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Research Report

# Body Mass Index and Memory Across 18 Years in the Wisconsin Longitudinal Study

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## Abstract

**Background:** Body weight is a modifiable risk factor for dementia, but results have been mixed as to the ages at which normal body weight is markedly preferable to overweight or obesity. This study assessed the association between change in body mass index (BMI) over 2 periods of the life course with change in memory between the ages of 65 and 72 for males and females.

**Methods:** Participants were 3 637 White high school graduates, born in 1939, from the Wisconsin Longitudinal Study. The statistical analyses were fixed-effects regression models, with moderation terms to test for sex differences. One set of models examined change in BMI between ages 54 and 65, and the other set examined change in BMI between ages 65 and 72. In both cases, cognitive change occurred between ages 65 and 72.

**Results:** Greater increases in BMI were associated with a greater decline in immediate recall for females only, both contemporaneously and following a lag. Increases in BMI were associated with greater contemporaneous—but not lagged—declines in both delayed recall and digit ordering for both males and females.

**Conclusions:** The present study adds to the evidence that for White, high school educated Americans, weight gain in midlife and young-old age is a risk factor for memory decline. Results vary according to the timing of the weight gain, the aspect of memory measured, and participant sex.

**Keywords:** Fixed-effects models, Midlife, Obese, Overweight

A meta-analytic study of over 1 million persons demonstrated that excess weight is a significant risk factor for dementia diagnosis (1). Adipose tissue may contribute to cognitive decline through neurovascular changes (the formation of white matter lesions in the brain) (2), endocrine pathways (adipokines such as leptin) (3), and immune responses (inflammation both in the brain and systemically) (4), among other mechanisms. The issue is significant both because over 40% of adults in the United States currently experience obesity and because body weight, unlike some other risk factors for cognitive decline and dementia, is considered modifiable (5,6).

However, the results of individual studies have been mixed, with higher body weight associated with significantly poorer cognitive performance in some studies and significantly better cognitive performance in others (7,8). A recent review concluded that mixed results are likely due to design differences across studies, including age at which body weight is assessed and how it is measured, length of follow-up, measurement of confounds such as comorbid conditions, and the sex and racial/ethnic composition of samples (9).

Additionally, although excess weight may cause cognitive decline, very initial dementia symptoms—apathy, loss of initiative, and changes in the sensory perception of food—might cause people to eat less and lose weight many years before they begin to experience serious problems in daily cognitive function (10). Thus, in the years immediately prior to diagnosis, people who will go on to have dementia weigh less than people who will not (1). Weight loss in the preclinical stages of dementia may contribute to the mixed results problem, given the wide age range of dementia diagnoses in the United States: The average age at diagnosis is 83.7 years, with a *SD* of 5.5 years (11). If weight loss occurs some years before clinical dementia, and age of onset of dementia varies, then in aggregate results, the observed relationship between body weight and cognition will depend strongly on the composition of the sample.

In the present study, we use a large longitudinal sample of older adults from a single birth cohort to assess the relationship between change in body mass index (BMI) and change in 3 measures of memory across an 18-year period from age 54 to 72. We further test for sex differences.

## Method

### Data

The Wisconsin Longitudinal Study (WLS) is a random sample of 1/3 of the cohort of men and women who graduated from Wisconsin high schools in 1957 ($N$ = 10 317). The sample is one of non-Hispanic White persons, given that in 1960, 97% of Wisconsin residents were non-Hispanic White (12). Participants were surveyed by paper and pencil in 1957 (age 18), by telephone interview and mail-back questionnaire in 1964 (age 25), 1975 (age 36), 1993 (age 54), and 2004 (age 65), and by in-person interview and mail-back questionnaire in 2011 (age 72). Our analyses omitted 5 558 participants who were not active in the study at ages 54, 65, and 72. Of these, approximately 37% (2 049) had died. Additionally, we omitted 1 053 participants who participated in all 3 waves but had incomplete cognitive data. Because the cognitive tasks were randomized to reduce overall survey length, approximately two-thirds of the omitted participants simply did not have cognitive tests included in their survey interview. Finally, we removed 11 people who never reported their weight, and 58 participants whose BMI fell into the underweight category (less than 18.5) at age 54, 65, or 72. Therefore, our analytic sample included 3 637 White participants who completed the cognitive battery and who consistently had a BMI of 18.5 or higher.

### Measures

#### Memory

At ages 65 and 72, participants completed a battery of cognitive tasks, including 3 measuring aspects of memory: immediate recall, delayed recall, and digit ordering. For recall, participants were read a list of 10 common words and asked to repeat as many as they could remember immediately, and again following a delay of approximately 10 min (13). Digit ordering was a modified protocol of the WAIS-III digit backward subtest (14). Participants reordered a series of digits from smallest to largest, beginning with a series of 3 and progressing until 2 failures or a correct 8-digit series. We calculated the percent of maximum possible scores for each test.

#### Body mass index

At ages 54, 65, and 72, participants were asked to self-report their weight in pounds and their height to the nearest quarter of an inch. Units were converted to kilograms and meters, respectively, for the calculation of BMI: kilograms per squared meters. We top-coded BMI at 40 for 69 observations at age 54, 139 observations at age 65, and 193 observations at age 72.

#### Covariates

There were 6 time-varying covariates measured at ages 54, 65, and 72. First, income was a measure of total personal income from all sources, including paid work, business ownership, Social Security and other pensions, government programs, and interest and investments. We divided continuous income into quartiles. Second, participants reported whether they currently smoked. Third, participants responded to the 20-item Center for Epidemiological Studies—Depression scale using a modified response scale, where participants reported the number of days in the past week they experienced each symptom (15). Thus, sum scores ranged from 0 to 140 and we took the natural log to normalize the distribution. Finally, participants reported whether a medical professional had ever diagnosed them with: diabetes; a heart attack or myocardial infarction, coronary heart disease, angina, congestive heart failure, or other heart problems; and high blood pressure or hypertension. The WLS began asking participants whether a medical professional had ever diagnosed them with stroke at age 65; therefore, we have this measure at ages 65 and 72 only.

### Statistical Modeling

We estimated fixed-effects regression models, which take the form

$$Y_{ij} - Y_{.j} = (\alpha_j - \alpha_j) + \beta_1(X_{ij1} - X_{.j1}) + \beta_2(X_{ij2} - X_{.j2}) + \ldots + \beta_n(X_{ijn} - X_{.jn})$$

where $Y_{ij}$ is the cognitive score at age $i$ for participant $j$; the $X_{ijn}$ indicate the values of BMI and the other covariates at age $i$ for participant $j$; and $Y_{.j}$ and $X_{.jn}$ are grand means that are subtracted from age-specific values. This model subtracts away the effects of time-invariant factors, both measured and unmeasured, such that only a time-varying factor can account for change in cognition.

A major reason for using fixed-effects models is that they strengthen what researchers can infer about causality in observational data: We can ensure sequential order by modeling how change in BMI between the ages of 54 and 65 is related to change in cognition between the ages of 65 and 72. However, the results of fixed-effects models are sensitive to how lags in the data are specified (16), and the design-related spacing of waves of data collection likely does not match the lags in the biological processes by which changing BMI influences changing cognition. In other words, there is no conceptual reason to hypothesize that BMI influences cognition for precisely the 11 years between the ages of 54 and 65. The lag might be shorter or longer or it may begin and end at different ages; moreover, there may be multiple mechanisms by which BMI influences cognition, each having its own timescale.

Thus, we modeled change in each outcome (immediate recall, delayed recall, and digit ordering) between age 65 and age 72 in both of the ways possible in the WLS: lagged and contemporaneous. Neither strategy is likely to be a perfectly accurate specification of the timing of the association between BMI and cognition. Nor can the statistical models adjudicate which timescale is correct. We present the results of both strategies only to maximize what can be learned from the WLS about the size and duration of the association under differing assumptions about how it operates in time. First, in lagged models, we examined cognitive change as a function of changes between the ages of 54 and 65 in BMI, income, status as a smoker, depressive symptoms, and diagnosis of diabetes, heart disease, and high blood pressure. Because of the importance of stroke to cognitive function, we included contemporaneous stroke history, as measured at ages 65 and 72. Second, in contemporaneous models, we examined cognitive change as a function of changes between the ages of 65 and 72 in BMI, income, status as a smoker, depressive symptoms, and diagnosis of diabetes, heart disease, high blood pressure, and stroke.

Finally, although time-invariant variables factor out of a fixed-effects model, a time-invariant variable may interact with a time-varying variable to influence change in cognition. Here, we test whether the effect of changing BMI on cognition differs for males

and females. The "main effect" of sex does not appear in the regression model because it is accounted for among the fixed effects.

### Missing Data

Within the analytic sample, 91% of participants provided complete data at age 54, 78% of participants provided complete data at age 65, and 75% of participants provided complete data at age 72. Depressive symptoms were the variable most likely to be missing, with 7% missing observations at age 54, 16% at age 65, and 18% at age 72. We generated 20 complete data sets using multiple imputation by chained equations before estimating our models. Results estimated using listwise deletion were substantively similar.

We also examined the data for evidence of attrition bias, as available upon request. The results we present in the main manuscript are robust to several different missing data scenarios.

## Results

Table 1 shows descriptive statistics for measures by sex and age. At age 65, the average female scored 66% on immediate recall, 46% on delayed recall, and 63% on digit ordering. These scores dropped to 58%, 39%, and 58%, respectively, at age 72. At age 65, the average male scored 58% on immediate recall, 36% on delayed recall, and 59% on digit ordering. These scores dropped to 52%, 31%, and 56%, respectively, at age 72. Average BMI increased from 26.1 at age 54 to 27.5 at age 65 and 28.5 at age 72 for females, and from 27.4 at age 54 to 28.3 at age 65 and 29.0 at age 72 for males. The average participant's *change* in BMI between 1993 and 2004 was 1.15 (not shown), with a *SD* of 2.54. In this time, 11% of participants lost 2 or more points of BMI and 41% gained 2 or more points. Likewise, average change in BMI between 2004 and 2011 was 0.87, with a SD of 2.66. In this time, 13% of participants lost 2 or more points of BMI and 36% gained 2 or more points.

Table 2 shows the fixed-effects regression models for the 3 memory tasks. For immediate recall, both lagged and contemporaneous BMI change were significant and interacted with sex, such that increases in BMI were associated with memory declines for females, but not for males. A 1-point increase in BMI between the ages of 54 and 65 was associated with a cognitive decline of 0.77 percentage points ($p < .01$) between the ages of 65 and 72. A 1-point increase in BMI between the ages of 65 and 72 was associated with a contemporaneous decline in memory of 0.63 percentage points ($p < .05$).

For both delayed recall and digit ordering, there were no sex interactions, and the contemporaneous effect was significant while the lagged effect was not. A 1-point increase in BMI between the ages of 65 and 72 was associated with a contemporaneous decline of 0.71 percentage points in delayed recall ($p < .001$) and of 0.72 percentage points in digit ordering ($p < .001$). These effects are modest in size, but nontrivial. For example, as BMI increased by 1 point, delayed recall and digit ordering decreased by approximately 0.7 percentage points. In comparison, developing high blood pressure was associated with decreases in these scores of approximately 2.8 percentage points. For increasing weight to equal the effect of developing high blood pressure, then a participant would need to gain 4 or more points in BMI, which happened to 13% of participants between age 54 and 65, and to 12% of participants between age 65 and 72.

**Table 1.** Descriptive Statistics by Sex and Age, Wisconsin Longitudinal Study 1993–2011, $N = 3\,637$

| | Females ($n = 1\,940$) | | | Males ($n = 1\,697$) | | |
|---|---|---|---|---|---|---|
| | M (*SD*) or % | M (*SD*) or % | M (*SD*) or % | M (*SD*) or % | M (*SD*) or % | M (*SD*) or % |
| | Age 54 | Age 65 | Age 72 | Age 54 | Age 65 | Age 72 |
| Immediate recall (%) | — | 65.69 (16.75) | 57.99 (14.26) | — | 57.59 (16.87) | 52.11 (13.81) |
| Delayed recall (%) | — | 45.68 (21.38) | 38.85 (18.12) | — | 36.09 (19.03) | 30.63 (16.15) |
| Digit ordering (%) | — | 63.20 (24.25) | 58.08 (21.17) | — | 58.89 (25.33) | 56.29 (25.33) |
| Body mass index (kg/m$^2$) | 26.09 (4.60) | 27.51 (5.02) | 28.51 (5.38) | 27.40 (3.64) | 28.29 (4.11) | 28.95 (4.52) |
| Income (quartiles) | 2.53 (1.09) | 2.19 (1.04) | 2.21 (1.06) | 2.89 (1.03) | 3.07 (0.96) | 3.02 (0.99) |
| Current smoker | 15.55% | 10.03% | 6.49% | 14.70% | 11.26% | 8.13% |
| Depressive symptoms | 16.37 (15.45) | 14.27 (14.04) | 15.91 (14.83) | 14.42 (13.49) | 11.89 (12.71) | 14.37 (13.79) |
| Diabetes | 2.73% | 8.97% | 13.78% | 3.12% | 12.44% | 20.69% |
| Heart disease | 3.76% | 9.75% | 18.18% | 6.07% | 19.29% | 30.93% |
| High blood pressure | 18.56% | 45.44% | 60.24% | 20.09% | 48.26% | 61.89% |
| Stroke | — | 2.06% | 4.18% | — | 3.77% | 6.49% |

*Notes*: Values are reported prior to multiple imputation and any linear transformations. Depressive symptoms ranged from 0 *lowest* to 140 *highest*.

**Table 2.** Fixed-Effects Regressions Indicating Associations Between Change in Body Mass Index and Percent Change in Cognition, Wisconsin Longitudinal Study ($N = 3\,637$)

| | Immediate Recall | | | | Delayed Recall | | Digit Ordering | |
|---|---|---|---|---|---|---|---|---|
| | Lagged | | Contemporaneous | | Lagged | Contemporaneous | Lagged | Contemporaneous |
| | Main Effects | Sex Interaction | Main Effects | Sex Interaction | Main Effects | Main Effects | Main Effects | Main Effects |
| | *B* (*SE*) | *B* (*SE*) | *B* (*SE*) | *B* (*SE*) | *B* (*SE*) | *B* (*SE*) | *B* (*SE*) | *B* (*SE*) |
| Body mass index (kg/m$^2$) | −0.53*** (0.13) | −0.06 (0.20) | −0.52*** (0.13) | −0.15 (0.20) | −0.20 (0.15) | −0.71*** (0.16) | −0.25 (0.18) | −0.72*** (0.17) |
| Income (quartiles) | 0.56* (0.28) | 0.48 (0.28) | 0.20 (0.34) | 0.19 (0.34) | 0.27 (0.32) | 0.31 (0.40) | 0.61 (0.39) | −0.08 (0.47) |
| Current smoker | −0.44 (1.08) | −0.47 (1.08) | 1.23 (1.56) | 1.34 (1.56) | 0.37 (1.27) | 0.94 (1.76) | 0.38 (1.52) | −0.35 (2.09) |
| Depressive symptoms | 0.97** (0.37) | 0.94* (0.37) | −1.42*** (0.40) | −1.41*** (0.40) | 0.89* (0.43) | −1.52** (0.46) | −0.26 (0.50) | −0.60 (0.54) |
| Diabetes | −2.91* (1.16) | −2.91* (1.16) | −3.01* (1.23) | −3.00* (1.22) | −2.00 (1.35) | −2.83 (1.42) | −1.13 (1.63) | −1.79 (1.70) |
| Heart disease | −2.90** (0.97) | −2.97** (0.97) | −1.85* (0.90) | −1.87* (0.90) | −3.99*** (1.14) | −0.20 (1.04) | −3.84** (1.35) | −2.91* (1.24) |
| High blood pressure | −5.27*** (0.65) | −5.27*** (0.65) | −3.10*** (0.80) | −3.02*** (0.80) | −5.14*** (0.76) | −2.72** (0.93) | −3.53*** (0.91) | −2.97** (1.10) |
| Stroke incidence between age 65 and 72 | −6.87*** (1.84) | −6.70*** (1.84) | −6.55** (1.88) | −6.50** (1.88) | −5.96** (2.13) | −5.82** (2.17) | −1.26 (2.64) | −0.51 (2.66) |
| Body mass index × Female | — | −0.77** (0.25) | — | −0.63* (0.26) | — | — | — | — |
| Intercept | 60.09 | 59.85 | 66.19 | 65.93 | 38.90 | 46.01 | 62.01 | 65.49 |
| $\sigma_u$ | 13.19 | 13.54 | 13.12 | 13.53 | 16.38 | 16.59 | 19.25 | 19.54 |
| $\sigma_e$ | 13.70 | 13.68 | 13.87 | 13.86 | 15.81 | 15.89 | 19.06 | 19.05 |

*Notes:* In the lagged models, change in the independent variables was between the ages of 54 and 65. In the contemporaneous models, change in the independent variables was between the ages of 65 and 72. In all models, change in cognition and stroke incidence were between the ages of 65 and 72. Body mass index was centered at 25. Depressive symptoms ranged from 0 *lowest* to 140 *highest*, and scores were logged for regression. There were no significant interactions by sex for delayed recall or digit ordering. ***$p < .001$; **$p < .01$; *$p < .05$.

## Discussion

This study assessed the relationship between BMI and memory functions—measured as immediate recall, delayed recall, and digit ordering—in a cohort of 3 637 White high school graduates as they aged from 54 to 72. The evidence was unequivocal that increasing weight was detrimental for performance. Greater increases in BMI were associated with a greater decline in immediate recall for females only, both contemporaneously and following a lag. Increases in BMI were associated with greater contemporaneous—but not lagged—declines in both delayed recall and digit ordering for both males and females.

Differences across the 3 measures of memory were anticipated, as immediate recall, delayed recall, and digit ordering tap short-term, long-term, and working memory to varying degrees (17). These functions rely on different regions of the brain, respond differently to normal aging and pathology, and are treated differently in clinical assessment and diagnosis. An effect of obesity for females, but not males, is consistent with research among both older (7) and younger (18) adults. However, reviews have concluded that the data are presently insufficient to draw firm conclusions about either cognitive domain or sex (9).

This study had several limitations of note. First, the WLS measure is BMI. Fat disposition changes with aging such that BMI alone is not always an accurate representation of adiposity (9). Second, participants self-reported whether a doctor had diagnosed them with cardiometabolic conditions. Undiagnosed or subclinical conditions are unaccounted for. Third, the WLS did not include a cognitive battery at age 54, so we were limited in our ability to examine the extent to which cognitive change may precipitate weight change. Finally, all participants were non-Hispanic White. This homogeneity is an advantage insofar as mixed results in previous research may be due to a stronger association between weight and cognition among White Americans than among Americans of color (19). However, rates of cognitive impairment are much higher in older adults of color, who are also more likely to be exposed to conditions such as food insecurity that affect weight trajectories (20).

However, this study also contributed several strengths. First, WLS participants have cognitive protective factors, including their White race and high level of educational attainment, and so the observation period of ages 54–72 likely precedes dementia-related weight loss for the average participant. The homogeneity of the sample also provides some natural controls for factors such as race/ethnicity that may influence the association between BMI and cognition (9). Second, our models include repeated measures of multiple possible confounders, including cardiometabolic conditions, depressive symptoms, and socioeconomic status (6). Finally, our fixed-effects regression analysis isolates within-person effects from between-person effects and accounts for sources of unobserved heterogeneity.

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Sara Kobielski conceived the study and performed the literature review and descriptive statistics. Sara M. Moorman conducted the regression analyses and wrote the paper.

## Conflict of Interest

None declared.

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