measures. This suggests that the significant variability about the rates of interindividual change in EXIT25 scores in this study may be environmentally determined and thus more amenable to intervention or prevention. In this regard, it is interesting to note that physical activity in old age appears to be specifically associated with measures of executive control and that aerobic exercise has a beneficial effect on age-related frontal cortical volume by functional magnetic neuroimaging.

In summary, a high prevalence of ECF impairment was observed in this sample of initially noninstitutionalized elderly retirees. ECF deficits progress over time, even in the absence of an abnormal MMSE score, and are significantly related to changes in disability. Current dementia case finding is insensitive to ECF and may underreport the incidence and prevalence of cognitive-related functional decline. Thus, ECF represents a relatively unexplored domain for investigation into and intervention on the functional declines associated with normal aging.

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