Journal of Gerontology: PSYCHOLOGICAL SCIENCES
2008, Vol. 63B, No. 3, P185–P192

Application of a Joint Multivariate Longitudinal–Survival Analysis to Examine the Terminal Decline Hypothesis in the Swiss Interdisciplinary Longitudinal Study on the Oldest Old

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In this work I aim at extending current knowledge on the terminal decline hypothesis by applying a joint multivariate longitudinal–survival analysis to the cognitive data of the Swiss Interdisciplinary Longitudinal Study on the Oldest Old. (In that study, 529 individuals between 79 and 85 years of age at study inception were assessed up to five times on a task of perceptual speed and one of verbal fluency.) I simultaneously estimated a multivariate, multilevel longitudinal model and a Weibull survival model to test whether individual performance and change in speed and fluency predict survival, controlling for retest effects, initial age, gender, overall health, socioeconomic status, and sensory functioning. Results revealed that age and performance level in fluency predicted survival, whereas level in speed and change in both cognitive variables did not. I discuss the relevance of fluency tasks in predicting mortality.

Key Words: Terminal decline—Change in cognitive performance and survival—Joint multivariate longitudinal-survival mode.

THE associations between cognitive performance and survival have been the focus of much research during the past decades. In particular, the hypotheses of terminal decline (defined as a long-term, moderate decline in cognitive performance that may predict mortality; Kleemeier, 1962) and of terminal drop (an abrupt decline in cognitive performance preceding mortality in the short run; Riegel & Riegel, 1972) have received wide attention in the cognitive aging literature. Several literature reviews discuss general common findings as well as potential sources of discordant results (Bäckman & MacDonald, 2006; Bosworth & Siegler, 2002). Current evidence seems to conclude that cognitive performance is related to imminent death. However, White and Cunningham's (1988) hypothesis that mortality prediction is limited to specific age-resistant cognitive domains (e.g., crystallized intelligence, Cattell, 1943; Horn, 1982) is not confirmed empirically. Rather, the terminal decline effect appears to be pervasive to other abilities. Moreover, the hypothesis by Riegel and Riegel that terminal decline effects weaken in very old age as a result of increasingly random causes of death does not hold up to recent empirical evidence (Ghisletta, McArdle, & Lindenberger, 2006; Sliwinski et al., 2006; Thorvaldsson, Hofer, & Johansson, 2006; for a recent review see Bäckman & MacDonald).

Several studies have reported perceptual speed to be predictive of mortality (e.g., Hassing et al., 2002; Maier & Smith, 1999), perhaps because of its role as a general mechanism underlying age-related differences on several cognitive tasks (Salthouse, 1996) and because it might reflect primary aging of the central nervous system (Birren, 1965). At the same time, other studies have found verbal fluency to predict mortality (e.g., Cosentino, Scarmeas, Albert, & Stern, 2006). Some have proposed verbal fluency to be related to mortality because it might indicate general brain functioning or even pathological states such as brain atrophy or system breakdown. Indeed, fluency measures have been shown to discriminate between patients affected by Alzheimer's dementias of different severities (e.g., Rascovsky, Salmon, Hansen, Thal, & Galasko, 2007), between patients with Alzheimer's, Parkinson's, and Huntington's disease (e.g., Troster et al., 1998), and between Parkinson's patients and healthy controls (e.g., Donovan, Richard, McDowall, & Abernethy, 1999).

The prime source of differences in findings concerning the cognition–survival links is methodological in nature. First, the usual differences in sample characteristics (e.g., age structure, health status, and gender composition) and measurement features (especially in terms of cognitive assessment) are often hypothesized to influence the results. Second, studies on the cognition–survival associations vary widely in their designs. Several studies assess cognitive performance only once and then relate this measure with survival status a few years thereafter. Such studies cannot infer about relationships between survivorship and cognitive change. Moreover, only a few of these longitudinal studies have more than two cognitive assessments. Hence, most longitudinal evidence rests on estimates of change that are vulnerable to measurement issues (Rogosa, 1988). Third, even when the designs are similar, the analytical procedures differ (Bosworth & Siegler, 2002; Ghisletta, McArdle, et al., 2006). Whereas some studies still estimate change by calculating simple difference scores (e.g., score at Time 1 minus score at Time 0), recent investigations based on longitudinal data make use of advanced analyses (e.g., Ghisletta, McArdle et al.; Rabbitt, Lunn, & Wong, 2006;

Table 1. Descriptive Statistics of Age and the Cognitive Variables by Occasion of Measurement

Age or Variable	Wave 1	Wave 2	Wave 3	Wave 4	Wave 5
Age	83.38 (2.64)	84.73 (2.64)	85.57 (2.59)	86.45 (2.54)	87.78 (2.54)
	[79.45–89.22]	[80.77–90.62]	[81.72–91.54]	[82.73–92.61]	[84.17–93.93]
Cross Out Test	50.00 (10.00)	47.46 (8.12)	49.58 (9.10)	49.41 (8.23)	49.09 (8.26)
	[0.33, 0.17]	[0.05, −0.30]	[0.05, −0.19]	[−0.29, −0.22]	[−0.12, −0.27]
Category Fruit Test	50.00 (10.00)	50.29 (9.74)	50.32 (10.21)	51.73 (11.47)	51.02 (11.10)
	[0.23, −0.43]	[0.42, 1.26]	[0.08, −0.41]	[0.76, 1.00]	[0.62, 1.32]

Note: For each variable, the means (with standard deviations in parentheses) are presented. Brackets indicate range for age, and skewness and kurtosis (in that order) for cross out and category. Numbers are as follows: Wave 1, $n = 529$; Wave 2, $n = 404$; Wave 3, $n = 337$; Wave 4, $n = 283$; Wave 5, $n = 226$.

Sliwinski et al., 2006; Thorvaldsson et al., 2006). In particular, multilevel models are now widely adopted to analyze longitudinal data (Laird & Ware, 1982), mainly because of the following: they separate constancy from change; they estimate constancy and change both at the group and at the individual level; they allow for the inclusion of observations with incomplete data; they are flexible with respect to the functional form of change and to the individual measurement schedules; and they are easily estimated with usual statistical software.

Once characteristics about constancy and change are estimated, they are usually compared across survivors and decedents. Recent statistical advances, though, allow for the direct inclusion of such characteristics in survival models. It is then possible to evaluate the effects of cognitive performance, in terms of both constancy and change estimated in a multilevel model, on the probability of surviving up to a given age, estimated in a survival model. Henderson, Diggle, and Dobson (2000) proposed a joint analysis that simultaneously estimates the parameters of a multilevel model applied to longitudinal data and those of a survival model, in which the individual longitudinal characteristics are specified as covariates. Guo and Carlin (2004) showed how to estimate this model with standard statistical software. Along with McArdle and Lindenberger, I applied this joint analysis to evaluate the terminal decline hypothesis (Ghisletta, McArdle, et al., 2006). In that study, we analyzed eight different cognitive variables, albeit one at a time. Indeed, current applications of this joint analysis are univariate in nature, in that constancy and change characteristics of only one variable are directly integrated in survival models. This approach ignores the potential shared information between multiple variables (such as correlated levels, slopes, and residuals).

The main objective in this study is to examine further the terminal decline hypothesis by focusing on the gradual cognitive performance decline preceding death rather than on a precipitous death-related terminal drop. To do so, I adapt the joint analysis to include a multivariate, rather than a univariate, longitudinal model and a survival model. The multivariate longitudinal component of the analysis estimates performance in a perceptual speed and a verbal fluency indicator together in a sample of Swiss octogenarians, approximately half of whom died during the study period. The survival component of the analysis estimates the survivorship prediction of individual differences in cognitive performance. Given that the main interest of this work lies in estimating change in cognition as a general long-term process, I analyze cognitive performance as a function of chronological age. I analyze both measures of perceptual speed and verbal fluency together because of their noted relevance in predicting survival. The hypothesis is that both measures are predictive of mortality because of their unique features: speed as the resource underlying most age-related differences in cognitive performance, and fluency because of its probable role in indicating general brain functioning. As a consequence, the model tested is multivariate in nature and assesses the relative importance of the two markers in the prediction of survival.

METHODS

Participants

The Swiss Interdisciplinary Longitudinal Study on the Oldest Old (SWILSO-O, Lalive d'Epinay, Pin, & Spini, 2001) is an interdisciplinary study on aging that involves sociology, social and cognitive psychology, social medicine, and econometrics. Two cohorts were assessed in the French-speaking region of Switzerland on an approximately yearly basis. The first cohort was assessed during nine waves from 1994 to 2004, with 340 participants at inception, and the second was assessed during five waves from 1999 to 2004, initially with 377 participants. Both cohorts were stratified by sex and region (urban vs semiurban) and composed of community-dwelling participants originally between about 80 and 85 years of age. The members of both cohorts were initially residing at home and hence probably lead to an overestimate of the overall health status of the general population. However, general characteristics of the sample such as socioeconomic status are representative of the population (Lalive d'Epinay et al.).

The cognitive measures were introduced in the SWILSO-O in 1999, and consequently the previous assessments of the first cohort cannot be considered here. In the end, our sample consisted of the 529 participants of both cohorts assessed after 1999 (i.e., on the fifth to the ninth and on the first to the fifth wave for the first and second cohort, respectively; cf. Ghisletta, Bickel, & Lövdén, 2006). The mean initial age was 83.38 years ($SD = 2.64$). Longitudinal selectivity effects in the SWILSO-O are weak (Ghisletta & Spini, 2004), despite the obvious reduction in sample size as the study progressed (cf. the note of Table 1), and no cohort effects on cognition were revealed.

We official registries of the Cantons Genève and Valais in December 2004 to determine the survival status and, in case of death, the exact date. At that time, 208 participants were dead and the mean age of death was 86.94 years ($SD = 2.90$). Men died on the average 1.27 years earlier than women did, with $t(206) = -3.23$, $p < .001$.

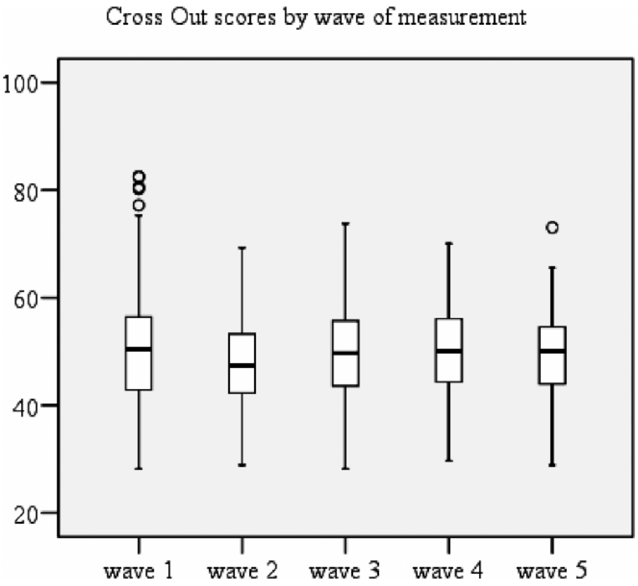

Figure 1. Box plot of the Cross Out Test scores by wave of measurement. Circles denote outliers (at more than 1.5 but less than 3 box lengths from a box boundary).

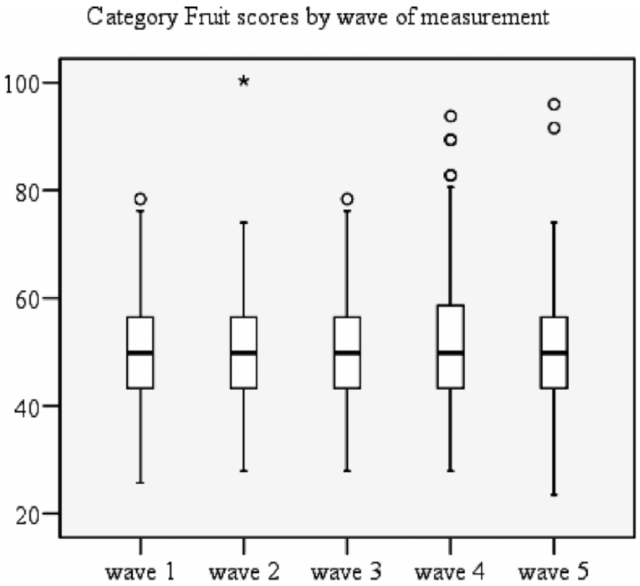

Figure 2. Box plot of the Category Fruit Test scores by wave of measurement. Circles denote outliers (at more than 1.5 but less than 3 box lengths from a box boundary). The asterisk denotes an extreme value (at more than 3 box lengths from a box boundary).

Cognitive Functioning

Two cognitive tasks were administered in the SWILSO-O: the Cross Out Test of the revised Woodcock–Johnson Psycho-Educational Battery (Woodcock & Johnson, 1989) and the Category Fruit Test (Cardebat, Doyon, Puel, Goulet, & Joanette, 1990). The former task assesses perceptual speed; each item consisted of a line in which a target figure on the left was to be identified among a series of similar but different distracting figures on the right. The target, which appeared five times in random order, was mixed with five other distracting figures, appearing less frequently, to form a total of 19 figures. The final score was the total number of target figures that were correctly identified during a 3-minute period.

During the latter task, participants had 2 minutes to name as many different fruits as possible. The final score consisted of the total number of different fruits named (for further details on the cognitive variables, see Ghisletta, Bickel, et al., 2006; Ghisletta & de Ribaupierre, 2005).

To facilitate the interpretation of the results, I scaled the cognitive scores to the *T* metric (M = 50, *SD* = 10) at Wave 1. I scaled the subsequent longitudinal scores with respect to Wave 1 to retain longitudinal changes in the means and variances. Table 1 presents descriptive statistics for the sample's age and cognitive performance by wave of measurement, whereas Figures 1 and 2 portray the distributions of the scores on the two cognitive variables at each wave of measurement. Only a few extreme values can be detected graphically and the overall skewness and kurtosis values are very close to zero, indicating that the distributions do not deviate from normality.

Retest Effects in the Multivariate Longitudinal Model

To obtain estimates of the multivariate longitudinal model with reduced statistical bias, I modeled retest effects. As done in several other studies (e.g., Ferrer, Salthouse, McArdle, Stewart, & Schwartz, 2005; McArdle, Prescott, Hamagami, & Horn, 1998), I created a set of dummy codes to mark the number of previous test exposures, starting at the second wave. Hence, at the first wave this code was not defined, while at the second, third, fourth, and fifth wave these codes estimated the first, second, third, and fourth retest effects, respectively. This strategy allows the estimation of occasion-specific and variable-specific retest effects and assumes the lack of cohort effects, which is the case here (cf. Ghisletta & de Ribaupierre, 2005).

Covariates in the Survival Model

I included several covariates to obtain unconfounded estimates of cognitive performance on survivorship, in particular, initial age, gender, socioeconomic status (SES), hearing and vision functioning, and health. The sample analyzed here included 274 women and 255 men. The SES indicator combined income, occupational status, and number of years of education to classify participants in lower (*n* = 289), middle (*n* = 185), or upper (*n* = 55) status. We assessed hearing functioning by means of three self-assessed questions concerning difficulties understanding other persons, difficulties having a conversation with someone, and general hearing problems (we calculated the sum of the three variables' scores, all with three possible answers). About half the individuals in the sample (*n* = 293) had no functional hearing problems, whereas very few (*n* = 9) had major problems. We assessed visual functioning by means of two self-assessed questions concerning general problems with vision and general visual capacities (we calculated the sum of the two variables' scores, both with three possible answers). Most participants (*n* = 381) reported no functional problems and very few (*n* = 19) reported serious problems with vision. Finally, general health combined one's self-assessed health (on a 5-point Likert scale) and one's general health status in accordance with a multidimensional classification of three states: robustness, frailty that did not affect activities of daily living (ADLs), and ADL dependence (we based this classification on participants' self-assessed sensory and mobility capacities, physical pain, memory problems, and general energy level, as well as on the ADL scale by Katz, Ford, Moskowitz, Jackson, & Jaffe, 1963; cf. Guilley et al., in press). Most participants were classified as frail ($n = 248$), although over half of them ($n = 131$) considered themselves in satisfying health. Only 4 participants were considered ADL dependent and in bad health, and 69 participants considered themselves in very good health and were classified as robust.

All covariates were self-assessed. I scaled the covariates to facilitate interpretations. I scaled the continuous covariates, initial age, hearing, vision, and general health, to have a mean of zero. Concerning the categorical covariates, I coded gender as 0 for men and as 1 for women, and I coded the SES as –1 for lower, 0 for middle, and 1 for upper status. The covariates do not intercorrelate highly (r ranging from –.26 to .32), so that multicollinearity in the survival model is not present.

Multivariate Longitudinal Model

First, I estimated a longitudinal model for each cognitive variable separately. Then, I used the two univariate specifications to define the multivariate model. I defined a multilevel model for longitudinal data with repeated measures (Level 1) nested within individuals (level 2; cf. Laird & Ware, 1982). I defined change over chronological age and the intercept at age 79 years (the initial age of the youngest participant). The model defines each individual's cognitive performance score on each variable as a function of that individual's intercept score at age 79 years, his or her slope score representing the linear change, and the final residual score (representing the usual error of prediction). Both intercept and slope are free of retest effects. I also tested quadratic effects of age and individual differences in retest effects, but the results were nonsignificant for both cognitive variables.

For each variable, I define the intercept and the linear age effect as the sum of a fixed and a random effect. Fixed effects represent the sample mean, whereas random effects represent individual variations around these sample means. With data of the kind analyzed here, the power to detect random effects of linear age is typically very low (Hertzog, Oertzen, Ghisletta, & Lindenberger, in press). I computed a systematic test for (a) the presence of these random effects and (b) their dependence on initial age and retest effects. The random effects of linear age were statistically significant for both Cross Out Test scores and Category Fruit Test scores, but they were not dependent on initial age or retest effects. The random effects of the two intercepts and of the two linear age effects specified in the multivariate longitudinal model are considered as covariates in the survival model.

Survival Model

Given that the joint longitudinal–survival analysis relies on a general maximum likelihood estimator, both the longitudinal and the survival models must adhere to this same principle. Consequently, survivorship must also be modeled parametrically, which excludes the use of the popular Cox model (Cox, 1972). The two parametric survival models tested here were the Weibull and the exponential. Death is the event of analysis and years to death after age 79 years defines time to the event in the survival models. The Weibull model conditions survival on the Weibull hazard function (characterized by parameter $r > 0$) and on the covariates already described here (initial age, gender, SES, hearing, vision, and health) and a final frailty term (Guo & Carlin, 2004). The frailty term allows the inclusion, within the survival model, of the random effects estimated in the longitudinal model.

When $0 < r < 1$, the hazard decreases as time increases, whereas if $r > 1$ then the hazard increases with passing time. When scale parameter $r = 1$, the Weibull model reduces to the exponential model, for which the survival hazard remains constant. Hence the former model nests statistically the second, and a likelihood ratio test based on 1 *df* can be applied to determine the statistical significance of r to test the statistical superiority of the Weibull over the exponential model. Results revealed that the survival process was more adequately described by the Weibull than by the exponential function, $\chi^2(N = 529, df = 1) = 252, p < .001$), so I present only the results of the Weibull model.

Joint Multivariate Longitudinal–Survival Analysis

The multivariate longitudinal model and the survival model estimate the effects of individual predictors in the form of individual-specific random effects around sample-averaged fixed effects. The overall objective is to estimate the effects of various covariates and of level of and change in cognitive performance on the probability of surviving to a given age. To this scope, the joint model allows one to include the random effects of the multivariate longitudinal model (i.e., individual differences in intercept of and in change in cognitive performance) in the survival model. The joint analysis estimates all terms of multivariate longitudinal and of the survival models simultaneously rather than incrementally, potentially augmenting statistical efficiency.[1] More detail can be found in Guo and Carlin (2004) and in Ghisletta, McArdle, and Lindenberger (2006).

RESULTS

All parameter estimates of the joint multivariate longitudinal and survival model are presented in Table 2. To facilitate the reading of this table, first I present the parameters of the multivariate longitudinal component; I follow these with the parameters of the survival component; and finally, I present the parameters representing the link between the longitudinal and the survival components. Again, all parameters of both components are estimated simultaneously in the final joint multivariate longitudinal and survival analysis. I present each parameter with its standard error and the probability value of its 1-*df* statistical t test. The 1% significance criterion ($\alpha = 0.01$) is adopted for interpretation.

For the multivariate longitudinal component, I first present the parameter estimates of the fixed effects, followed by those of the random effects. For the Cross Out Test (CO) variable (columns 2–4), the average longitudinal trajectory starts at 53.49 at age 79 years, declines by 1.08 points each year, and is countered by moderate retest effects after the second, third, and fourth wave (the first retest effect was fixed at zero to avoid

Table 2. Parameter Estimates of the Joint Multivariate Longitudinal–Survival Model

	Cross Out			Category Fruit		
	PE	*SE*	*p*	PE	*SE*	*p*
Parameters from the multivariate longitudinal component						
Fixed effects						
γ_k^{00} (intercept)	53.49	0.8090	<.0001	53.17	0.9082	<.0001
γ_k^{10} (linear age)	−1.08	0.1452	<.0001	−0.84	0.1864	<.0001
$\beta_{2,k}^{2}$ (1st retest)	= 0			1.19	0.6292	.0588
$\beta_{3,k}^{2}$ (2nd retest)	2.14	0.4828	<.0001	1.18	0.7559	.1182
$\beta_{4,k}^{2}$ (3rd retest)	2.83	0.5976	<.0001	3.24	0.9366	.0006
$\beta_{5,k}^{2}$ (4th retest)	3.41	0.8129	<.0001	3.01	1.2544	.0169
Random effects						
variances (σ^2)						
$\sigma^2(u_{j,k}^{0})$	87.85	13.2654	<.0001	84.46	16.4853	<.0001
$\sigma^2(u_{j,k}^{1})$	0.91	0.2940	.0021	1.08	0.4031	.0079
$\sigma^2(r_{i,j,k})$	28.04	1.5424	<.0001	41.75	2.1566	<.0001
covariances (σ)						
$\sigma(u_{j,\mathrm{CO}}^{0}, u_{j,\mathrm{CF}}^{0})$	29.27	11.8831	.0141			
$\sigma(u_{j,\mathrm{CO}}^{1}, u_{j,\mathrm{CF}}^{1})$	0.47	0.2599	.0712			
$\sigma(u_{j,\mathrm{CO}}^{0}, u_{j,\mathrm{CO}}^{1})$	−6.31	1.8421	.0007			
$\sigma(u_{j,\mathrm{CF}}^{0}, u_{j,\mathrm{CF}}^{1})$	−4.31	2.3228	.0641			
$\sigma(u_{j,\mathrm{CO}}^{0}, u_{j,\mathrm{CF}}^{1})$	−0.86	1.8769	.6474			
$\sigma(u_{j,\mathrm{CF}}^{0}, u_{j,\mathrm{CO}}^{1})$	−2.38	1.6260	.1433			
$\sigma(r_{i,j,\mathrm{CO}}, r_{i,j,\mathrm{CF}})$	4.46	1.1292	<.0001			
Parameters from the survival component						
α^0 (intercept)	1.97	0.0550	<.0001			
α^1 (initial age)	0.08	0.0086	<.0001			
α^2 (gender)	0.06	0.0419	.1580			
α^3 (SES)	0.02	0.0309	.6129			
α^4 (hearing)	−0.00	0.0022	.1795			
α^5 (vision)	0.00	0.0021	.1153			
α^6 (health)	0.01	0.0023	.0112			
R	0.24	0.0178	<.0001			
Parameters from the joint component						
γ_k^{0} (effect of $u_{j,k}^{0}$)	−0.01	0.0085	0.2723	0.01	0.0044	.0023
γ_k^{1} (effect of $u_{j,k}^{1}$)	−0.10	0.1396	0.4763	0.14	0.1139	.2356

Note: PE = parameter estimate; *SE* = standard error of that parameter estimate; *p* = probability value of the 1-*df* significance *t* test of that parameter estimate; = 0 = parameter was not estimated but fixed at zero; CO = Cross Out Test; CF = Category Fruit Test; SES = socioeconomic status. Parameters of the fixed and random effects of the multivariate model are presented separately. The deviance statistic, –2LL (total number of estimated parameters), is 20,214 (36).

a counterintuitive, albeit nonsignificant, positive estimation). The picture is similar for the Category Fruit Test (CF) variable (columns 5–7). The average intercept was estimated at 53.17, the yearly decline was somewhat weaker, 0.84 points, and only the third retest effect proved reliable. Given the nature of the cognitive tasks, with the CO being much less familiar than the naming of different fruits, this is not surprising.

Individual differences in starting level were reliable for both variables, as evinced by the estimated random effects (87.85 for CO and 84.46 for CF). Random effects were also significant for linear age effects, but, as expected, of much weaker magnitudes (0.91 for CO and 1.08 for CF). The only reliable covariance of the random effects was that between the intercept and the linear age effect for CO (–6.31, corresponding to $r = -.71$). The residual variance estimate of the speed task was smaller than that of the fluency task (28.04 vs 41.75). Finally, the residual variance components correlated significantly (covariance of 4.46, corresponding to $r = .13$), indicating potential common external influences (e.g., testing method).

For the survival component, only a significant effect of initial age was revealed, estimated at approximately 0.08, which corresponds to an estimated odds ratio of about 2.28 for an increase of 10 years in age. (Note, however, that this index need not be constant during the life period studied here.) The other covariates did not significantly influence the probability of dying at a given age (although general health was close to the cutoff significance level). Given that the covariates do not intercorrelate strongly, this cannot be due to multicollinearity.

Finally, the last section of Table 2 shows the parameter estimates relative to the effects of individual differences in intercept of and change in the two cognitive variables on survival. The speed variable was not associated with survival, neither in its intercept nor in its linear age effects. Verbal fluency, however, proved to be a significant predictor of survival. Indeed, variations in the intercept of the fluency marker significantly predicted the probability of dying ($p = .0023$). A 1-*SD* difference in this cognitive performance is associated with an estimated odds ratio of approximately 1.14. Change in the verbal fluency performance was not predictive of survival.[2]

Discussion

In this article I aimed at advancing the current comprehension of the terminal decline hypothesis by applying, for the first time to my knowledge, a joint multivariate longitudinal–survival analysis. The analysis not only simultaneously modeled the longitudinal development in cognition with the survival process, but also the effects of the former vis-à-vis other potential predictors of death. More precisely, the multivariate longitudinal model estimated the intraindividual trajectories of cognitive performance of the participants, the interindividual differences in these intraindividual trajectories, and the interrelationships between these trajectories. These are some of the main objectives of longitudinal research outlined by Baltes and Nesselroade (1979), and they partially explain why multilevel models have become such a popular analytical approach to longitudinal data. At the same time, survival analyses remain the prime analytical procedure to estimate the relative importance of multiple factors related to survival time. In this application, the effects of initial age, gender, SES, hearing and visual functioning, and general health were considered vis-à-vis interindividual differences in level of and change in performance on speed and fluency.

The results of the joint longitudinal–survival analysis revealed that only initial age and level of performance in verbal fluency were predictive of survival, whereas cognitive decline, performance in perceptual speed, gender, SES, hearing, and visual functioning were not. Most probably the lack of overall predictability of death in this sample is due to sampling criteria. All SWILSO-O participants were initially living at home, and at age 80 years this is clearly a sign of positive selection. With the sample being probably healthier than general population members of the same age, mortality prediction was low to begin with in the SWILSO-O.

Moreover, the sample was stratified with respect to sex and consequently the men in the SWILSO-O likely represent a positive selection of the Swiss male population of the same age. This might explain the lack of gender differences in survival in the results. As for SES, hearing, and visual functioning, extant findings are unclear. For instance, when variables more directly associated with mortality such as general health status are controlled for, as was done here, other variables such as hearing and visual functioning may lose predictability power (Anstey, Luszcz, Giles, & Andrews, 2001). Furthermore, our SES indicator, which combined income, occupational status, and number of years of education, allowed us to classify participants in a lower, middle, or upper status. Perhaps the trichotomous nature of this indicator with its limited range curbed the estimation of its association with survival.

The results of the longitudinal model do, however, agree with those of several other longitudinal studies on cognitive aging. Indicators of perceptual speed are typically age sensitive, hence following longitudinal trajectories similar to those of fluid abilities. Verbal fluency tasks, in contrast, show less decline because they require both fluid and crystallized abilities for correct answers (Mayr & Kliegl, 2000; Salthouse, 1993). As expected, the present results show that the decline in CO scores was slightly greater than that of CF scores. Moreover, the estimated retest effects were stronger for the speed than for the fluency variable. Given the differential ecological validity of the two tasks (naming fruits vs finding a novel, abstract graphical representation among other similar but slightly different stimuli), this result was expected. The estimation of retest effects adopted here may be subject to criticism, prime among which is that it may confound cohort and retest effects. Nevertheless, previous analyses revealed that the two SWILSO-O cohorts, which are only 5 years apart, are not different with respect to cognitive performance. Moreover, the age range of the two cohorts combined here is of approximately 10 years, and the longitudinal observation period lasts about 5 years. Thus, the present analysis must rely to a minor extent on the convergence assumption between cross-sectional age differences and longitudinal age changes (Bell, 1953), and this further reduces the likelihood of cohort effects. Moreover, the statistical procedure adopted here to estimate retest effects has proved useful in a number of independent longitudinal studies (e.g., Ferrer et al., 2005; Ghisletta, McArdle, et al., 2006; Rabbitt et al., 2006).

Verbal Fluency as a Potentially Important Predictor of Mortality

As argued by Bäckman and MacDonald (2006), verbal fluency appears to be a particularly salient ability in the evaluation of the terminal decline hypothesis because of its hybrid fluid-crystallized nature. Consequently, fluency tasks, with their intermediate cognitive demands, may be easy enough for survivors while too difficult for those about to die. This conclusion is further supported by our recent work (Ghisletta, McArdle et al., 2006). We assessed survival prediction of eight different cognitive tasks in the Berlin Aging Study, where the sample had an initial age range of 70–103 years and was assessed up to 11 times over about 13 years. Relevant to the present results, performance level in the Category task (requiring participants to name as many animals as possible) and in the Word-Beginning task (name as many words starting with the letter *s* as possible) were also predictive of survival. However, at the same time, change in performance in both indicators did not affect survivorship. This is probably due to the reduced statistical power within multilevel models to estimate variance in change compared with variance in level (Hertzog et al., in press).

Although overall performance in verbal fluency has shown to discriminate between groups of patients affected by different types of dementias (see the introductory paragraphs of this article), a more careful examination of task performance allows one to gain further insight into the mechanisms possibly involved in such discriminations. Troyer, Moskovitch, and Winocur (1997) analyzed verbal fluency performance in terms of two strategies—clustering (generating words within subcategories, e.g., fruits in a fruit salad, fruits grown on trees, fruits picked in one's garden) and switching (shifting between subcategories). The authors compared younger and older healthy participants and found that, on semantic (or category) fluency, younger participants generated more words and switched more frequently than did older participants, whereas on phonemic (or initial letter) fluency, older participants produced larger clusters than did younger participants. Clustering and switching have also been found to be relevant in further understanding performance in fluency tasks of patients affected by Alzheimer's, Parkinson's, and Huntington's disease (e.g., Donovan et al., 1999; Troster et al., 1998). A possible explanation is that switching is related to frontal-lobe functioning (Troyer et al.), confirming that left prefrontal dysfunction is related to decline in both phonemic and semantic fluency in Alzheimer's patients (Kitabayashi et al., 2001).

At the same time, it appears that verbal fluency performance is also indicative of more general health status. Indeed, diabetic persons performed significantly worse on tests of verbal fluency than did healthy controls (Wahlin, Nilsson, & Fastbom, 2002), and stroke risk is associated with fluency decline (even after controlling for age and education; see Brady, Spiro, McGlinchey-Berroth, Milberg, & Gaziano, 2001). Furthermore, there is evidence that the severity of amyotrophic lateral sclerosis (Lou Gehrig's disease) correlates negatively with verbal fluency performance (Rippon et al., 2006). Finally, Harris and associates (2006) found a significant correlation between telomere length and fluency performance in a sample of nondemented people who were 79 years of age, even after the researchers controlled for general mental abilities at age 11 years. Telomere length is associated with several vascular conditions, among which are myocardial infarction and diabetes, and their consideration for the prediction of survival is gaining increased interest in the scientific community (cf. Bäckman & MacDonald, 2006).

Limitations and Conclusions

Clearly, although this study used quite a sophisticated analytical procedure, some potentially important features were omitted. Prime among these is the dissociation between normative age-graded and nonnormative influences on survival (Baltes & Nesselroade, 1979). More precisely, we included a general health indicator, but we could not include more exact information about participants' health status. Preclinical dementia (Sliwinski, Hofer, Hall, Buschke, & Lipton, 2003), other pathologies severe enough to result in death or dropout (Rabbitt et al., 2006), such as cancer, coronary heart disease, and stroke (Anstey, Mack, & von Sanden, 2006; Hassing, et al., 2002), and genetic information (polymorphisms and telomeres, cf. Bäckman & MacDonald, 2006) were not available in the SWILSO-O. Only self-assessed health indicators, combined in the general health status variable, could be included in the survival model. Given that here this general indicator was not predictive of survival time, the inclusion of more precise health-related variables is clearly warranted in future work.

In conclusion, I obtained the results of this work by applying a joint multivariate longitudinal and survival model, representing a state-of-the-art analysis of change and survival. The longitudinal model could also have been specified to investigate sudden drops in cognitive performance immediately preceding death by replacing the time-since-birth (i.e., chronological age) with the time-to-death basis (e.g., Thorvaldsson et al., 2006). This alternative time basis would have been more appropriate to investigating the terminal drop hypothesis (Sliwinski et al., 2006) rather than focusing on terminal decline as was done here. Although perceptual speed was not related to survivorship, performance level in verbal fluency was. This confirms the potentially central role of this ability in improving our comprehension of the terminal decline process (Bäckman & MacDonald, 2006). Future studies on cognitive predictors of mortality will likely benefit from including tasks that measure abilities of intermediate cognitive demands. More specifically, future studies ought to include semantic and phonemic fluency tasks and record participants' answers to allow an examination of the application of clustering and switching strategies.

ACKNOWLEDGMENTS

This research was supported by the Swiss National Science Foundation Priority Program "Switzerland: Towards the Future" (5004-047750/047752, Principal Investigator Christian Lalive d'Epinay), the Département de la Santé et de l'Action Sociale de la République et Canton de Genève, and the Département de la Santé du Canton du Valais. Parts of these analyses were presented at the 10th Congress of the Swiss Society of Psychology, Zürich, Switzerland, in September 2007. My special thanks go to all participants and staff members of the Swiss Interdisciplinary Longitudinal Study on the Oldest Old.

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Received August 20, 2007
Accepted December 12, 2007
Decision Editor: Thomas M. Hess, PhD

End Notes

[1] I fit the joint model by using the NLMIXED procedure in SAS (SAS Institute, 2002) because this allows me to define the likelihood function for both the multivariate longitudinal model and the survival model. For the former part, I adapted the syntax of Thiébaut and Jacqmin-Gadda (2004) and that of Marshall, De la Cruz-Mesia, Barón, Rutledge, and Zerbe (2006); for the survival and the final joint part, I adapted the syntax of Guo and Carlin (2004).

[2] Results of separate joint univariate longitudinal–survival analyses (one for speed and one for fluency) are very similar, except that in the univariate model with only fluency, visual functioning predicted survival. This is because visual functioning predicts performance in the speed task, but not in fluency. Given that the multivariate model includes also speed, visual functioning loses its relationship with survival. For simplicity, I present only the results of the joint multivariate longitudinal–survival analyses.