Power Analyses

Since we generally did not find significant associations of cognitive reserve variables or sex with biomarker values, we wanted to ensure that we had adequate power in the study to detect any important associations. We used simulations to estimate minimum detectable effect sizes at alpha=0.05 for these variables given the sample size. Using sex and PiB changes over time as an example, holding the observed variability constant, we found the minimum detectable regression coefficient for log(PIB) over time to be 0.006. At 5 years of follow up, that corresponds to a minimum detectable difference between males and females of 0.03 for log(PIB). If, say, we had males and females starting with PiB values of 1.5 at baseline, and the females stayed constant, we would have power to detect changes over time in the males leading to predicted PiB as small as 1.55 after 5 years. We could thus detect quite small differences between males and females over time. Using education/occupation and PiB changes over time as another example, we found the minimum detectable regression coefficient for log(PIB) over time to also be 0.006. If, say, we had groups with the mean education/occupation and education/occupation 1 standard deviation from the mean, both starting with PiB values of 1.5 at baseline, and the mean group stayed constant, we would have power to detect changes over time in the other group leading to predicted PiB as small as 1.55 after 5 years. The small magnitude of these detectable effects suggests that we had adequate power to detect associations of interest. Results for the other cognitive reserve variables and APOE were consistent with this conclusion.

We also used simulations to estimate minimum detectable effect sizes at alpha=0.05 for the high education and low education groups, looking at the APOE4 x Cognitive midlife interaction in amyloid deposition, and found that the minimum detectable effect sizes for the high and low education groups differed by only 0.003. Differences in power between the high and low education groups would thus seem to be very small.

Table e-1: Midlife cognitive activities (mean values) split by education level (Edu) and cognitive activity levels (CA).

Variable	High Edu & High CA n = 128	High Edu & Low CA n = 77	Low Edu & High CA n = 73	Low Edu & Low CA n = 115	P-value
Artistic activities	0.5	0.1	0.4	0.0	0.005
Computer activities	3.9	1.3	3.2	1.0	<0.0001
Craft activities	1.3	0.6	2.6	0.9	<0.0001
Group activities	1.4	0.6	0.9	0.4	<0.0001
Play games	2.6	0.7	3.1	1.4	<0.0001
Play music	1.1	0.5	0.8	0.2	0.0002
Read books	4.0	1.0	3.7	0.6	<0.0001
Read magazines	4.7	2.2	4.4	2.3	<0.0001
Read newspapers	6.6	5.9	6.6	5.9	<0.0001
Social activities	1.5	1.0	1.5	0.9	0.0002

The P-values come from an ANOVA testing for an overall difference among the groups
Rating of scores for each of the cognitive activities - 0.0=once a month or less; 0.5=2-3 times a month; 1.5=1-2 times per week; 3.5=3-4 times per week; 5.5=5-6 times per week; 7.0=every day

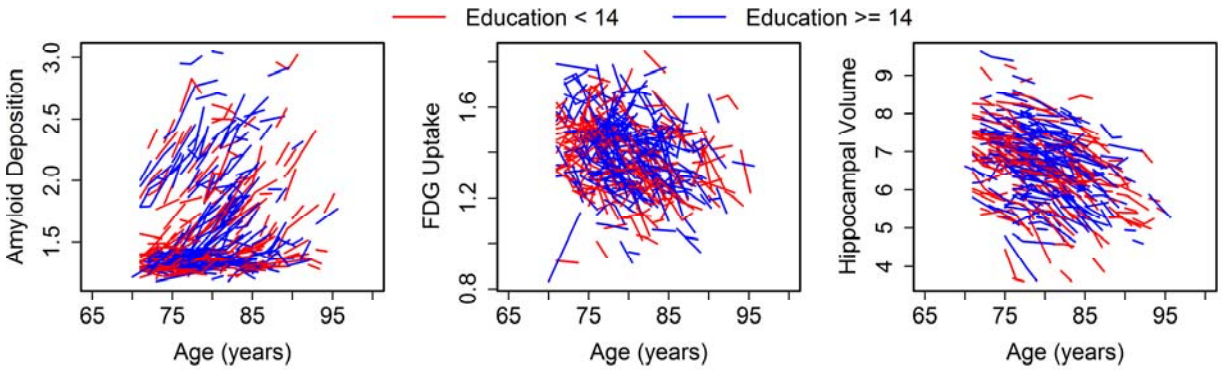

Figure e-1: Spaghetti plots of biomarker values in individual subjects lined up by age.

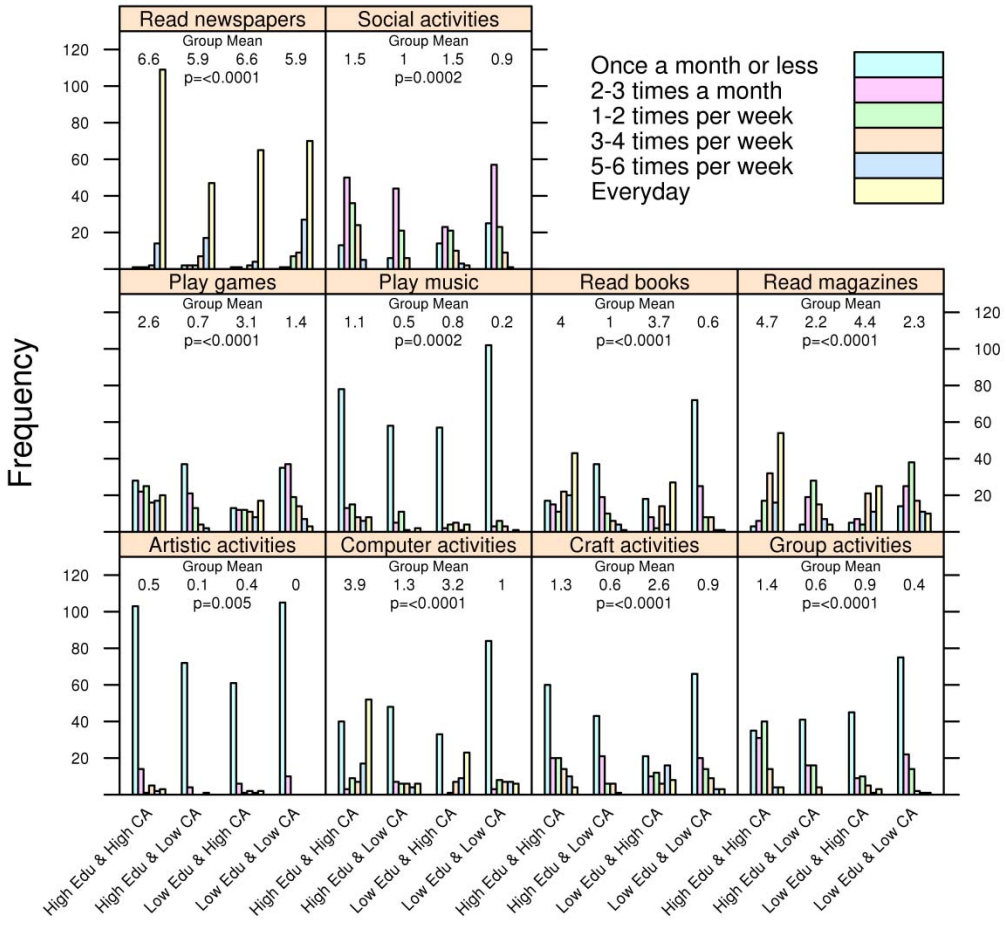

Figure e-2: Frequencies of each of the midlife cognitive activities displayed after stratification by education level (Edu) and cognitive activity levels (CA).

MIDLIFE PHYSICAL ACTIVITY QUESTIONNAIRE

Patient #: _____

In the following questions, we are interested in your physical activities when you were **50 – 65** years old.

For each of the physical activities listed below, please indicate on average, how often you have performed the activity when you were **50 to 65 years old**						
Physical activities when you were 50-65 years old	Once a month or never	2-3 times a month	1-2 times per week	3-4 times per week	5-6 times per week	Every day
Light activities like laundry, vacuuming, making beds, dusting, light yard-work, repairs, or home maintenance	☐	☐	☐	☐	☐	☐
Light exercise like bowling, walking leisurely, stretching, golfing with a golf cart, slow dancing	☐	☐	☐	☐	☐	☐
Moderate activities like scrubbing floors, washing windows, shoveling or snow-blowing light snow, digging, gardening, moving boxes, furniture, or garbage cans, raking leaves, painting, carpentry	☐	☐	☐	☐	☐	☐
Moderate exercise like brisk walking, hiking, aerobics, strength training, golfing without a golf cart, swimming, tennis doubles, moderate use of exercise machines (exercise bike), yoga, martial arts, weight lifting.	☐	☐	☐	☐	☐	☐
Heavy activities like carrying heavy objects/masonry, farm work, heavy digging, pushing a mower, shoveling or snow-blowing moderate or heavy snow, hard manual labor	☐	☐	☐	☐	☐	☐
Vigorous exercise like jogging, backpacking, bicycling uphill, tennis singles, racquetball, intense/extended use of exercise machines, skiing	☐	☐	☐	☐	☐	☐
When you were 50-65 years old, did you participate in any regular activity or program (either on your own or in a formal class) designed to obtain exercise or improve your physical fitness?	☐ Yes			☐ No		

(Continued on next page)

MIDLIFE COGNITIVE ACTIVITY QUESTIONNAIRE

Patient No.: _____

We are also interested in activities you performed when you were **50 to 65 years** .

For each of the activities listed below, please indicate on average, how often you performed the activity when you were **50 to 65 years old**

Cognitive activities when you were 50-65 years old	Once a month or never	2-3 times a month	1-2 times per week	3-4 times per week	5-6 times per week	Every day
Read newspapers. Examples include: Post Bulletin, Minneapolis Star-Tribune, St. Paul Pioneer Press, Chicago or New York times, Wall Street journal	☐	☐	☐	☐	☐	☐
Read magazines. Examples include: Business, sports, arts, hobby magazines	☐	☐	☐	☐	☐	☐
Read books. Examples include: novels, fiction, non-fiction	☐	☐	☐	☐	☐	☐
Play games. Examples include: Playing cards, crossword puzzles, other puzzles, bridge, checkers, other board games	☐	☐	☐	☐	☐	☐
Play Music. Examples include: Playing a musical instrument, being in a choir, playing in an orchestra or a band	☐	☐	☐	☐	☐	☐
Artistic activities. Examples include: Painting, drawing, sculpting, other arts	☐	☐	☐	☐	☐	☐
Craft activities. Examples include: Woodworking, pottery, ceramics, quilting, quilling, sewing	☐	☐	☐	☐	☐	☐
Group activity. Examples include: Bible study, book club, stock club, other organized discussion groups	☐	☐	☐	☐	☐	☐
Social activities such as going to the theater, movies, concerts, going out with friends, travel, etc.	☐	☐	☐	☐	☐	☐
Computer activities. Examples include: Use of Internet, email, computer games, conducting web searches/ research, on-line purchases, etc.	☐	☐	☐	☐	☐	☐
	<1 hour	1-2 hours	3-4 hours	5-6 hours	7-8 hours	> 8 hours
Television. How many hours per day did you spend watching TV?	☐	☐	☐	☐	☐	☐