In multiple facets of subjective memory decline sex moderates memory predictions

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Abstract

Introduction: Two established subjective memory decline facets (SMD; complaints, concerns) are early indicators of memory decline and Alzheimer’s disease. We report (1) a four-facet SMD inventory (memory complaints, concerns, compensation, self-efficacy) and (2) prediction of memory change and moderation by sex.

Methods: The longitudinal design featured 40 years (53 to 97) of non-demented aging (n = 580) from the Victoria Longitudinal Study. Statistical analyses included confirmatory factor analyses and conditional latent growth modeling.

Results: The four-facet SMD Inventory was psychometrically confirmed. Longitudinal analyses revealed significant variability in level and change for SMD and memory. Prediction analyses showed complaints and concerns predicted lower level and steeper memory decline; however, follow-up moderation analyses revealed selective predictions for females. Memory compensation predicted decline overall. Lower memory self-efficacy predicted steeper decline selectively for males.

Discussion: Although traditional and novel SMD facets predicted memory decline, differential sex moderation was observed. SMD research benefits from conceptual complementarity and precision prediction.

KEYWORDS
memory compensation, memory complaints, memory concerns, memory self-efficacy, subjective memory decline, Victoria Longitudinal Study

1 | INTRODUCTION

1.1 Background

The subjective experience of cognitive decline (SCD) in an asymptomatic period of aging may be an early indicator of future objective decline and clinical transitions into mild cognitive impairment (MCI) and Alzheimer’s disease (AD).1 SCD, especially when differentiated and combined into complaints and concerns (worries), has been associated cross-sectionally with concurrent AD-type pathology, such as amyloid beta (Aβ) deposition,2,3 and longitudinally with greater risk of cognitive decline4 and progression to AD.5 Subjective memory decline (SMD) is a domain-specific concept nested within the broader umbrella of SCD. The two traditional constituents of SMD, subjective memory complaints and memory concerns, have predicted objective memory decline in normal aging as well as MCI and AD.5,6 Specifically, SMD has shown associations with dementia,6,7 hippocampal and gray matter atrophy,8,9 Aβ deposition,10 as well as incident cognitive and memory decline.11,12 Conceivably, SMD could reflect subjective sensitivity to memory failures associated with early AD-related pathological changes.

Some inconsistencies in SCD and SMD results13,14 may be related to variations in assessment (single items, scales), breadth of content domain (general cognition, episodic memory), research design...
(cross-sectional, longitudinal), and potential moderation of SMD effects by factors such as sex.\textsuperscript{9,15} Broader coverage in SMD conceptualization, measurement, and testing may produce complementary insights and enhanced prediction precision.\textsuperscript{16} Accordingly, we explored SMD as measured by brief subscales of four conceptually complementary facets relevant to aging: memory complaints, concerns, compensation, and self-efficacy.\textsuperscript{17,18} We evaluated SMD facet prediction patterns for longitudinal episodic memory change over a broad band of aging (53 to 97 years) for the overall sample and as stratified by sex.

In recent years, variability and change in memory performance in asymptomatic aging has been well established. Accelerated decline in episodic memory remains an important objective signal of future MCI and AD risk.\textsuperscript{19} However, longitudinal studies of memory trajectories show substantial variability in level (differences across the Y-axis at any age) and slope (differences in individualized patterns across the X-axis; Figure 1).\textsuperscript{20,21} Multiple domains of predictors (eg, genetic, biomedical, functional) have been associated with differential level and slope of longitudinal memory.\textsuperscript{20,21}

The two established SMD facets are a self-perceived decline in memory (complaints) and concerns about that decline.\textsuperscript{1} Two testable supplemental aspects of subjective memory beliefs are discussed in related literatures: memory compensation and memory self-efficacy.\textsuperscript{22-26} Memory compensation refers to awareness of memory decline and potential actions to address complaints or concerns about everyday memory deficits. Actions include techniques used to remedy or forestall perceived performance deficits and declines.\textsuperscript{24,27} Memory self-efficacy refers to the concept that beliefs about one’s own memory ability and decline (and the extent to which memory aging may be controlled) play an important role in everyday memory situations.\textsuperscript{25,28} We selected items from two established aging-related memory knowledge and beliefs inventories that reflected the four provisional SMD facets to create a multi-faceted SMD Inventory.

The extent to which memory-related phenomena in aging may differ by sex is broadly indicated for hippocampal volume,\textsuperscript{29} memory performance,\textsuperscript{30} memory resilience,\textsuperscript{31} and memory implications of AD genetic risk.\textsuperscript{21} Given the well-established presence of sex differences in the incidence and etiology of AD,\textsuperscript{32} it is also possible that SMD (a potential pre-prodromal phase of objective impairment and AD) may differ by sex. Recent studies of SCD and SMD have reported sex differences in basic frequency,\textsuperscript{33} cognitive performance and disease progression to MCI,\textsuperscript{34} and dementia risk.\textsuperscript{33,35} We follow an established stratification approach to investigating sex moderation in dementia-related phenomena, with main analyses performed separately for males and females.\textsuperscript{21}

### 1.2 | Research goals

In a sample of cognitively normal older adults we investigated whether the standard facets of SMD could be usefully supplemented by two additional facets. We selected a non-demented longitudinal sample for two reasons. Specifically, they provided a foundational benchmark for (1) developing new SMD facets as they represent existing variability in memory-related self-awareness, concerns, efficacy beliefs, and compensation and (2) testing and comparing predictions of normal memory change across SMD facets as moderated by sex. The analytic strategy included psychometric evaluation, longitudinal growth and prediction modeling, and moderation analyses by sex. After establishing the SMD Inventory, our first research goal (RG1) used latent growth models (LGM) to model variability and change in both SMD and episodic memory. For research goal 2a (RG2a), we used conditional latent growth models (CLGM) to test whether SMD facet level predicted memory level or change. For research goal 2b (RG2b), we investigated sex-specific predictions of episodic memory performance by SMD facets.

### 2 | METHODS

#### 2.1 | Participants

Participants were volunteer community-dwelling older adults from the Victoria Longitudinal Study (VLS), a Canadian large-scale longitudinal sequential study of biomedical, clinical, and cognitive aging.\textsuperscript{22} Written consent was provided by all participants and data collection procedures were certified by prevailing ethics guidelines and boards. Longitudinal data were assembled from ongoing VLS samples, with up to three waves of data per individual (\(M\) interval \(W1-W2 = 4.4\) years; \(W2-W3 = 4.6\) years). Individualized trajectory distributions were constructed for both SMD and memory (Figure 1) such that age was the metric of change. These documented procedures\textsuperscript{20} produced a 40-year
FIGURE 1  Variability in episodic memory level and change. We observed extensive variability in memory performance (Y-axis) and change in the current sample of older adults (n = 580) across a 40-year band of aging (53 to 97 years; X-axis). The black lines portray individualized memory trajectories. The red line is the latent growth curve representing the best-fitting function for the memory trajectory distribution.

2.2 Measures

As per VLS design and procedures, all memory tasks and SMD items described below were administered at each wave to all returning participants.

2.2.1 Episodic memory

The VLS used standard episodic memory tasks consisting of: the VLS word recall, the Rey Auditory Learning task, and the Benton Facial Recognition task (see supporting information). All tasks were used in developing the one-factor episodic memory latent variable (Table S1 in supporting information).

2.2.2 Subjective memory decline

We initially defined and examined four facets of self-perceived decline in memory: (1) memory complaints, (2) memory concerns, (3) memory compensation, and (4) memory self-efficacy. We used two established memory beliefs inventories to derive the present SMD indicators. The Metamemory in Adulthood (MIA) questionnaire is a 108-item instrument measuring eight facets of metamemory (including memory beliefs, affect, and knowledge) as relevant to aging. The Memory Compensation Questionnaire (MCQ) is a 45-item instrument which measures awareness and use of everyday memory techniques.
by older adults. Three independent researchers selected items from the MIA and MCQ for their potential to reflect the targeted SMD facets, establishing initial face and consensual validity. Both psychometric validity (eg, item-total correlations) and factorial validity (eg, confirmatory factor analysis [CFA] loadings) were also examined to confirm the selected items and facets. See Table S2 in supporting information for further details. All items (Table 2) were in 5-point Likert-scale format and coded so that higher scores indicated worse SMD.

Memory Complaints (Facet 1): The first standard SMD facet reflects whether one believes that their memory has declined with time. Typically, this facet is represented by a single item (eg, “Do you feel like your memory is becoming worse?”). This subscale included three items.

Memory Concerns (Facet 2): The second standard SMD facet reflects the extent to which one is worried about one’s decline in memory performance. This subscale included seven items.

Memory Compensation (Facet 3): This SMD facet refers to the scenario in which awareness and concerns regarding memory failures could lead to differential efforts to compensate for memory decline and enhance memory performance. This subscale included five items.

Memory Self-Efficacy (Facet 4): This SMD facet refers to beliefs about overall mastery of everyday memory decline or specific ability to manage memory change and continue effectively using memory in life situations. This subscale included four items.

Note. Abbreviations: APOE, apolipoprotein E; CES-D, Center for Epidemiologic Studies-Depression scale; MMSE, Mini-Mental State Examination; NEO-Anxiety, NEO Personality Inventory – Anxiety Subcategory Score.

2.3 Statistical analyses

2.3.1 Foundational analyses

Modeling Plan and Fit. CFA and invariance testing in Mplus 8.2 was used to establish the best fitting longitudinal model of both episodic memory...
and SMD. Model fit for all analyses was determined using standard fit indices: (1) a non-significant $\chi^2$ indicating a good fit; (2) comparative fit index (CFI) for which $\geq 0.95$ is a good fit and values between 0.90 and 0.94 an adequate fit; (3) root mean square error of approximation (RMSEA), for which a value $\leq 0.05$ would be considered good fit and between 0.06 and 0.08 would be considered adequate fit; and (4) standardized root-mean-square residual (SRMR) for which a value of $\leq 0.08$ is considered good fit. We also tested longitudinal measurement invariance for both episodic memory and SMD to establish construct equivalence across time prior to examining performance and change characteristics (see supporting information).

Episodic Memory Model. A one-factor episodic memory model fit the data well and partial scalar invariance was observed (Table S1).

Subjective Memory Decline Model. From the four objectively defined facets (Table 2), the four-facet model of SMD was found to fit the data well and residual invariance was observed (Table S1).

Missing Data. For all test-level variables, missing data rates across all waves were low: below 5%, except for W3 of the Rey Auditory Learning Test for which testing error occurred. Similarly, the observed retention rates were high: 81.7% for W1-W2, and 82.7% for W2-W3. We followed a recommended protocol for estimating missing data, which uses maximum likelihood estimation methods to allow for the inclusion of data from all participants, even those with missing data for subsequent waves. See supporting information (1.4) for missing data description and protocols.

2.3.2 | RG 1: Latent growth modeling of episodic memory and SMD

LGM was used to investigate variability and change in episodic memory and the four SMD subscales. A centering age of 75 years represented level, as it is the approximate middle point of the 40-year band of data and is a relevant inflection age in non-demented memory aging. We tested four unconditional growth models: (1) a fixed intercept model, representing no interindividual or intraindividual variation; (2) a random intercept model, which assumes interindividual variability, but no intraindividual change; (3) a random intercept fixed slope model, which also assumes interindividual variation in level, with all individuals changing at the same rate; and (4) a random intercept random slope model, which assumes interindividual variation in level and change. A significant chi-square difference test was used to select the best fitting model.

2.3.3 | RG2a: Prediction of episodic memory level and change by SMD facets

For the first part of the second research goal, we used CLGM to investigate SMD facet predictions of memory performance (level) and change (slope). All factor scores were independently calculated and used in subsequent analysis models. All four SMD facets were included in the LGM to control for the effects of other SMD facets in facet-specific predictions.

2.3.4 | RG2b: Prediction of episodic memory level and change by SMD facet and sex

The previous CLGM was stratified by sex to test sex moderation using the $D$ statistic. A significant $D$ would indicate that a model constraining males and females across intercepts and slope was significantly worse than an unconstrained model.

3 | RESULTS

3.1 | RG1: Latent growth modeling of episodic memory and SMD

Episodic memory performance showed interindividual variability in level ($b = 15.72$ [13.26, 18.17], $P < .001$) and slope ($b = 0.03$ [0.02, 0.03], $P < .001$; Table S3 in supporting information). The four-facet model of SMD also showed significant interindividual variability in level ($b = 0.09$ [0.07, 0.1], $P < .001$) and slope ($b < 0.001$, $P < .001$; Table S4 in supporting information), but the effects of slope were non-significant. As slope was not significant, SMD level was used in subsequent prediction analyses. See Table S5 in supporting information for means and distribution information for episodic memory and SMD.

3.2 | RG2a: Prediction of memory level and change by SMD facet

First, higher memory complaints predicted lower memory performance ($b = -1.20$ [−0.3, 2.1], $P = .007$) and change ($b = -0.06$ [−0.02, −0.1], $P = .003$). Second, higher concerns predicted lower memory level ($b = -0.98$ [−0.2, −1.8], $P = .02$) and steeper decline ($b = -0.05$ [−0.01, −0.08], $P = .01$). Third, more memory compensation predicted less memory decline ($b = 0.11$ [0.2, 0.1], $P = .03$). The memory self-efficacy facet was not associated with memory level or change.

3.3 | RG2b: Prediction of memory level and change by SMD facet and sex

Using stratified CLGMs, we observed several sex-specific SMD facet-memory predictions ($D = 105.80$, $P < .001$). Complaints: The complaints prediction of steeper memory decline was significant for females only ($b = -0.05$ [−0.01, −0.1], $P = .04$). Concerns: Although more memory concerns predicted lower memory level for both females ($b = -1.23$ [−0.13, −2.3], $P = .03$) and males ($b = -1.40$ [−0.33, −2.5], $P = .01$), the prediction of steeper decline was significant only for females ($b = -0.06$ [−0.01, −0.1], $P = .01$). Self-Efficacy: Selectively for males, lower memory self-efficacy predicted both lower memory level ($b = 2.13$ [0.17, 4.0], $P = .03$) and
steeper decline ($b = 0.14 [0.04, 0.25], p = .008$). Compensation: The compensation prediction of memory decline for the overall sample did not appear by sex.

4 | DISCUSSION

This study explored whether the two established SMD facets of complaints and concerns$^{1,5,15}$ could be (1) replicated with existing inventory data in the VLS and (2) usefully supplemented by selected facets of subjective memory aging, as reported in neighboring literatures (eg, memory beliefs, strategies, and compensation)$^{17,24}$ We empirically confirmed four facets to establish the VLS SMD Inventory. The principal goals were to (1) investigate variability and change in episodic memory and SMD, (2a) explore SMD facet prediction of episodic memory change across 40 years of non-demented aging, and (2b) test potential sex-specific associations of SMD facets and memory level and change.

For the first goal, we confirmed a significant random intercept, random slope LGM for both memory and SMD. The longitudinal memory results replicated other studies with similar samples,$^{21}$ showing variability in memory trajectory patterns, including rate of decline. The SMD results also demonstrated significant variability in both level and change, revealing varying trajectories of subjective memory. Previous studies have reported similar variability in complaints among cognitively normal$^{16,45}$ and cognitively impaired$^{46}$ older adults. Overall, the substantial heterogeneity in longitudinal trajectory patterns provided a platform for the remaining research goals.

For the second goal, we used CLGM to test SMD facet predictions of memory level and change.$^{14,17,40}$ Regarding the traditional SMD facets, both greater complaints and concerns predicted lower memory level and steeper decline. Previous studies reported similar significant associations, but with the combination of memory complaints and concerns.$^{5,6,11}$ Our results show that these predictions of memory decline can be detected with both facets independently. Regarding the novel facets, higher levels of memory compensation activities predicted shallower memory decline trajectories. Awareness of everyday memory decline can lead not only to worries and further decline but also recruitment and deployment of memory compensation techniques.$^{22,27,40}$ Arguably, this compensation phenomenon is the other side of the SMD coin: producing a beneficial aspect in asymptomatic memory aging. As such, memory compensation may be a behavioral mechanism underlying cognitive resilience or reserve.$^{27,31}$ To be sure, not all compensation efforts are equally effective and not all effective techniques are marshalled productively. How memory compensation fits in the larger construct of SMD—and whether it may be a dynamic resource for reducing or counter-balancing complaints and concerns—requires further research. Given the memory compensation prediction finding, future research might also focus on the role of executive function as a potential mediator of associations between compensation use and memory decline.

In the sex stratification analyses, we found several instances of significant moderation by sex on SMD-related memory predictions. Most notably, for the two established facets, we observed that the above-noted prediction effects operated selectively for females. To date, attention to sex- or gender-related aspects of memory complaints and related clinical or cognitive outcomes have appeared infrequently and results have been mixed.$^{33,47}$ Our results extend longitudinal findings in which complaints were associated with increased dementia risk over a 15-year follow-up period for females only.$^{35}$ Potential interpretations include both sex and gender considerations. Females may be more sensitive to changes in cognition due to social role differences (ie, health-care gatekeeper for themselves and their family) and biological differences (ie, post-menopausal estrogen changes associated with more rapidly declining memory), leading to a more accurate appraisal of current (and accumulating) memory deficits.$^{35}$

Regarding the second standard SMD facet, increased concerns predicted both lower memory level and steeper decline in females, but only lower level in males. These results qualify the full-sample pattern noted above, consistent with some previous reports that did not test for sex differences.$^{1,11,48}$ Sex-specific memory concerns prediction patterns of objective memory have not been previously reported. However, one study reported that females with SMD concerns had increased all-cause dementia risk, but males did not.$^{52}$ The connection to our results is that accelerated memory decline often precedes AD diagnosis.$^{19}$

Memory self-efficacy did not predict memory performance for the full sample, but produced notable sex differences. For aging males only, a lower sense of memory mastery was associated with lower memory levels and steeper decline. One parallel result showed that higher instrumental self-efficacy was associated with better verbal memory performance (2.5 years later) in males only.$^{59}$ Although memory self-efficacy has been studied in related literatures, it has not been widely connected to SMD or the differentiating role of sex. In contrast, memory compensation predicted memory decline only in the full sample, not separately or differentially by sex. Previous research has illustrated the promise and complexity of compensation-cognition associations.$^{24,25,27,40}$

Our models were conducted such that the effects of each facet were covaried for the effects of the other facets. In a post hoc check, we included two additional baseline covariates; education (years) and depression (Center for Epidemiological Studies-Depression score). There were no changes to prediction patterns in the overall prediction models (RG2a), with minor changes in the sex-stratified analyses (RG2b). For females, controlling for education resulted in minor changes to memory level predictions (memory complaints now predicted level; memory concerns no longer predicted level). Controlling for depression resulted in memory complaints no longer predicting decline. For males, controlling for education removed the previous effects of memory self-efficacy on memory level or decline. We recommend further investigation of these and other potential influences on SMD and memory associations.

Although the two traditional facets of SMD have been confirmed as leading components of subjective awareness and beliefs about emerging cognitive deficits in asymptomatic aging, we have observed an important qualification and extension. The qualification is that our prediction models revealed potentially important sex differences in
strength of the association with longitudinal memory change. The extension is that two complementary aspects of SMD (memory self-efficacy and compensation) were found to play contributing roles in determining memory performance and change. As noted earlier, observers have proposed that, because of its conceptual heterogeneity, systematically varying formats and approaches of SMD may aid in optimizing its measurement, validation, and application.15,16

There were several strengths and limitations to this study. First, VLS participants are relatively educated and healthy at intake and the present sample was selected to be cognitively normal (asymptomatic for AD). Although not entirely representative of a broad population of older adults, this sample may reflect a growing and independent subset of aging adults in developed nations; therefore, the potential range of generalizability may extend to asymptomatic older adults in these regions. Second, our original study plan included a fifth possible SMD facet of memory anxiety. However, this facet was not separable from the standard memory concerns facet in initial analyses. Conceivably, in a more memory impaired group, a higher degree of concern (ie, anxiety) may be discriminable from concerns and worries. Upon review of the SMD items and the latent SMD model, the memory concerns and memory anxiety latent factors were highly correlated at each of the three waves (r range = 0.77 to 0.93) and were combined into one facet for the present analyses. Third, we note that the memory compensation facet demonstrated relatively lower internal reliability.50 However, our subsequent analyses established optimal model fit for a four-factor latent structure of SMD, residual invariance across time, as well as satisfactory indicator variable loadings onto the four facets (> 0.4). Fourth, we tested baseline SMD facet level (not change) as a predictor of memory change. The four-factor SMD model produced non-significant slope effects, thus precluding the use of SMD change as a predictor. Among the strengths of this study is, first, indicators for both episodic memory and SMD were from well-established inventories that contributed to two latent variables deployed in longitudinal analyses. Second, we achieved greater breadth of coverage using a multi-faceted approach to SMD. Our approach reflects the reported heterogeneity in the conceptualization and etiology of SMD.15,16 Third, our sample was reasonably large and our application of age as the metric of change effectively co-varied age in all analyses.21 The research design allowed analyses to be conducted across a 40-year band of aging (53 to 97 years).

In sum, the main research goals were (1) to develop a multi-facet SMD inventory in the context of an existing longitudinal data base and (2) to test SMD facet predictions of memory change within the entire sample and as stratified by sex. The full sample results demonstrated significant variability in both memory and SMD. The SMD memory prediction analyses were qualified by several sex-specific results. Memory complaints, memory concerns, and memory self-efficacy demonstrated sex-specific prediction of memory trajectories. The traditional facet of memory complaints predicted memory change in females only. Memory concerns predicted memory level across sex groups but predicted memory change in females only. Results indicated that two novel facets of SMD may supplement traditional approaches to SMD among certain groups. Overall, the present results pertain to relatively normally aging older adults and extend into very late life. However, they also point to the importance of the investigation of these facets and predictive associations in more cognitively diverse or even at-risk or impaired groups. Subjective memory decline may indicate early changes in memory function that are (initially) undetectable using objective neuropsychological testing but that nevertheless vary by sex, providing an early opportunity for precision risk assessment and personalized attention.

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SUPPORTING INFORMATION
Additional supporting information may be found online in the Supporting Information section at the end of the article.

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