Understanding Ageing: Further Commentary on the Limitations of Cross-Sectional Designs for Ageing Research

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Ageing · Methodology · Cognition

Abstract

Critical issues regarding the utility of age-heterogeneous cross-sectional samples for estimating associations among rates of change are briefly reviewed and further examined in response to the four insightful commentaries on our original discussion paper. These general issues are considered in terms of current practice in gerontological studies. Several of the commentaries refer to additional problems (e.g., selection/attrition, cohort differences) with cross-sectional designs for inferring correlated rates of change, often modeled as shared age-related variance. The commentators concurred with, and performed simulations that support, our primary contention that the influence of mean population trends over time has a major confounding influence on cross-sectional estimates of association. While this confound has been acknowledged and demonstrated in a number of publications over this century, cross-sectional studies and covariance modeling remain common practice in gerontological studies. We question the value of this practice for advancing aging theory and would like to see greater emphasis placed on longitudinal studies and the use of cross-sectional designs and analytic methods that permit separation of age-related mean trends from estimates of association between age-related variables.

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Introduction

Hofer and Sliwinski [1] describe some limitations of cross-sectional research for the analysis of associations among age-related variables. Further details and simulation results are provided by Hofer and Flaherty [2]. A major point of these papers is that when associations among age-related variables are of interest, simple age-related mean differences – average trends across individuals of different ages – will comprise and upwardly bias covariance estimates. Indeed, positive and large associations among age-related processes will occur even when rates of change across variables are independent, and thus uncorrelated. Although average population changes might reflect common causal mechanisms and functional constraints, mean trends provide a weak basis for understanding the structural and causal processes associated with individual differences in aging.

Most theories of cognitive aging have been based on cross-sectional studies. Indeed, the analysis of cross-sectional samples of individuals varying broadly in age has been a dominant research paradigm in gerontology, particularly in the area of cognitive aging research, where it appears as the widely held belief that age-heterogeneous cross-sectional studies can lead to an understanding of the interdependence among aging-related processes [3–6]. This is not to say that there has been limited longitudinal research in this regard. Schaie and Hofer [7] review 24 current longitudinal studies of aging; results from these

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studies will undoubtedly have a major impact on the field of aging.

Describing the ubiquitous age-related mean changes in a population is clearly an important goal and has been the focus of much research on aging using both cross-sectional and longitudinal designs. However, the study of individual differences in aging is equally important, permitting the evaluation of genetic influences, environmental risk factors, and structure and pattern of aging processes. Several questions have driven our critical analysis of research designs, emphasizing research outcomes regarding aging-related changes using cross-sectional and longitudinal studies. If population average change is all we could know about such processes, what would be gained by examining the covariances among these processes? How could we understand whether these changes occur independently or whether they occur as a result of the same influences or within the same system of variables? Indeed, what information is carried by cross-sectional covariances among age-related processes?

It was on this basis that we sought to understand how different methodological designs will lead to different expectations of covariances among processes. We regard mean trends to be a relatively unacknowledged source of covariation in current age-heterogeneous studies. This is not at all a new issue, however. That mean trends, or differences, will produce covariation has been described and illustrated over the last century across a range of substantive and statistical literatures. The problem is similar in form to the ecological fallacy [8], Simpson's [9] and Lord's [10] paradox, and the time-correlation problem [11, 12]. Cattell [13], Kelley [14], Merz and Kalveram [15], and Reinert [16], among others, describe how heterogeneity related to 'maturity' or time will lead to a common factor. Cattell [13] discusses approaches for dealing with the 'time trend' and advocates careful factor rotation over the analysis of partial correlations. The effect of age-related mean trends on factor structures is developed further by Meredith and Horn [17] in the context of evaluating factorial invariance. Indeed, we found that these issues have been raised repeatedly in publications questioning the utility of cross-sectional studies for understanding change [18–20], and it is clear that age-heterogeneous cross-sectional studies are more confounded than other designs for understanding the process of change.

We found it useful to demonstrate the nature of the problem by beginning with a simple longitudinal model that incorporates an average population trend and individual differences about this trend. The use of this model to generate data and expectations for cross-sectional sam-

ples provides a direct demonstration of the differences between cross-sectional and longitudinal approaches. Longitudinal methods permit the separation of population trends (fixed effects) and individual differences about the trends (random effects), whereas age-heterogeneous cross-sectional approaches typically do not. The contribution of mean trends to estimates of covariance in such cross-sectional samples is particularly troublesome for statistical analyses that focus on the shared age-related covariance [21, 22], since similarity among mean trends will dominate this proportion of covariance. In describing this association as confounded, we do not at all diminish the importance of mean trends in research on aging and are careful to state this. We question, however, whether age-related mean trends should have much weight in the development of theories and hypotheses regarding associations among aging-related processes. We emphasize this point because it does not appear to be common knowledge that age-related covariance is confounded in this manner or that such confounds profoundly limit inferences about patterns of aging across individuals.

We acknowledge that the study of change is best based on the analysis of individuals over time and that longitudinal studies should, therefore, be the standard for understanding aging. Nevertheless, cross-sectional data contain information regarding differential rates of aging in addition to average population trends. We examine alternative cross-sectional approaches: the use of narrow age cohort (NAC) and sequential narrow age cohort (SNAC) designs. We demonstrate that, as time elapses, individual differences in rates of change have an increasing effect on the covariance among age-related processes. We have shown this both analytically [1, 2] and in simulation [2] using a linear model of change, though, of course, different patterns and magnitudes of change, nonrandom attrition, and cohort effects are among the many influences that may alter these estimates of covariance. On the basis of our derivation, we make the statement that partialling for age-related variance in a single age-heterogeneous cross-sectional sample, by removing individual differences related to the average between-person mean trend, results in a loss of information regarding individual differences in rates of change. Partialling for age in a single age-heterogeneous sample is similar to a single NAC sample of approximately the same average age. The information that is lost is the changing magnitude of association across NAC samples under the expectation that change across individuals is correlated.

What is important about the single NAC design (or age-partial association) is that finding weak or no associa-

tions among age-related variables serves as evidence for the independence of individual differences in aging-related changes, as it is unlikely that initial individual differences would be completely cancelled by individual differences in rates of aging. Therefore, the NAC design is most useful if weak or no associations are found, as otherwise the sources of individual differences remain much less certain. In this way, a single NAC sample (or age-partialled covariances) can provide evidence for dissociation among age-related processes.

When only cross-sectional information is available, we prefer the use of the sequential age-homogeneous sample analysis, which permits the evaluation of differences in covariance across age-based groups, to variance decomposition analyses that are typically applied to age-heterogeneous samples. Age-heterogeneous samples can easily be stratified in this manner, and associations can be based on age-partialled covariances within each age group to eliminate the effect of mean trend association with the age variance within NAC samples.

Discussion of Commentaries

We will use the very constructive comments offered by our colleagues to expand and further evaluate the major points of our article. In general, we find that the commentaries are in agreement with the major points of our discussion paper and have usefully emphasized points related to the general issues we raise.

Anstey

Anstey [23] reviews the methodological reasoning that many researchers have used to understand the process of aging with cross-sectional data and describes both the utility and limitations of cross-sectional research. We are not sanguine about the utility of age-heterogeneous cross-sectional research for evaluating associations. Nevertheless, cross-sectional research can elucidate general population age trends and prevalence rates, and it can help form policy decisions when the focus is on population level processes. We concur that age-heterogeneous studies can be useful for descriptive purposes, and we agree that a common practice should be to perform and report the age-partial analysis.

We would like to take this opportunity to clarify the NAC design. Anstey states that it is not possible to understand age or aging within such a design; however, this is only true if there are no individual differences in *rates* of aging. NAC samples eliminate mean differences related to

age by treating age as a constant. However, age-homogeneous samples still contain information regarding differential rates of aging (see equation 6 [1]). This is the central reason that the NAC and SNAC designs are useful for evaluating the independence or interdependence of aging-related changes across individuals. These designs are closely associated with the recommendations of Wohlwill [19, 20] that age be used as an index and not as an explanatory variable. These designs emphasize the concept of age as a continuum over which correlated individual differences in rates of change, due to either functional relations or common causation, unfold and lead to the expectation of increasing covariances among processes.

Li and Schmiedek

Li and Schmiedek [24] provide a very useful and positive commentary, illustrating other potential sources of influence on individual change patterns and demonstrating further the limitations of cross-sectional studies for understanding associations among aging-related changes. Clearly, models that are sensitive to the dynamics and lead-lag patterns of change over time will provide us with necessary information regarding the cascade of events associated with the causes and effects of aging.

The NAC/SNAC design controls only for the between-individual mean trends. It still has all of the other confounds and limitations of cross-sectional and age-heterogeneous longitudinal studies. These other limitations, including cohort differences and selective attrition, are important considerations for the interpretation of both cross-sectional and longitudinal research. Li and Schmiedek very clearly demonstrate how cohort and mortality might differentially affect the outcome of associations in NAC samples. These influences are directly pertinent to the evaluation of SNAC results, such as the dedifferentiation hypothesis [16]. We must be alert to population heterogeneity and nonrandom selection [25], the effects of which remain unknown in cross-sectional studies but are seen in terms of changing participation status in longitudinal studies. Associations among rates of change across individuals will also be a function of form and magnitude of change in individual trajectories at different ages. Although these may be highly limiting factors, the fact that NAC samples contain information on the correlated rates of change permits an opportunity for cross-sectional data to enhance our understanding of the structure of aging-related changes.

We certainly resonate with the process orientation and the focus on functional explanations. We are excited about the prospects of understanding aging using sam-

pling methods and statistical advances that are sensitive to the dynamic nature of developing and ageing systems.

Molenaar

Molenaar [26] demonstrates our basic points regarding the confound of fixed and random effects in age-heterogeneous cross-sectional designs [1, 2]. In more general terms, Molenaar questions the utility of between-individual information, obtained from either cross-sectional or longitudinal designs, and points out that between-person differences may provide little to no information regarding within-person processes. These are critically important points and should encourage greater attention on within-individual processes in regards to changes with age.

In response to Molenaar's comments, we must clarify our notation. We have not treated age inconsistently or in an ambiguous manner in our development of the covariance expectations. Equation 1 is a simple model for an individual i 's score at time t . This is a standard linear equation for a single time point score extracted from a longitudinal series of observations for individual i . The common notation for these models (known as mixed models, hierarchical linear models, or random effects models) is based on vector and matrix notation – see, e.g., Rovine and Molenaar [27]. Molenaar argues that t should be subscripted by i in equation 1 on the basis that it should be random. However, time is not random within person; it is quite deterministic. For a longitudinal series, time (or age) is the index that orders the observations. We must assume that equation 1 and the surrounding text were interpreted by Molenaar as describing a sample level quantity. When our discussion moves to age-heterogeneous cross-sectional samples, the covariance expectations correctly include t_i , as time becomes a sampled quantity (i.e., a random effect as in random-effects Anova).

Our equations 3–5 [1] are the covariance expectations in a sample of individuals that do vary in age, and t is appropriately subscripted, as Molenaar notes. Equations 6 and 7 refer to NAC samples which by definition do not exhibit differences in age, and so t is fixed within group. In NAC samples, where individuals are all of the same age, the expectation of t_i is zero, and these terms drop from the expectation for a particular NAC group, as shown in equation 6. We could have subscripted with further notation to specify the particular age of each NAC group (e.g., $t_i = c$, where $c = 70, 75, 80$) but chose simply to represent this as a fixed value for each age group, each 'representing a single slice of time'. Our use of this notation should be clear, however, in the example presentation of $t = 1, 2, 3, 4$, shown in equation 7 and in the descrip-

tion of this usage in the accompanying text. Therefore, we have not treated age in an ambiguous manner in our derivation of covariance expectations. Equations 5 and 6 deal with age-heterogeneous and age-homogeneous samples, respectively. We apologize if this proved confusing and hope that we have adequately clarified these derivations.

Molenaar demonstrates that fixed age effects produce covariances and that partialling for age in a regression analysis can account for the fixed age effects (mean trends). This is exactly the point of our criticism of cross-sectional studies in gerontological research – average population differences are implicitly the focus of covariance decomposition. What is typically examined in ageing research is the age-related component (i.e., shared age-related variance, age-mediation effect) – the portion of variance related to age that is partialled out – and this component of variance is predominantly composed of the fixed age effects. We reemphasize that the unpartialled associations in cross-sectional data refer mainly to the mean trends, seen as age-related differences in an age-heterogeneous cross-sectional sample. We are in agreement that age-partialled effects, obtained statistically or using sample stratification (i.e., SNAC design), should be the focus of analysis in cross-sectional studies. However, we must note that age in these circumstances is obtained by between-person observations (influenced by cohort, differential selection) and may not reflect the age trend within individuals that can be estimated with longitudinal data.

In his final simulation, Molenaar uses a model that allows correlated random age slopes. He concludes that the resulting age-partial correlations must be explained by *either* correlated random intercepts (i.e., correlated individual differences in level of performance) or correlated random regression coefficients (i.e., correlated rates of aging). Thus, Molenaar provides an alternative demonstration of our major thesis: in the presence of age-partial associations, it is *impossible* to disambiguate the source of covariation using the age-partial approach on age-heterogeneous cross-sectional data or in a single NAC sample.

Molenaar concludes that the residual (partial) correlation that contains information regarding correlated random rates of change is 'not a vice, but a virtue, because it makes it possible in the next modeling step to introduce random change components ... to explain these partial correlations'. However, Molenaar does not explain how this next step could and should be taken given the confound with correlated initial individual differences. In the context of a longitudinal study, random change components are directly estimated and can, therefore, be intro-

duced into the modeling process. The strength of the SNAC approach is that information regarding correlated rates of change is accessible and separable from correlated initial individual differences. That random effects will have increasing contributions to cross-sectional NAC correlations over time was a major point of our argument and the reason for our statement regarding the 'loss of information' in age-partial analysis. However, as we demonstrated previously [1, 2], this 'next modeling step' *cannot* be taken in the context of a conventional, age-heterogeneous cross-sectional design, where the residual correlations would remain stubbornly ambiguous.

Salthouse and Nesselroade

We have several comments regarding the limitations of longitudinal data sets enumerated by Salthouse and Nesselroade [28]. First, and most importantly, these limitations may apply to 'longitudinal data sets', but are not necessarily inherent to longitudinal designs. In contrast, our criticisms identify inherent weaknesses of cross-sectional studies of age-heterogeneous samples that cannot be overcome through refinements to study design or careful measurement approaches. Second, of the five limitations identified by Salthouse and Nesselroade, four apply to cross-sectional designs as well. Most cross-sectional aging studies that support common factor models [5, 6] use samples of convenience and hence are not representative of the population (limitation No. 2). Many cross-sectional designs include only a small number of variables, and in a recent review, Schaie and Hofer [7] describe 24 ongoing longitudinal studies of aging, most of which utilize a very rich assessment battery (limitation No. 3). Salthouse and Nesselroade state that test-retest correlations between measurements are typically high and that these correlations imply that the systematic variance in change (i.e., individual differences in age effects) is small (limitation No. 4). We are obliged to point out that Verhaeghen and Salthouse [6] demonstrate that small ratios of age-related to total variance characterize most cross-sectional studies, with age effects accounting for between 7% (for working memory) and 27% (for processing speed) of the total variance. An advantage of longitudinal designs is that they allow statistical identification and unambiguous separation of age-related systematic variance from other sources of variation (e.g., stable individual differences), even if it is quite small. Analytical techniques cannot unambiguously disentangle these different sources of variations in cross-sectional designs of age-heterogeneous samples. Therefore, relatively small amounts of age-specific variability present more of a problem for

cross-sectional than for longitudinal designs. Finally, Salthouse and Nesselroade argue that few attempts have been made to distinguish true age effects from practice effects, unsystematic fluctuations, and other factors (limitation No. 5). We concur, but again are obliged to point out that cross-sectional studies face the same problems and afford fewer opportunities to overcome them than do longitudinal designs. Unmeasured and differential practice effects (e.g., differential prior experience and underperformance related to novel task demands) are rarely examined in cross-sectional aging research, the primary exceptions being studies that use extensive practice to study age differences in asymptotic performance [29–32]. Most cross-sectional and longitudinal studies have ignored the potential influence of short-term fluctuations in performance, although the role of intraindividual cognitive variability has become an area of intensive interest in recent longitudinal studies [33–35]. In fact, only longitudinal designs can measure and control for unsystematic (and systematic) fluctuations in performance [36]. Sliwinski et al. [37] demonstrated how susceptible cross-sectional studies are to the influence of 'factors other than endogenous maturation' by illustrating the influence of unidentified preclinical dementia on cognitive age effects estimated at cross-section. Only longitudinal follow-up allows the separation of changes attributable to disease processes (nonnormative influences) from those attributable to endogenous maturation (normative influences) [38–40].

The authors, in building their argument that the amount of variance attributable to differential aging effects is small, cite test-retest correlations from several very-long-term longitudinal studies. First of all, we must note that test-retest correlations between two occasions of measurement provide relatively little information regarding systematic changes in performance [41]. This issue aside, we believe that the authors have provided compelling evidence for the contrary position, namely that the amount of variance attributable to differential changes is potentially large. The authors cite longitudinal studies that report declining test-retest correlations, as the interval between measurement occasions increases: 0.86 for a 7-year interval, 0.78 for a 42-year interval, and 0.63 over 66-year interval. All of these correlations were computed on composite scores which presumably have very high instantaneous reliabilities. Therefore, we can assume that most if not all of the unexplained variation in these test-retest analyses is attributable to individual differences in dynamic processes influencing performance (i.e., individual differences in rates of aging). Increasing amounts of

the unexplained variation in performance could be attributable to individual differences in change, as the interval between measurement increases: 26% of the total variance ($1-0.86^2$) over 7 years, 39% ($1-0.78^2$) over 42 years, and over the lifespan (66 years), the majority of the variability (60%, or $1-0.63^2$) could be attributable to individual differences in change. The lower bound estimate for the proportion of variability potentially attributable to individual differences in aging (26%) is the same as the upper bound of variability attributable to age-related variability estimated at cross-section (27%). Thus, longitudinal studies (even those spanning less than 10 years) can potentially produce more robust estimates of age effects than can cross-sectional studies that measure age differences across a broader age span [42, 43].

The NAC design, particularly in its sequential (SNAC) form, permits an alternative evaluation of association among aging-related changes. The SNAC design is essentially a test of age as a moderator. The test of interaction described by Salthouse and Nesselroade can be evaluated using a continuous variable approach and examining the three-way interaction term of age and the two dependent processes. However, the multiple-group approach we describe is often the recommended approach for evaluating moderation [44]. We find the SNAC design useful for evaluating changes in association across age groups, given that the association between the random effects will increase with age and result in increasing associations (under assumptions that selection and attrition are negligible). Evidence for the utility of this multiple-group approach is seen in early developmental applications and in aging research evaluating differentiation and dedifferentiation [16].

Linear models of change necessarily imply increases in variance. However, increases in variability across age groups are unlikely to occur in populations and in the analysis of empirical studies, where change may be nonlinear and where selection is nonrandom and operates in a way that those who exhibit the least change are the most likely to continue participation in longitudinal samples or be available for age-heterogeneous cross-sectional samples. The example based on the WAIS III standardization data is not at all inconsistent with nonrandom selection on heterogeneous characteristics, with survivors at subsequent ages being nonrandom samples of previously available populations [25]. One of the central critiques of Salthouse and Nesselroade's comments with regard to the expectation and lack of finding of increasing variability across NAC samples can be understood in terms of attrition and selection effects [33]. The expectations of the

NAC and SNAC designs must be understood in the context of this selection. Furthermore, we must regard this as a problem for *all* cross-sectional studies, since the process of selection occurs at the level of the population and, therefore, influences the acquisition of all samples varying in age, regardless of whether they will be followed over time.

The authors conclude by reiterating the value of cross-sectional approaches that examine shared age-related variability in cognitive performance. However, they do not specify exactly what value such an approach offers with respect to advancing and testing theory. The authors agree with our contention that analyses of between-person variability provide a weak basis for inferences regarding age-related changes at the level of the individual. Because theories of cognitive aging seek to explain the mechanisms that cause age-related change in cognitive function, there seems to be little direct value in conventional cross-sectional approaches that focus on the analysis of shared age effects, since these estimates may be dominated by the effects of mean trends (average between-individual differences). While we doubt that merely being sensitive to such design limitations will be helpful, we are in complete agreement that 'it is no longer premature to emphasize rates of change and changes in rates of change' in longitudinal studies and expect that progress in aging theory will come from studies that observe individuals over time. We regard the challenges associated with longitudinal studies of aging as more tractable than the confounds that exist within cross-sectional studies.

Summary Statement

There can be no doubt that mean trends are a confounding influence on associations in conventional analysis of age-heterogeneous cross-sectional studies. We have shown analytically that mean trends are a component of the covariance in cross-sectional studies of individuals varying in age. We have also demonstrated that information regarding 'rates of change' can be obtained from cross-sectional information using NAC samples. These alternative designs based on SNAC samples can be performed on existing age-heterogeneous cross-sectional data.

No research design is optimal for all purposes. However, some designs are less useful than others for particular purposes. Understanding aging requires analysis of change within individuals. We propose that there are real limits on the understanding of the direct and indirect

effects of aging processes that may be gained by (1) simple comparison of mean trends over individuals of different ages and (2) cross-sectional designs that are confounded by these mean trends. This is not to say that mean trends are unimportant or undeserving of our attention. However, when individual differences in aging are the focus of analysis, evidence based on such designs will lead to common factor solutions, shared age-related variance, and overestimates of covariances that may be spurious in terms of associations among individual-level change processes with age.

Longitudinal designs permit much stronger tests of association between rates of change but are not without limitations. The point raised by Salthouse and Nesselrode [28] that 'the strongest conclusions will come when results from different methods, each based on different sets of assumptions, converge' is quite reasonable and reiterates a basic tenant of the scientific approach. However, their contention is true only to the extent that each method is informative regarding the phenomena under study. We have described how different methodological approaches are confounded to different degrees. Such confounds will necessarily lead to different conclusions, and therefore some designs must be given greater emphasis for answering questions that focus on the individual differences in processes affected by aging. In this case, lack of convergence should lead to the acceptance of results from the more appropriate methodological approach [42, 43]. While the NAC/SNAC design provides an alternative cross-sectional model, the best evidence regarding individual differences in aging will be obtained from individuals followed over time as they age.

We would like to conclude by stating that valid inferences regarding the aging process based on the NAC/SNAC approach, as with any cross-sectional design, rest on a number of assumptions. One key assumption for using the NAC/SNAC approach bears reiterating: non-trivial individual differences in rates of aging exist. Conventional age-heterogeneous approaches that rely on age-partial analyses require a different assumption (demonstrated by Molenaar's final simulation) for obtaining interpretable and unambiguous results: that *no* individual differences in rates of aging exist. However, it is the very fact (and this fact has been well established) that individuals exhibit different and correlated rates of cognitive aging that provides the empirical impetus for cognitive aging research and theory development. Therefore, the key assumption for conventional cross-sectional studies of association in age-heterogeneous samples undercuts their own utility.

These analyses should tell us that it is not sufficient to be sensitive to limitations of conventional cross-sectional approaches, but that we must change our research practice in order to advance theory. The purpose of our original articles [1, 2] is to suggest a refinement to conventional cross-sectional approaches and encourage the use of longitudinal methods to overcome critical limitations and potentially advance aging theory.

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Links to longitudinal studies of aging can be found at: www.personal.psu.edu/smh21/. We thank Jason Allaire, Andrea Piccinin, and Michael Rovine for their helpful comments on the manuscript.

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