

Title: Are subjective memory complaints indicative of objective cognitive decline or depressive symptoms? Findings from the English Longitudinal Study of Ageing

Abstract

Older adults often complain about their memory ability, but it is not clear to what extent subjective memory complaints accurately reflect objective cognitive dysfunctions. The concordance between objective and subjective cognitive performance may be affected by depressive symptoms and by declining insight into cognitive deficits. This study aims to examine longitudinal associations between subjective memory complaints, objective cognitive performance and depressive symptoms. 11,092 participants aged 50 years and above from the English Longitudinal Study of Ageing were followed-up every 2 years over a 6-year period. Two processes latent growth curve models (LGCM) examined associations between levels and changes in several cognitive abilities and subjective memory complaints, unadjusted for depression symptoms. Then three processes LGCM examined associations between levels and changes in depressive symptoms, subjective memory complaints and objective cognitive abilities in the overall sample, and separately among persons with mild cognitive impairment at baseline. More subjective memory complaints were associated with poorer performance in all cognitive domains at baseline. Steeper decline in immediate recall, verbal fluency and processing speed performance was associated increasing subjective memory complaints both in the overall sample and among persons with mild cognitive impairment. Increasing depressive symptoms were associated with both objective and subjective cognitive decline in the overall sample, and only with subjective memory decline among cognitively impaired persons. Self-reported memory complaints may have the potential to identify decline in objective cognitive performance that cannot be explained by depressive symptoms. Among cognitively impaired persons depressive symptoms may amplify subjective but not objective cognitive decline.

Are subjective memory complaints indicative of objective cognitive decline or depressive symptoms? Findings from the English Longitudinal Study of Ageing

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Introduction

The topic of subjective memory complaints is of major interest in current research on cognitive aging and dementia. Subjective memory complaints are reported by 25% to 50% of community-dwelling older adults (for a review see Jonker et al., 2000), and the prevalence of such complaints increases with advancing age (Montejo et al., 2011). Memory complaints are associated with neuroimaging biomarkers of amyloid- β and neurodegeneration (Amariglio et al., 2015), and they predict an increased risk of dementia before cognitive dysfunctions are detected by objective cognitive tests (Jessen, 2014; Jessen et al., 2010). Even single-item measures for subjective memory complaints have been shown to predict objective memory dysfunctions, cortical thinning in brain regions affected by Alzheimer's Disease (AD) (Schultz et al., 2015), and an increased risk of late-onset AD (Geerlings et al., 1999).

Understanding the interplay between objective and subjective cognitive function could have important implications for the early identifications and treatment of persons at risk for cognitive impairment and dementia. According to meta-analytic evidence, cross-sectional associations between subjective memory complaints and objective memory performance are of low magnitude (Beaudoin and Desrichard, 2011; Crumley et al., 2014), suggesting that older adults do not make accurate evaluations of their cognitive performance. A first explanation for this finding is that older adults may use different comparison standards to rate their current cognitive performance. It was suggested that the use of repeated measures of subjective memory complaints could help older adults calibrate current subjective memory ratings against their previous ratings, leading to more accurate evaluations of their memory performance (Zimprich et al., 2003). Consistent with this hypothesis, some studies found that the association between changes in objective cognitive performance and changes in subjective memory complaints was two to four times larger than the association between baseline levels of these

processes (Mascherek and Zimprich, 2011; Parisi et al., 2011; Zimprich et al., 2003). However, this trend may be absent in the oldest old (Pearman et al., 2014).

Second, the discordance between objective and perceived cognitive performance may reflect declining insight into cognitive performance among persons with cognitive dysfunctions. Consistent with this interpretation, some findings suggest the presence of anosognosia for cognitive deficits among older adults with mild cognitive impairment (MCI) (Galeone et al., 2011; Vogel et al., 2004), and mild AD (Kalbe et al., 2005). Among the few studies that examined bi-directional prospective associations between subjective and objective cognition findings are mixed, leaving an unresolved question about the longitudinal concordance or discordance between these processes. Persons with poorer initial objective memory performance experienced either an increase in subjective memory complaints, suggesting subjective-objective concordance (Jorm et al., 2001), or a decrease in subjective memory complaints, suggesting subjective-objective discordance (i.e., declining insight into memory deficits) (Snitz et al., 2015). As for the opposite direction of the effect, more initial memory complaints predicted faster decline in objective memory performance (Jorm et al., 2001), language and executive function performance (Snitz et al., 2015), suggesting subjective-objective concordance. The concordance or discordance between subjective and objective cognition may depend on the cognitive abilities assessed (Snitz et al., 2015).

Third, the relation between objective cognitive performance and subjective memory complaints may be influenced by depressive symptoms. Depression has been consistently associated with both subjective memory complaints (for a review see Jonker et al., 2000) and objective cognitive dysfunctions in late life (e.g., Baudic et al., 2004; Brailean et al., 2016; Comijs et al., 2001; Koenig et al., 2014; Lockwood et al., 2002; Morimoto and Alexopoulos, 2013; Sheline et al., 2006). It was suggested that subjective memory complaints may be more indicative of depressive symptoms than of objective cognitive dysfunctions (Burmester et al.,

2016; Reid and Maclullich, 2006). If subjective cognitive complaints had an affective aetiology, then depressive symptoms may account for the association between objective and subjective cognitive function. A study by Zimprich et al. (2003) found that changes in subjective memory complaints were associated with both changes in objective cognitive performance and changes in depressive symptoms, but the study was limited by the availability of only two assessment occasions. More longitudinal studies are needed to understand the interplay between the trajectories of depressive symptoms, objective cognitive abilities, and subjective cognitive complaints.

The primary aim of this study is to examine associations between levels and changes in several cognitive abilities (i.e., immediate recall, delayed recall, processing speed and verbal fluency) and subjective memory complaints in community dwelling older adults. Consistent with previous reports, we expect steeper decline in objective cognitive performance to be associated with increasing subjective memory complaints over time. We also expect that more initial subjective memory complaints would predict faster decline in objective cognitive performance, and that poorer baseline cognitive performance would predict an increase in subjective memory complaints over time. Additionally, we explore whether persons with probable mild cognitive impairment at baseline show fewer cognitive complaints over time, reflecting declining awareness into cognitive deficits. Secondly, this study aims to examine the role of depressive symptoms in the relation between subjective memory complaints and objective cognitive abilities. If subjective memory complaints are more indicative of depressive symptoms than of objective cognitive dysfunctions, then accounting for depressive symptoms should reduce the strength of the associations between levels and changes in subjective memory complaints and objective cognitive abilities.

Materials and methods

Participants

Data were taken from the English Longitudinal Study of Ageing, an ongoing study exploring physical, emotional, cognitive, social and economic functioning in later life in a nationally representative sample of the English population (Stephoe et al., 2013). Ethical approval for all data collection was granted by the NHS Research Ethics Committees under the National Research and Ethics Service, and all participants provided informed consent. The ELSA sample was broadly representative of the English population, as suggested by a socio-demographic profile comparable to that of the national census. The baseline sample was drawn from the 1998, 1999 and 2001 Health Surveys for England (HSE) and it included participants born before 1 March 1952, living in a private household in England from HSE, who had given their consent to follow-up. Individual response rates were 67%, consisting of N=11391 core members aged 50 and above who were included in the current study. This sample undertook baseline assessments in 2002-2003, followed by three follow up assessments: 2004 - 2005 (wave 2), 2006 – 2007 (wave 3), and 2008 – 2009 (wave 4).

Measures

Episodic memory was assessed using the Ten-Word Delayed Recall Test. Ten words were presented and the number of words recalled immediately was used as a measure of immediate recall, whereas the number of words recalled after a five-minute interval was used as a measure of delayed recall. Scores for immediate recall and delayed recall could each range from 0 to 10, with higher scores indicating better performance.

Verbal fluency was assessed using the animal naming task requiring participants to name as many animals as possible within one minute. Scores ranged from 0 to 50, with higher scores indicating a higher number of animals named. This task is thought to measure executive

functioning, although processes such as semantic memory and language ability are also involved (Abwender et al., 2001; Henry and Phillips, 2006).

Processing speed was assessed using a Letter Cancellation Task. Participants were given a clipboard to which was attached a page of 780 random letters of the alphabet set out in a grid. They were asked to cross out as many of the 65 target letters (P and W) as possible in 1 minute, and to perform the task as quickly and accurately as possible. The average score for the number of target letters correctly identified (0 to 65) was used as a measure of processing speed, with higher scores indicating better performance.

Subjective memory was assessed by asking participants to rate their current memory ability on a 5-Likert scale, where 1 = poor memory, 2 = fair memory, 3 = good memory, 4 = very good memory, and 5 = excellent memory.

Depressive symptoms were assessed using the sum of 8 binary yes-no items drawn from the Center for Epidemiological Studies-Depression Scale (CES-D) (Radloff, 1977). The 8-item version of CES-D (i.e., felt depressed, was happy, felt lonely, enjoyed life, felt sad, everything was an effort, restless sleep, could not get going) is a reliable and valid instrument for assessing depressive symptoms in older adults (Karim et al., 2015). The total score ranged from 0 to 8, with a higher score indicating more depressive symptoms.

Statistical analysis

Univariate latent growth curve models (LGCM)

First, univariate LGCM, as a function of time in study, were fitted independently for each outcome measure (i.e., subjective memory, immediate recall, delayed recall, verbal fluency, processing speed and depressive symptoms). Univariate LGCM examined:

- a) the baseline level of the outcome measure (i.e., intercept);

- b) the rate of outcome change (i.e., slope) and its form (i.e., linear or non-linear);
- c) the correlation between the initial level of the outcome and the rate of change in the outcome (e.g., persons who start off with poorer memory performance show steeper decline in memory performance over time);
- d) the effects of baseline covariates on the intercept and slope of each outcome.

In our models the intercept of each outcome measure was centred at baseline (2002-2003) and a linear form of the latent growth trajectory was tested. The slope of the growth factor is a random effect that can vary between individuals, and it represents changes in each outcome measure over 6 years of follow-up. Individuals were assessed at roughly the same intervals (every 2 years). Intercepts and slopes of all outcome measures were adjusted for baseline age (in years), gender and level of education. Age was centred at its mean value (65.3 years) to help with model estimation and with the interpretation of the estimates. Education was included as a categorical variable, where 1 = no educational qualification; 2 = secondary education (i.e., Certificate of Secondary Education; General Certificate of Education (GCE) Ordinary Level; GCE Advanced Level); 3 = tertiary education (i.e., higher education below degree; completed degree). Of note, the no qualification category includes persons who left school without any formal qualifications. Schooling in England was made compulsory for children up to 14 in 1918, and school leaving age remained at 14 until 1947. The first qualification in that period was the School Certificate, but this was usually taken at age 16, after many people had left school, hence the relatively high percentage of persons without a formal qualification.

Two processes LGCM

After determining the form of the trajectory and ensuring good model fit in univariate LGCM, two processes LGCM were fitted to examine associations between levels and changes in subjective memory ratings and each objective cognitive ability. In addition to the parameters

estimated in univariate LGCM models, parallel processes LGCM models simultaneously estimated:

- a) cross-sectional associations between subjective memory and each objective cognitive ability at baseline;
- b) the prospective effect of baseline subjective memory on changes in each cognitive ability;
- c) the prospective effect of each baseline cognitive ability on changes in subjective memory;
- d) parallel associations between changes in subjective memory and changes in each cognitive ability.

All models were adjusted for age, gender and education.

Three processes LGCM

Finally, we conducted three processes LGCM models to examine the pattern of associations between levels and changes in subjective memory, depressive symptoms and each objective cognitive ability, adjusting for age, gender and education. An example of three processes LGCM is presented in Figure 1. In addition to the parameters estimated in univariate LGCM models, three processes LGCM models simultaneously estimated:

- a) cross-sectional associations between subjective memory, each cognitive ability, and depressive symptoms at baseline;
- b) the prospective effect of baseline subjective memory on changes in each cognitive ability and changes in depressive symptoms;
- c) the prospective effect of baseline cognitive ability on changes in subjective memory and changes in depressive symptoms;
- d) the prospective effect of baseline depressive symptoms on changes in subjective memory and changes in each cognitive ability;

- e) parallel associations between changes in subjective memory, changes in each cognitive ability, and changes in depressive symptoms.

All LGCM analyses were conducted in MPlus Version 7.2 (Muthén and Muthén, 1998–2012). Maximum Likelihood Robust (MLR) estimation was used for all models. MLR is considered to produce unbiased estimates under the missing at random (MAR) assumption (Little and Rubin, 1987). Model fit was evaluated based on the model Chi-square with a *p* value above 0.05 indicating good model fit (Hu and Bentler, 1999); the comparative fit index (CFI) (Bentler, 1990) and the Tucker Lewis index (TLI) (Tucker and Lewis, 1973) with values above 0.95 indicating good fit; the root mean square error of approximation (RMSEA) (Steiger, 1990) with values below 0.06 indicating good fit.

Several sets of sensitivity analyses were conducted based on the final three processes LGCM models. A first set of models was estimated in the overall sample after additionally adjusting for potential confounders selected on the basis of previous research (Blazer, 2003; van den Kommer et al., 2013), and included as binary variables: longstanding illness (reporting a longstanding illness, disability or infirmity that limits daily activities – yes/no), smoking status (ever smoker/never smoker), loneliness (feeling lonely most of the time for the past week – yes/no), physical activity (participating in sports or physical activity of moderate intensity at least once a week – yes/no), alcohol consumption (drinking alcohol daily – yes/no). A second set of models was conducted in the subsample with probable mild cognitive impairment, as defined by a score of at least 1 standard deviations below the sample mean on any cognitive task at baseline (N=3421). These models were also re-estimated after excluding persons with baseline dementia. A third set of models was estimated in the subsample with normal cognition at baseline.

Results

Descriptive statistics

The flow chart of the study sample is presented in Supplementary Figure 1. Participants were aged 50 years and above, with a mean age of 65.3 at baseline. Females represented 57% of the study sample. About 43% of participants had no education qualification, 35% had primary or secondary education, and 22% had tertiary education. About 33% of participants rated their memory as poor or fair. Mean depression scores in the overall sample were $M = 1.61$, $SD = 2.00$, and only 17% of respondents endorsed 4 or more symptoms on the 8-item version of CES-D, indicating probable clinical depression (Steffick, 2000). The rates of physician diagnosed dementia, as reported by participants or informants, were: $N = 63$ (0.6%) at baseline; $N = 82$ at wave 2; $N = 125$ at wave 3; $N = 146$ at wave 4 (including new and continuing cases). About 30% of participants ($N = 3446$) scored below 1SD on at least one cognitive task at baseline and were considered as having probable mild cognitive impairment. About 28% of persons with normal cognition, 42% of those with probable mild cognitive impairment, and 85% of those with dementia rated their memory as “poor” or “fair” (with the remaining rating their memory as “good”, “very good”, or “excellent”). Baseline depression scores were significantly higher ($t = -19.20$, $p < 0.001$) among persons who rated their memory as poor or fair ($M = 2.12$, $S.D. = 2.23$) compared to persons who rated their memory as good, very good or excellent ($M = 1.36$, $S.D. = 1.82$). Dropout was associated with female gender, older age, lower levels of education, more depressive symptoms, more subjective memory complaints and poorer objective cognitive performance at baseline (see Supplementary Table 1).

Univariate LGCM

Results presented in Table 1 are based on univariate LGCM fitted separately for subjective memory, each objective cognitive ability, and depressive symptoms in the overall

sample. All models were adjusted for age, gender and education. Univariate models testing linear change for each outcome measure showed very good fit: CFI \geq 0.98, TLI \geq 0.98, RMSEA \leq 0.03 (90 % CI [0.02, 0.03]). Observed and estimated means for each outcome measure are plotted in Supplementary Figures 1-6. The slopes of subjective memory and all cognitive abilities were negative and statistically significant, indicating decline in all cognitive abilities as well as in subjective memory ratings (i.e., increasing memory complaints) over time. The negative slope of depressive symptoms indicates an amelioration of depression symptoms over time. The variance of the intercept and slope of each outcome measure was statistically significant, indicating inter-individual differences in initial levels and rates of change. Significant negative correlations between intercept and slope were found for subjective memory, processing speed, and depressive symptoms, indicating that participants with higher baseline scores showed more decline over time in each outcome measure, which may reflect an effect of regression to the mean. Findings from the univariate model for subjective memory suggest that males showed more memory complaints at baseline ($\beta = 0.04$, S.E. = 0.01, $p < 0.01$) and over time ($\beta = 0.07$, S.E. = 0.03, $p < 0.01$). Older age was associated with increasing subjective memory complaints over time ($\beta = -0.15$, $p < 0.01$), and higher educational attainment was associated with fewer subjective memory complaints at baseline (secondary education qualification vs. no qualification: $\beta = 0.10$, S.E. = 0.01, $p < 0.001$; tertiary education versus no education: $\beta = 0.17$, S.E. = 0.01, $p < 0.001$).

Two processes LGCM

Supplementary Table 2 shows findings from two processes LGCM examining the associations between subjective memory and each objective cognitive ability, adjusting for age, gender and education. All models fitted the data well: CFI \geq 0.98, TLI \geq 0.98, RMSEA \leq 0.02 (90 % CI [0.01, 0.03]). With respect to cross-sectional associations, lower baseline levels of

subjective memory were associated with lower baseline levels of immediate recall, delayed recall, verbal fluency, and processing speed. With respect to parallel longitudinal associations, steeper decline in subjective memory was associated with steeper decline in immediate recall, verbal fluency, and processing speed. Regarding prospective associations, the intercept of subjective memory was significantly associated with the slopes of immediate and delayed recall; given that the slopes of both immediate recall ($B < 0.01$; S.E. = 0.02; $p = 0.97$) and delayed recall ($B = 0.02$; S.E. = 0.02; $p = 0.45$) were positive in these models, the findings indicate that persons with higher baseline subjective memory ratings (i.e., fewer complaints) showed less subsequent improvement (i.e., practice effects) in immediate and delayed recall performance. As for the opposite direction of the effect, there was a significant positive association between the intercept of delayed recall and the slope of subjective memory; given that the slope of subjective memory was negative in this model ($B = -0.08$; S.E. = 0.01; $p < 0.001$), the findings indicate that persons with better initial delayed recall performance showed less decline in subjective memory ratings over time (i.e., fewer complaints).

Three processes LGCM

Table 2 presents findings from three processes LGCM that simultaneously estimated associations between levels and changes in subjective memory, each objective cognitive ability, and depressive symptoms in the overall sample. All models fitted the data well: CFI ≥ 0.99 , TLI ≥ 0.99 , RMSEA ≤ 0.02 (90 % CI [0.01, 0.02]). The pattern of associations between subjective memory and objective cognitive abilities remained the same when simultaneously modelling their associations with levels and changes in depressive symptoms. With respect to cross-sectional baseline associations, higher depressive symptoms were associated with more subjective memory complaints, as well as poorer performance in all cognitive domains. With respect to parallel longitudinal associations, a higher increase in depressive symptoms was associated with steeper decline in subjective memory ratings (i.e., increasing complaints), as

well as steeper decline in immediate and delayed recall performance. As for prospective associations, the intercept of depressive symptoms was negatively associated with the slopes of verbal fluency; given that the slope of verbal fluency was negative ($B = -0.07$; $S.E. = 0.08$, $p = 0.42$) in this model, these findings indicate that persons with higher initial depressive symptoms showed more decline in verbal fluency. The intercept of depressive symptoms was also negatively associated with the slope of delayed recall; given that the slope of delayed recall was positive ($B = 0.04$; $S.E. = 0.03$; $p = 0.11$), these findings suggest that persons with higher baseline depressive symptoms showed less improvement in delayed recall (i.e., practice effects). The intercepts of verbal fluency and immediate recall were positively associated with the slope of depressive symptoms; given that the slope of depression was negative in both models (model 1: $B = -0.14$; $S.E. = 0.03$; $p < 0.001$; model 4: $B = -0.11$; $S.E. = 0.03$; $p < 0.001$), these findings indicate that persons with higher initial levels of verbal fluency or immediate recall showed less decline in depressive symptoms. The intercept of subjective memory ratings was positively associated with the slope of depressive symptoms only in the model that included processing speed (i.e. model 3); given that the slope of depressive symptoms was negative ($B = -0.08$; $S.E. = 0.03$, $p < 0.01$), these findings indicate that higher initial subjective memory ratings (i.e., fewer complaints) were associated with less decline in depressive symptoms. There was a significant positive association between the intercept of depressive symptoms and the slope of subjective memory in models that included immediate recall, delayed recall and verbal fluency; given the negative slope of subjective memory ($B = -0.09$; $S.E. = 0.02$; $p < 0.001$), these findings suggest that higher initial depressive symptoms were associated with less decline in subjective memory ratings (i.e., fewer complaints).

Sensitivity analysis results

Adjusting for additional confounders (i.e., longstanding illness, smoking, loneliness, physical activity, alcohol consumption) did not alter the pattern of findings from three processes LGCM, with the exception of the effects of baseline immediate recall and verbal fluency on changes in depression symptoms, and the effect of baseline depression symptoms on changes in verbal fluency, which were no longer statistically significant (results not presented).

Findings from three processes LGCM among persons with probable mild cognitive impairment at baseline (mean age = 70.7) are presented in Table 3. All models fitted the data well: CFI \geq 0.96, TLI \geq 0.95, RMSEA \leq 0.04 (90 % CI [0.03, 0.04]). The pattern of results was similar with findings in the overall sample, with the following exceptions: a) initial subjective memory ratings were no longer significantly associated with changes in immediate and delayed recall; b) initial depression symptoms were no longer significantly associated with changes in delayed recall and verbal fluency; c) initial immediate recall and verbal fluency were no longer significantly associated with changes in depressive symptoms; d) changes in depressive symptoms were no longer significantly associated with changes in immediate and delayed recall. The pattern of results remained the same when excluding persons with baseline dementia (N=63) from the subsample with probable MCI.

Three processes LGCM analyses conducted in the subsample of persons with normal cognition (N=7651) revealed a similar pattern of results as those conducted in the overall sample, with the following exceptions: a) higher initial depression symptoms predicted significantly steeper decline in immediate recall ($\beta = -0.14$, $p < 0.01$); b) better initial immediate recall performance was associated with fewer memory complaints over time ($\beta = 0.18$, $p <$

0.01); c) initial subjective memory ratings were no longer significantly associated with improvements in immediate recall (practice effects).

Finally, it should be noted that the LGCM analyses presented modelled subjective memory complaints (scores from 1 to 5) and depressive symptoms (scores from 0 to 9) as continuous variables, alongside objective cognitive abilities. This is because both subjective memory complaints and depression symptoms are ordered categorical variables with an underlying continuous concept; Shapiro-Wilk test suggests that the subjective memory variable is normally distributed at each wave; depression symptoms were not normally distributed, but MLR estimation is robust to non-normality. To ensure that our modelling approach did not affect substantive conclusions we compared the results from models that treated these variables as continuous with models that treated the variables as categorical. First, univariate models for subjective memory and depression symptoms as categorical variables were fitted using the Delta parameterization in Mplus following the method described by Wang and Wang (2012) (see pages 196-201). The thresholds of the categorical variables were held invariant over time to ensure the same metric over time. Then 3 processes LGCM models were fitted with subjective memory and depression symptoms as categorical outcomes and cognitive abilities as continuous outcomes. In summary, our findings suggest: *a*) a similar standardized coefficient of the subjective memory/depression symptoms slope (i.e., where the change in the slope is expressed in slope standard deviations); *b*) a similar effect of baseline predictors (i.e., age, gender, education, cognitive abilities) on changes in subjective memory/depression symptoms; *c*) a similar pattern of associations between slopes when modelling depression symptoms and subjective memory complaints as categorical versus continuous variables. Given that our modelling approach did not have a notable impact on the statistical significance, magnitude and directions of the effects, we conclude that our findings are robust.

Discussion

This study adds to the literature by clarifying the longitudinal interplay between subjective memory complaints, objective cognitive abilities, and depressive symptoms in a large nationally representative sample of older adults. We found that persons with poorer initial cognitive performance showed more initial subjective memory complaints. These associations were of small to moderate magnitude, consistent with recent meta-analytic findings (Burmester et al., 2016). Persons experiencing steeper decline in verbal fluency, processing speed and immediate recall showed increasing subjective memory complaints over time. Unlike previous studies (Mascherek and Zimprich, 2011; Parisi et al., 2011; Zimprich et al., 2003), we did not find a trend for stronger associations between changes in subjective memory complaints and changes in objective cognitive abilities compared to associations between baseline levels of these processes. Regarding prospective associations, persons with better initial delayed recall performance showed fewer memory complaints over time. Contrary to our expectations, persons with more initial subjective memory complaints did not experience faster decline in objective cognitive performance, which is at odds with evidence by Jorm et al. (2001). Our findings suggest that subjective cognitive complaints do not predict but rather accompany objective cognitive decline. Taken together, our findings build on previous evidence supporting the longitudinal concordance between levels and changes in subjective and objective cognition among community dwelling older adults (Hulur et al., 2014; Parisi et al., 2011; Zimprich et al., 2003).

The pattern of associations between subjective memory complaints and objective cognitive abilities did not change when simultaneously accounting for their association with levels and changes in depressive symptoms in three processes LGCM, and when additionally controlling for potential confounders. Our findings are consistent with findings by Snitz et al. (2008) and Zimprich et al. (2003), and with evidence suggesting that in population based

studies the correspondence between subjective and objective cognition is not affected by depressive symptoms (for a review see Burmester et al., 2016). Increasing depression severity was associated with steeper objective and subjective memory decline. Higher initial depression symptoms were associated with more verbal fluency decline, but fewer subjective memory complaints over time. In summary, subjective memory complaints accompany objective cognitive decline, whereas depression symptoms accompany both objective and subjective cognitive decline. These findings suggest that the co-occurrence of depression symptoms and subjective memory complaints may be attributable to objective cognitive decline.

Among persons with initial probable cognitive impairment, subjective memory complaints accompanied objective cognitive decline, suggesting preserved insight into cognitive functioning (Galeone et al., 2011; Vogel et al., 2004). Initial depression severity did not influence the rate of objective cognitive decline. Also, increasing depressive symptoms were associated with increasing subjective memory complaints, but not with objective cognitive decline. Taken together, these findings suggest that among cognitively impaired persons depression does not predict or accompany objective cognitive decline, but it may amplify the negative subjective evaluation of cognitive decline. Of note, the threshold for probable mild cognitive impairment (i.e., 1 SD below the sample mean on any cognitive task) was chosen to ensure adequate sample size needed to facilitate model convergence, but it may have only captured persons with mild cognitive dysfunctions.

Strengths of this study include the relatively large sample size, the longitudinal follow-up period, and the use of a complex modelling approach to examine the interplay between levels and changes in objective cognition, subjective memory complaints and depressive symptoms. This study has several limitations. First, subjective memory complaints were assessed using a single item measure and we lacked multidomain cognitive complaint measures. Our approach is consistent with evidence supporting the predictive value of single

memory complaint items for objective memory dysfunctions (Schultz et al., 2015), and evidence that subjective memory complaints indicate multiple cognitive dysfunctions beyond the memory domain (Benito-Leon et al., 2010; Minett et al., 2005; Snitz et al., 2008). However, future studies would benefit from including more comprehensive assessments of specific complaints in multiple cognitive domains (Rabin et al., 2015). Second, the presence of practice effects may have limited the absolute decline in cognitive abilities, although we consider practice effects to be insignificant given the relatively long interval between assessments (i.e., 2 years) and the use of different word lists for the memory task across follow-ups. Third, our models did not adjust for multiple testing, thus reducing the probability of failing to detect a true effect (i.e., type 2 error), but increasing the probability of detecting a false effect (i.e., type 1 error) (Gelman et al., 2012). We considered that correcting for multiple testing would be overly conservative in the context of LGCM given that each model simultaneously estimated multiple correlated parameters. Fourth, the high dropout rate (largely due to mortality) is a limitation inherent to longitudinal studies of ageing. Although we dealt with missing data using the maximum likelihood estimation under the missing at random assumption, findings may be affected by the selective dropout of older and less healthy individuals. Finally, our findings are not generalizable to clinical populations. Future research should clarify the predictive value of subjective memory complaints for cognitive decline and dementia among persons with clinically significant depressive symptoms.

In conclusion, this study found that subjective memory decline accompanies objective cognitive decline and both objective and subjective cognitive decline are associated with increasing depressive symptoms among community dwelling older adults. This suggests that self-reported memory complaints may have the potential to identify noticeable changes in objective cognitive performance that are not attributable to depressive symptoms. Depression

may amplify the negative subjective evaluation of cognitive decline among cognitively impaired persons.

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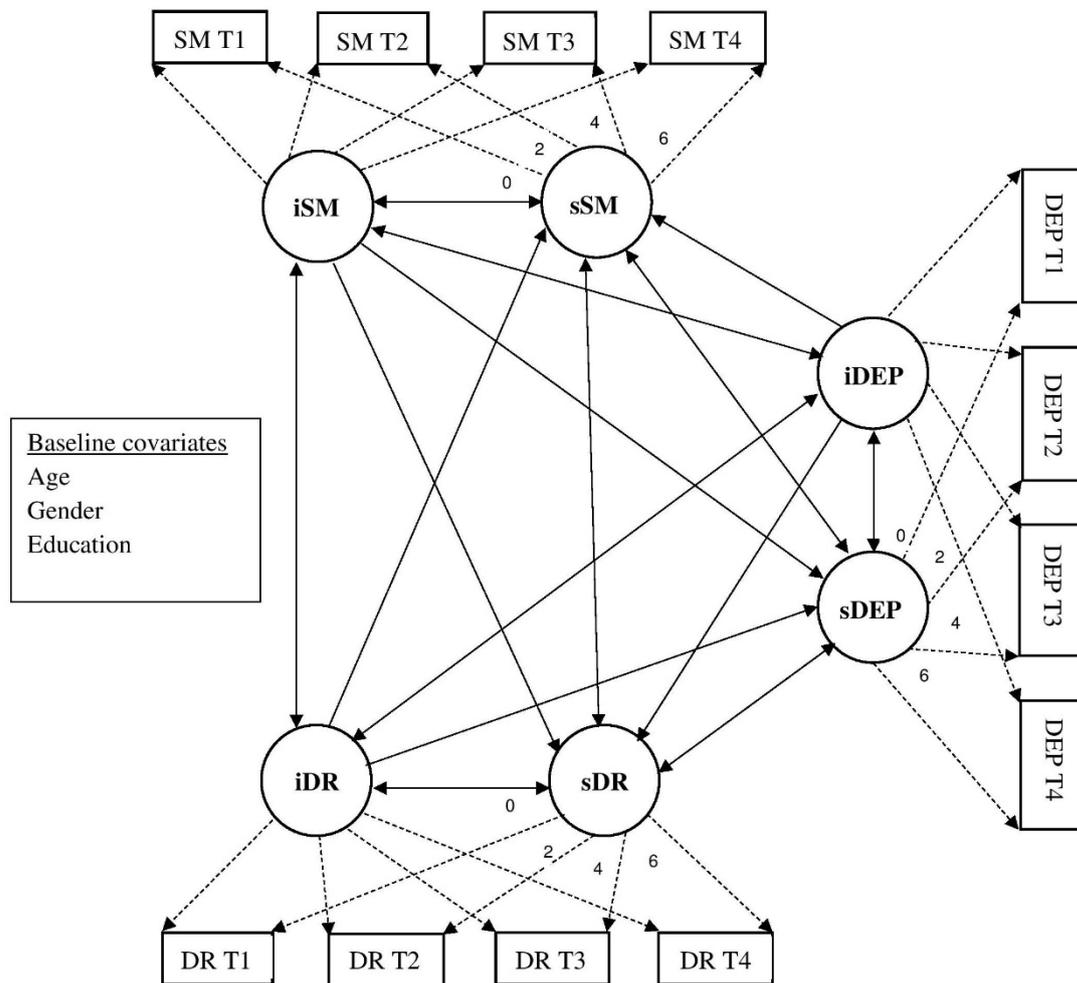
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Figure 1. LGCM model of the associations between subjective memory complaints, delayed recall performance and depressive symptoms



Note: Three processes LGCM illustrating cross-sectional, prospective and parallel associations between subjective memory complaints, objective delayed recall performance, and depressive symptoms. iSM = intercept of subjective memory; sSM = slope of subjective memory; iDR = intercept of delayed recall; sDR = slope of delayed recall; iDEP = intercept of depression; sDEP = slope of depression. Single-headed arrows represent regression effects. Double headed arrows represent correlations. All intercepts are centred at baseline. The slopes represent changes in each outcome measure over 6 years (with assessments conducted every 2 years). All intercepts and slopes were regressed on baseline age, gender, and education.

Table 1. Estimates for Univariate Latent Growth Curve Models

Measure	Intercept		Slope				Correlation of intercept and slope			
	Estimated mean	S.E.	Estimated variance	S.E.	Estimated mean	S.E.	Estimated variance	S.E.	r	S.E.
Subjective memory	2.72***	0.03	0.49***	0.01	-0.06***	0.01	<0.01***	<0.01	-0.30***	0.04
Immediate recall	4.42***	0.05	0.85***	0.04	-0.04**	0.05	0.01**	<0.01	0.03	0.11
Delayed recall	2.73***	0.06	1.53***	0.05	-0.03*	0.01	0.02***	<0.01	-0.08	0.06
Verbal fluency	17.86***	0.19	17.37***	0.54	-0.12**	0.04	0.16***	0.03	0.06	0.07
Processing speed	14.31***	0.17	15.56***	0.51	-0.18***	0.04	0.10***	0.03	-0.25***	0.05
Depressive symptoms	1.37***	0.06	2.14***	0.07	-0.04**	0.01	0.02***	<0.01	-0.29***	0.04

Note: *** $p < 0.001$; ** $p < 0.01$; * $p < 0.05$. Results presented are based on LGCM models conducted separately for each of the outcome measures, after adjustment for age, gender, and education. The value of the slope reflects the yearly change in the outcome measure.

Table 2. Three processes LGCM associations between initial levels and changes in subjective memory, objective cognitive abilities and depressive symptoms in the overall sample

<i>Model 1</i>	B	S.E.	β	<i>Model 2</i>	B	S.E.	β
Immediate recall and depression				Delayed recall and depression			
Correlation intercept immediate recall with intercept depression	-0.33***	0.03	-0.24	Correlation intercept delayed recall with intercept depression	-0.40***	0.03	-0.22
Effect of intercept immediate recall on slope depression	0.02**	0.01	0.17	Effect of intercept delayed recall on slope depression	0.01	0.01	0.10
Effect of intercept depression on slope immediate recall	-0.01	<0.01	-0.09	Effect of intercept depression on slope delayed recall	-0.01**	<0.01	-0.12
Correlation slope immediate recall with slope depression	<-0.01**	<0.01	-0.30	Correlation slope delayed recall with slope depression	<-0.01*	<0.01	-0.14
Immediate recall and subjective memory				Delayed recall and subjective memory			
Correlation intercept immediate recall with intercept subjective memory	0.18***	0.01	0.27	Correlation intercept delayed recall with intercept subjective memory	0.23***	0.02	0.27
Effect of intercept subjective memory on slope immediate recall	-0.02*	0.01	-0.13	Effect of intercept subjective memory on slope delayed recall	-0.02**	0.01	-0.13
Effect of intercept immediate recall on slope subjective memory	0.01	<0.01	0.12	Effect of intercept delayed recall on slope subjective memory	0.01***	<0.01	0.22
Correlation slope immediate recall with slope subjective memory	<0.01***	<0.01	0.35	Correlation slope delayed recall with slope subjective memory	<0.01	<0.01	0.11
Depression and subjective memory				Depression and subjective memory			
Correlation intercept subjective memory with intercept depression	-0.30***	0.02	-0.29	Correlation intercept subjective memory with intercept depression	-0.30***	0.02	-0.29
Effect of intercept subjective memory on slope depression	0.01	0.01	0.04	Effect of intercept subjective memory on slope depression	0.01	0.01	0.05
Effect of intercept depression on slope subjective memory	<0.01*	<0.01	0.09	Effect of intercept depression on slope subjective memory	0.01**	<0.01	0.11
Correlation slope subjective memory with slope depression	<-0.01***	<0.01	-0.22	Correlation slope subjective memory with slope depression	<-0.01***	<0.01	-0.22

<i>Model 3</i>	B	S.E.	β	<i>Model 4</i>	B	S.E.	β
Processing speed and depression				Verbal fluency and depression			
Correlation intercept processing speed with intercept depression	-1.08***	0.09	-0.19	Correlation intercept verbal fluency with intercept depression	-1.26***	0.10	-0.21
Effect of intercept processing speed on slope depression	<0.01	<0.01	0.01	Effect of intercept verbal fluency on slope depression	<0.01*	<0.01	0.10
Effect of intercept depression on slope processing speed	<0.01	0.01	0.01	Effect of intercept depression on slope verbal fluency	-0.02*	0.01	-0.08
Correlation slope processing speed with slope depression	<0.01	<0.01	0.01	Correlation slope verbal fluency with slope depression	-0.01	<0.01	-0.10
Processing speed and subjective memory				Verbal fluency and subjective memory			
Correlation intercept processing speed with intercept subjective memory	0.49***	0.05	0.18	Correlation intercept verbal fluency with intercept subjective memory	0.70***	0.05	0.24
Effect of intercept subjective memory on slope processing speed	-0.02	0.02	-0.04	Effect of intercept subjective memory on slope verbal fluency	-0.01	0.02	-0.02
Effect of intercept processing speed on slope subjective memory	<-0.01	<0.01	-0.03	Effect of intercept verbal fluency on slope subjective memory	<0.01	<0.01	0.04
Correlation slope processing speed with slope subjective memory	<0.01*	<0.01	0.18	Correlation slope verbal fluency with slope subjective memory	0.01***	<0.01	0.26
Depression and subjective memory				Depression and subjective memory			
Correlation intercept subjective memory with intercept depression	-0.30***	0.02	-0.29	Correlation intercept subjective memory with intercept depression	-0.30***	0.02	-0.29
Effect of intercept subjective memory on slope depression	0.01	0.01	0.07	Effect of intercept subjective memory on slope depression	0.01	0.01	0.05
Effect of intercept depression on slope subjective memory	<0.01*	<0.01	0.07	Effect of intercept depression on slope subjective memory	<0.01*	<0.01	0.08
Correlation slope subjective memory with slope depression	<-0.01***	<0.01	-0.21	Correlation slope subjective memory with slope depression	<-0.01***	<0.01	-0.22

Notes: *** $p < 0.001$; ** $p < 0.01$; * $p < 0.05$; B = nonstandardized estimate; β = standardized estimate;

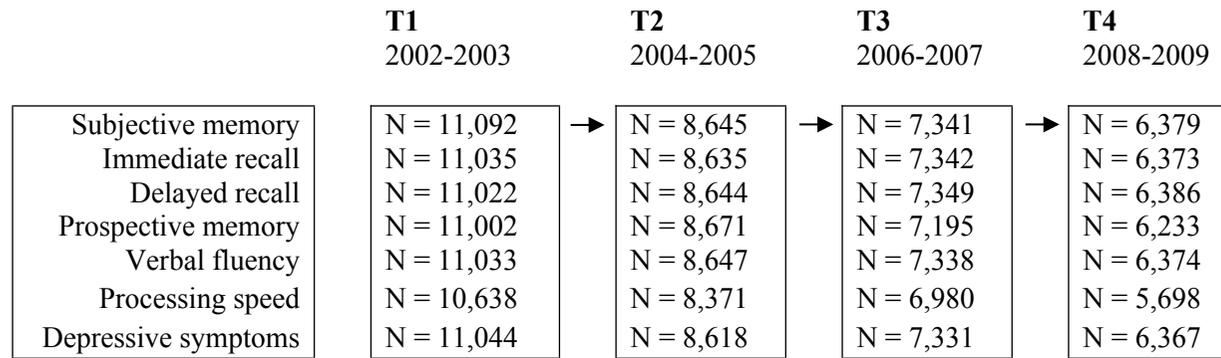
Table 3. Three processes LGCM associations between initial levels and changes in subjective memory, objective cognitive abilities and depressive symptoms among persons with initial probable cognitive impairment

<i>Model 1</i>	B	S.E.	β	<i>Model 2</i>	B	S.E.	β
Immediate recall and depression				Delayed recall and depression			
Correlation intercept immediate recall with intercept depression	-0.32***	0.06	-0.24	Correlation intercept delayed recall with intercept depression	-0.32***	0.06	-0.17
Effect of intercept immediate recall on slope depression	0.04	0.02	0.17	Effect of intercept delayed recall on slope depression	0.01	0.01	0.04
Effect of intercept depression on slope immediate recall	-0.01	0.01	-0.08	Effect of intercept depression on slope delayed recall	-0.01	0.01	-0.06
Correlation slope immediate recall with slope depression	<-0.01	<0.01	-0.16	Correlation slope delayed recall with slope depression	<-0.01	<0.01	-0.07
Immediate recall and subjective memory				Delayed recall and subjective memory			
Correlation intercept immediate recall with intercept subjective memory	0.14***	0.03	0.24	Correlation intercept delayed recall with intercept subjective memory	0.18***	0.03	0.23
Effect of intercept subjective memory on slope immediate recall	0.01	0.02	0.05	Effect of intercept subjective memory on slope delayed recall	0.03	0.02	0.12
Effect of intercept immediate recall on slope subjective memory	<0.01	0.01	0.04	Effect of intercept delayed recall on slope subjective memory	0.01*	<0.01	0.21
Correlation slope immediate recall with slope subjective memory	<0.01*	<0.01	0.33	Correlation slope delayed recall with slope subjective memory	<0.01	<0.01	-0.03
Depression and subjective memory				Depression and subjective memory			
Correlation intercept subjective memory with intercept depression	-0.40***	0.04	-0.33	Correlation intercept subjective memory with intercept depression	-0.40***	0.04	-0.33
Effect of intercept subjective memory on slope depression	<0.01	0.02	0.01	Effect of intercept subjective memory on slope depression	0.01	0.02	0.03
Effect of intercept depression on slope subjective memory	0.01**	<0.01	0.24	Effect of intercept depression on slope subjective memory	0.01***	0.01	0.27
Correlation slope subjective memory with slope depression	<-0.01**	<0.01	-0.27	Correlation slope subjective memory with slope depression	<-0.01**	<0.01	-0.26

<i>Model 3</i>	B	S.E.	β	<i>Model 4</i>	B	S.E.	β
Processing speed and depression				Verbal fluency and depression			
Correlation intercept processing speed with intercept depression	-1.14***	0.19	-0.17	Correlation intercept verbal fluency with intercept depression	-0.32***	0.06	-0.17
Effect of intercept processing speed on slope depression	<-0.01	<0.01	-0.06	Effect of intercept verbal fluency on slope depression	0.01	0.01	0.04
Effect of intercept depression on slope processing speed	0.01	0.02	0.05	Effect of intercept depression on slope verbal fluency	-0.01	0.01	-0.06
Correlation slope processing speed with slope depression	0.01	0.01	0.16	Correlation slope verbal fluency with slope depression	<-0.01	<0.01	-0.07
Processing speed and subjective memory				Verbal fluency and subjective memory			
Correlation intercept processing speed with intercept subjective memory	0.36***	0.09	0.13	Correlation intercept verbal fluency with intercept subjective memory	0.18***	0.03	0.23
Effect of intercept subjective memory on slope processing speed	0.01	0.04	0.01	Effect of intercept subjective memory on slope verbal fluency	0.03	0.02	0.12
Effect of intercept processing speed on slope subjective memory	<-0.01	<0.01	-0.06	Effect of intercept verbal fluency on slope subjective memory	0.01*	<0.01	0.21
Correlation slope processing speed with slope subjective memory	0.01*	<0.01	0.37	Correlation slope verbal fluency with slope subjective memory	<0.01	<0.01	-0.03
Depression and subjective memory				Depression and subjective memory			
Correlation intercept subjective memory with intercept depression	-0.40***	0.04	-0.33	Correlation intercept subjective memory with intercept depression	-0.40***	0.04	-0.33
Effect of intercept subjective memory on slope depression	0.01	0.02	0.05	Effect of intercept subjective memory on slope depression	0.01	0.02	0.03
Effect of intercept depression on slope subjective memory	0.01**	<0.01	0.22	Effect of intercept depression on slope subjective memory	0.01**	<0.01	0.23
Correlation slope subjective memory with slope depression	<-0.01**	<0.01	-0.26	Correlation slope subjective memory with slope depression	<-0.01**	<0.01	-0.26

Notes: *** p < 0.001; ** p < 0.01; * p < 0.05; B = nonstandardized estimate; β = standardized estimate;

Supplementary Figure 1. Flow chart of the study sample



Supplementary Table 1. Baseline characteristics for participants who completed the study and those who dropped out

	Completers		Dropped out		Chi2(df)	P value
	%		%			
Gender (female)	56		53		11.9(1)	<0.01
Education						
No qualification	35		52			
Primary or secondary	38		32		48.4(1)	<0.001
Tertiary	27		16		177.0(1)	<0.001
	Mean	S.D.	Mean	S.D.	T test(df)	P value
Age	63.5	9.3	67.3	11.3	-19.6(11389)	<0.001
Depression	1.4	1.9	1.8	2.1	-9.4(11042)	<0.001
Subjective memory	3.0	0.9	2.9	1.0	21.3(11033)	<0.001
Immediate recall	5.7	1.7	5.0	1.8	21.4(11020)	<0.001
Delayed recall	4.3	2.0	3.5	2.2	6.0(11090)	<0.001
Verbal fluency	20.3	6.2	17.8	6.4	21.2(11031)	<0.001
Processing speed	19.3	5.7	17.6	6.1	14.6(10636)	<0.001

Study completers = participants with data at all four waves; dropped out cases = participants who left the study at wave 2, 3, or 4.

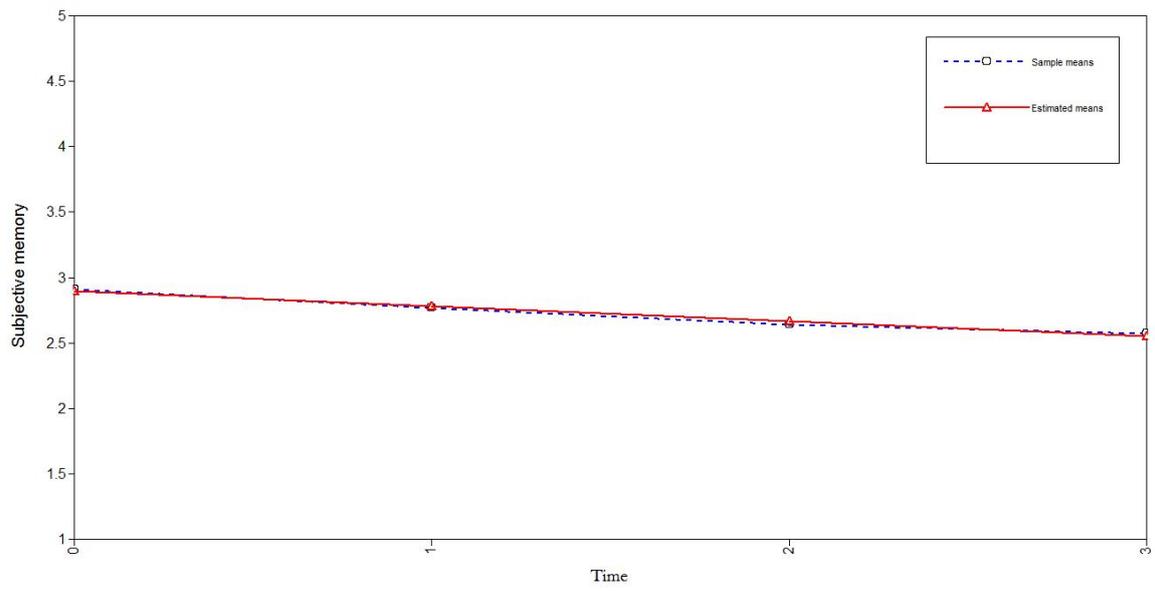
Supplementary Table 2. Two processes LGCM associations between initial levels and changes in subjective memory and objective cognitive abilities

<i>Model 1</i>				<i>Model 2</i>			
Subjective memory and immediate recall				Subjective memory and delayed recall			
	B	S.E.	β		B	S.E.	β
Correlation intercept immediate recall with intercept subjective memory	0.18***	0.01	0.27	Correlation intercept delayed recall with intercept subjective memory	0.23***	0.02	0.27
Effect of intercept subjective memory on slope immediate recall	-0.01*	0.01	-0.11	Effect of intercept subjective memory on slope delayed recall	-0.02**	0.01	-0.10
Effect of intercept immediate recall on slope subjective memory	<0.01	<0.01	0.08	Effect of intercept delayed recall on slope subjective memory	0.01***	<0.01	0.19***
Correlation slope immediate recall with slope subjective memory	<0.01***	<0.01	0.35	Correlation slope delayed recall with slope subjective memory	<0.01	<0.01	0.11

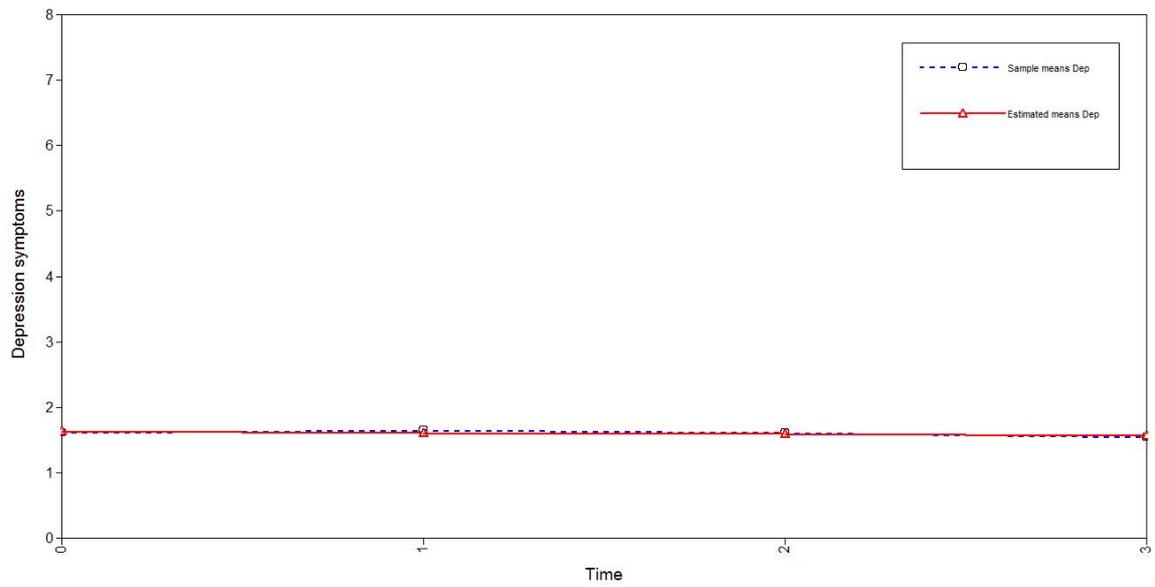
<i>Model 3</i>				<i>Model 4</i>			
Subjective memory and processing speed				Subjective memory and verbal fluency			
	B	S.E.	β		B	S.E.	β
Correlation intercept processing speed with intercept subjective memory	0.48***	0.05	0.18	Correlation intercept verbal fluency with intercept subjective memory	0.70***	0.05	0.24
Effect of intercept subjective memory on slope processing speed	-0.02	0.02	-0.04	Effect of intercept subjective memory on slope verbal fluency	<0.01	0.02	<-0.01
Effect of intercept processing speed on slope subjective memory	<-0.01	<0.01	-0.05	Effect of intercept verbal fluency on slope subjective memory	<0.01	<0.01	0.02
Correlation slope processing speed with slope subjective memory	<0.01*	<0.01	0.17	Correlation slope verbal fluency with slope subjective memory	0.01***	<0.01	0.27

Notes: *** p < 0.001; ** p < 0.01; * p < 0.05; B = nonstandardized estimate; β = standardized estimate;

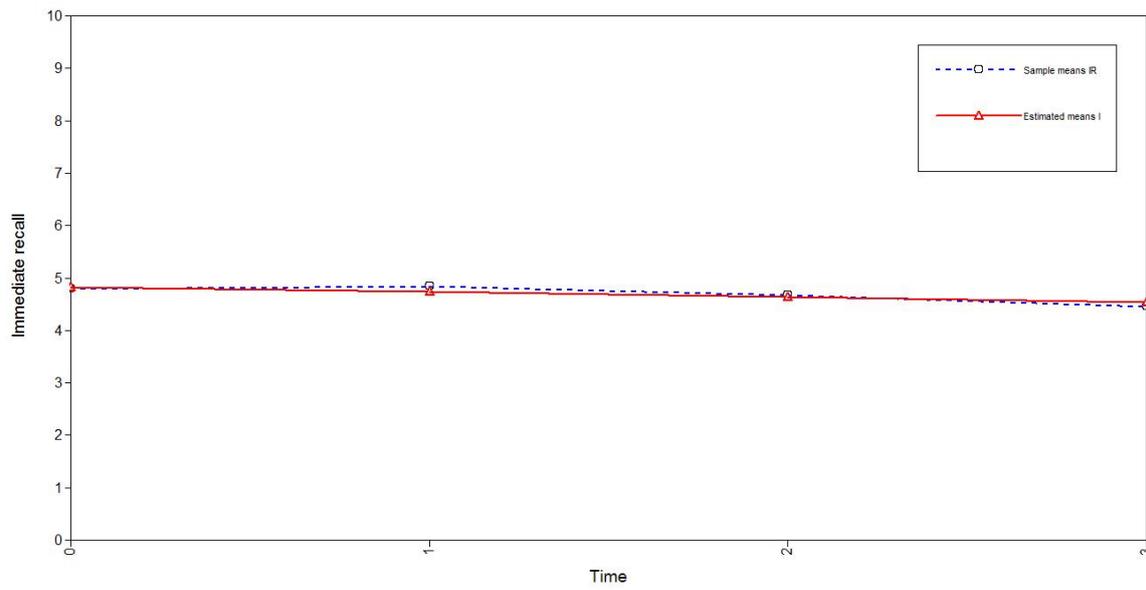
Supplementary Figure 1. Observed and estimated means for subjective memory complaints



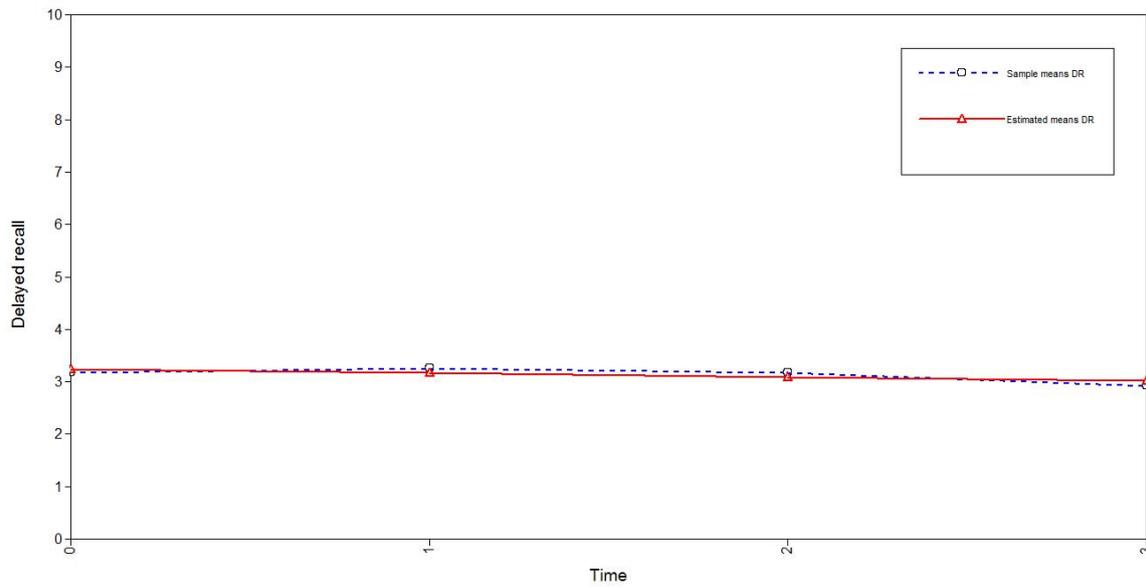
Supplementary Figure 2. Observed and estimated means for depression symptoms



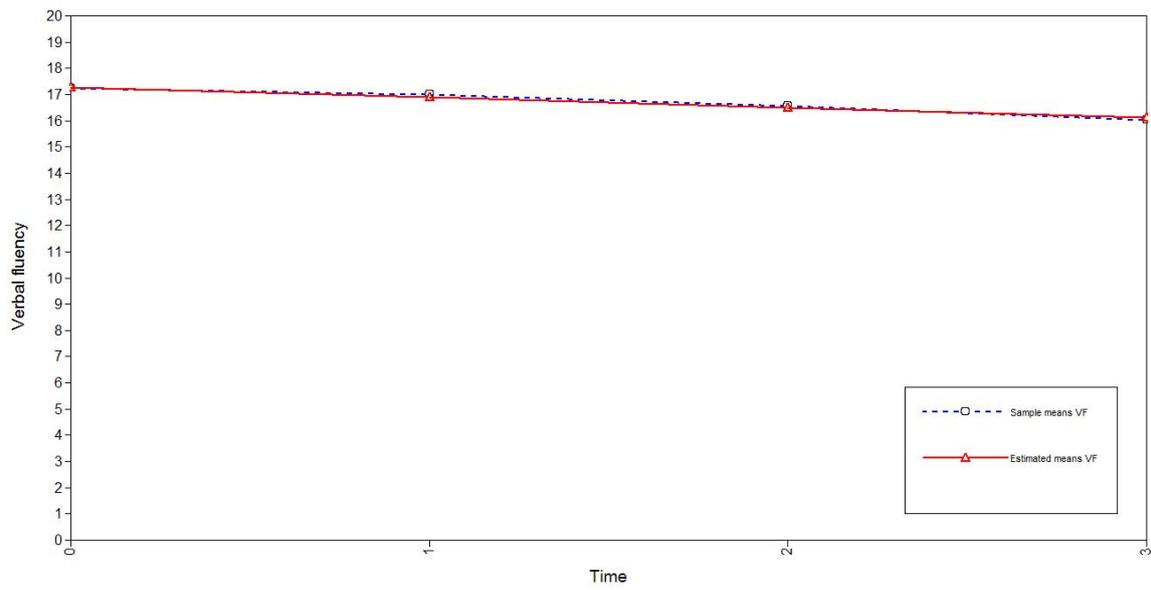
Supplementary Figure 3. Observed and estimated means for immediate recall



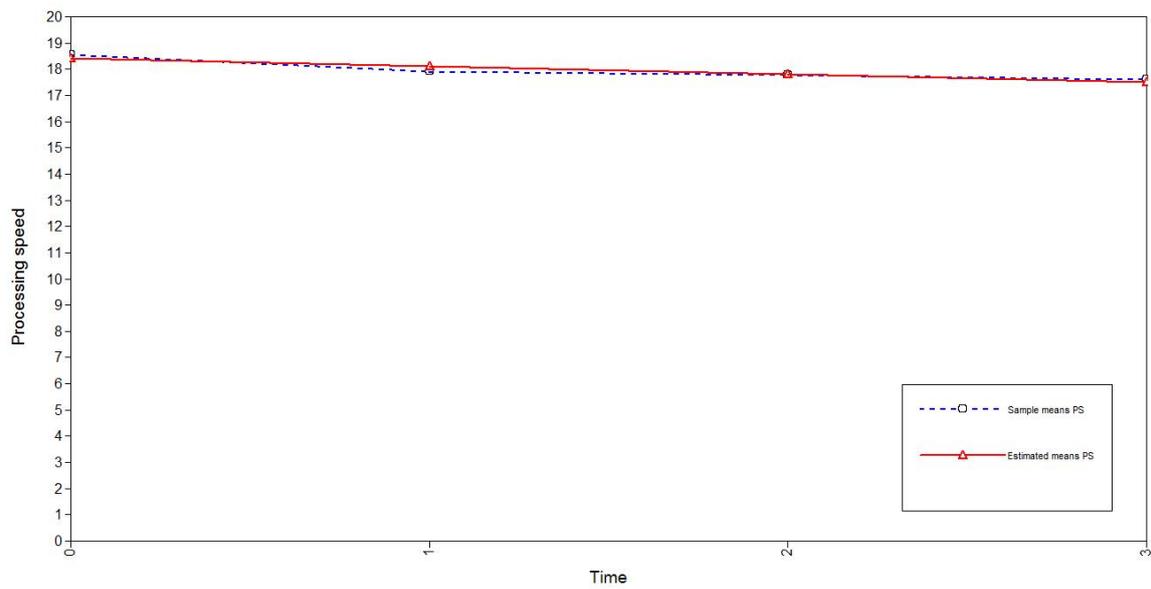
Supplementary Figure 4. Observed and estimated means for delayed recall



Supplementary Figure 5. Observed and estimated means for verbal fluency



Supplementary Figure 6. Observed and estimated means for processing speed



Conflict of interest: All authors declare that they have nothing to disclose.