

The association between dietary protein intake and sources and the rate of longitudinal changes in brain structure

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Supplemental Table S1 Dietary Protein Sources Classification and Codes

| Protein sources | ID | items |
|-----------------|-------|--|
| red meat | 26066 | Beef |
| | 26100 | Lamb |
| | 26117 | Pork |
| Processed meat | 26122 | Processed meat |
| Poultry | 26121 | Poultry |
| Eggs | 26088 | Egg and egg dishes |
| cheese | 26099 | High fat cheese |
| | 26103 | Medium and low-fat cheese |
| Nuts | 26107 | Unsalted nuts and seeds |
| | 26108 | Salted nuts and seeds |
| yogurt | 26102 | Low fat yogurt |
| | 26096 | Full fat yogurt |
| Whole grains | 26105 | Muesli |
| | 26076 | Bran cereal |
| | 26077 | Oat cereal (non sugar) |
| | 26078 | Oat cereal (sugar) |
| | 26079 | Other cereal (sugar) |
| | 26074 | Whole meal bread |
| | 26114 | Whole meal pasta, brown rice and other wholegrains |
| | 26086 | Soy desserts and yogurt |
| Legumes | 26136 | Soy milk |
| | 26115 | Peas and sweetcorn |
| | 26137 | Meat substitutes - soy |
| | 26101 | Legumes and pulses |
| | 26150 | Whole milk |
| milk | 26131 | Semi skimmed milk |
| | 26133 | Skimmed milk and cholesterol-lowering milk |
| sea food | 26109 | Oily fish |
| | 26149 | White fish and tinned tuna |
| | 26070 | Breaded/battered fish |

The questionnaire was first introduced as part of the Assessment visit towards the end of recruitment for the last 70,000 participants. Participants who had provided UK Biobank with e-mail addresses were also invited, via e-mail, to complete the questionnaire online on four separate occasions between Feb 2011 and April 2012.

Assessment center: April 2009 to September 2010

1st e-mail invitations: Feb 2011 - April 2011

2nd email invitations: June 2011 - Aug 2011

3rd email invitations: Oct 2011 – Dec 2011

4th email invitations: April 2012 – June 2012

Supplemental Table S2 Baseline characteristics of study participants on white matter hyperintensities(N=2679)

| | Total | Female | Male | P-value |
|---|----------------------|-------------------|-------------------|---------|
| N | 2679 | 1386 | 1293 | |
| age, y (mean (SD)) | 52.70 (7.41) | 51.71 (7.15) | 53.77 (7.54) | <0.001 |
| sex (%) | | | | |
| female | 1386 (51.7) | 1386 (100.0) | 0 (0.0) | |
| male | 1293 (48.3) | 0 (0.0) | 1293 (100.0) | |
| MET (%) | | | | |
| low | 466 (17.4) | 229 (16.5) | 237 (18.3) | 0.404 |
| medium | 1101 (41.1) | 582 (42.0) | 519 (40.1) | |
| high | 1112 (41.5) | 575 (41.5) | 537 (41.5) | |
| TDI (mean (SD)) | -2.00 (2.64) | -1.92 (2.68) | -2.08 (2.59) | 0.127 |
| smoke (%) | | | | |
| never | 1719 (64.2) | 905 (65.3) | 814 (63.0) | 0.221 |
| ever smoker | 960 (35.8) | 481 (34.7) | 479 (37.0) | |
| race (%) | | | | |
| others | 75 (2.8) | 41 (3.0) | 34 (2.6) | 0.691 |
| white | 2604 (97.2) | 1345 (97.0) | 1259 (97.4) | |
| drink (%) | | | | |
| never | 54 (2.0) | 34 (2.5) | 20 (1.5) | 0.126 |
| ever drinker | 2625 (98.0) | 1352 (97.5) | 1273 (98.5) | |
| education (%) | | | | |
| below | 1204 (44.9) | 605 (43.7) | 599 (46.3) | 0.176 |
| college or above | 1475 (55.1) | 781 (56.3) | 694 (53.7) | |
| BMI (%) | | | | |
| Underweight | 16 (0.6) | 13 (0.9) | 3 (0.2) | <0.001 |
| Normal weight | 1124 (42.0) | 718 (51.8) | 406 (31.4) | |
| Overweight and obesity | 1539 (57.4) | 655 (47.3) | 884 (68.4) | |
| cancer (%) | 219 (8.2) | 133 (9.6) | 86 (6.7) | 0.007 |
| CVD (%) | 73 (2.7) | 7 (0.5) | 66 (5.1) | <0.001 |
| hypertension (%) | 519 (19.4) | 160 (11.5) | 359 (27.8) | <0.001 |
| DM (%) | 79 (2.9) | 25 (1.8) | 54 (4.2) | <0.001 |
| energy (mean (SD)) | 8773.90 (2260.05) | 8228.82 (2004.52) | 9358.19 (2370.56) | <0.001 |
| total protein (mean (SD)) | 81.75 (22.74) | 78.14 (20.17) | 85.63 (24.63) | <0.001 |
| animal protein (mean (SD)) | 53.05 (20.13) | 50.81 (18.60) | 55.45 (21.41) | <0.001 |
| vegetable protein (mean (SD)) | 28.71 (9.62) | 27.33 (9.03) | 30.18 (10.02) | <0.001 |
| proportion of animal protein (mean (SD)) | 0.64 (0.12) | 0.64 (0.12) | 0.64 (0.11) | 0.74 |
| Proportion of vegetable protein (mean (SD)) | 0.36 (0.12) | 0.36 (0.12) | 0.36 (0.11) | 0.74 |
| animal/vegetable (mean (SD)) | 0.26 (0.24) | 0.26 (0.25) | 0.25 (0.23) | 0.725 |

Data for continuous variables are presented as mean (SD). Data for categorical variables are presented as n (%).

Abbreviations: MET, metabolic equivalent; BMI, body mass index; CVDs, cardiovascular diseases; SD, standard deviation; TDI, Townsend deprivation index; DM, diabetes mellitus

Supplemental Table S3 Association between dietary protein intake and longitudinal change rate of total brain, white matter, grey matter volume(N=2723)

| | Total brain volume | | white matter volume | | grey matter volume | |
|-------------------|------------------------|-------|------------------------|-------|------------------------|-------|
| | β (SE) | P | β (SE) | P | β (SE) | P |
| total protein | | | | | | |
| model1 | 2.775e-06(1.220e-05) | 0.820 | -3.584e-06 (2.288e-05) | 0.876 | 7.845e-06 (1.611e-05) | 0.626 |
| model2 | 2.124e-05(1.731e-05) | 0.220 | 6.691e-06 (3.249e-05) | 0.837 | 3.283e-05 (2.29e-05) | 0.152 |
| model3 | 2.115e-05(1.729e-05) | 0.221 | 7.123e-06 (3.245e-05) | 0.826 | 3.218e-05 (2.291e-05) | 0.160 |
| animal/protein | | | | | | |
| model1 | 7.233e-04 (2.306e-03) | 0.754 | -2.733e-03 (4.324e-03) | 0.527 | 3.927e-03 (3.044e-03) | 0.197 |
| model2 | 7.57e-04 (2.332e-03) | 0.746 | -3.06e-03 (4.376e-03) | 0.484 | 4.249e-03 (3.085e-03) | 0.168 |
| model3 | 6.455e-04 (2.330e-03) | 0.782 | -3.267e-03 (4.37e-03) | 0.455 | 4.227e-03 (3.085e-03) | 0.171 |
| vegetable/protein | | | | | | |
| model1 | -7.232e-04 (2.306e-03) | 0.754 | 2.733e-03 (4.324e-03) | 0.527 | -3.927e-03 (3.044e-03) | 0.197 |
| model2 | -7.57e-04 (2.332e-03) | 0.746 | 3.06e-03 (4.376e-03) | 0.484 | -4.249e-03 (3.085e-03) | 0.168 |
| model3 | -6.455e-04 (2.33e-03) | 0.782 | 3.267e-03 (4.37e-03) | 0.455 | -4.227e-03 (3.085e-03) | 0.171 |
| vegetable protein | | | | | | |
| model1 | -8.835e-06 (2.873e-05) | 0.759 | -2.383e-07 (5.388e-05) | 0.996 | -1.779e-05 (3.794e-05) | 0.639 |
| model2 | 1.121e-05 (3.761e-05) | 0.766 | 2.808e-05 (7.057e-05) | 0.691 | -5.531e-06 (4.976e-05) | 0.911 |
| model3 | 1.364e-05 (3.758e-05) | 0.717 | 3.378e-05 (2.581e-05) | 0.792 | -6.269e-05 (4.978e-05) | 0.900 |
| animal protein | | | | | | |
| model1 | 5.507e-06 (1.370e-05) | 0.688 | -4.464e-06 (2.568e-05) | 0.862 | 1.393e-05 (1.809e-05) | 0.441 |
| model2 | 1.573e-05 (1.581e-05) | 0.32 | 6.170e-07 (2.967e-05) | 0.983 | 2.836e-05 (2.091e-05) | 0.175 |
| model3 | 1.523e-05 (1.579e-05) | 0.335 | -2.856e-08 (2.964e-05) | 0.999 | 2.794e-05 (2.092e-05) | 0.182 |
| animal/vegetable | | | | | | |
| model1 | 2.835e-04 (1.136e-03) | 0.803 | -1.294e-03 (2.130e-03) | 0.544 | 1.761e-03 (1.500e-03) | 0.240 |
| model2 | 2.843e-04 (1.149e-03) | 0.805 | -1.458e-03 (2.156e-03) | 0.499 | 1.894e-03 (1.520e-03) | 0.213 |
| model3 | 2.358e-04 (1.146e-03) | 0.84 | -1.533e-03 (2.153e-03) | 0.477 | 1.870e-03 (1.52e-03) | 0.219 |

Model 1 was adjusted for age, and sex.

Model 2 was based on model 1 and additionally adjusted for Townsend Deprivation Index, total energy intake, education level, physical activity, smoking, alcohol intake, race, body weight status.

Model 3 was based on model 2 and further adjusted for baseline cancer, CVDs, hypertension, and diabetes

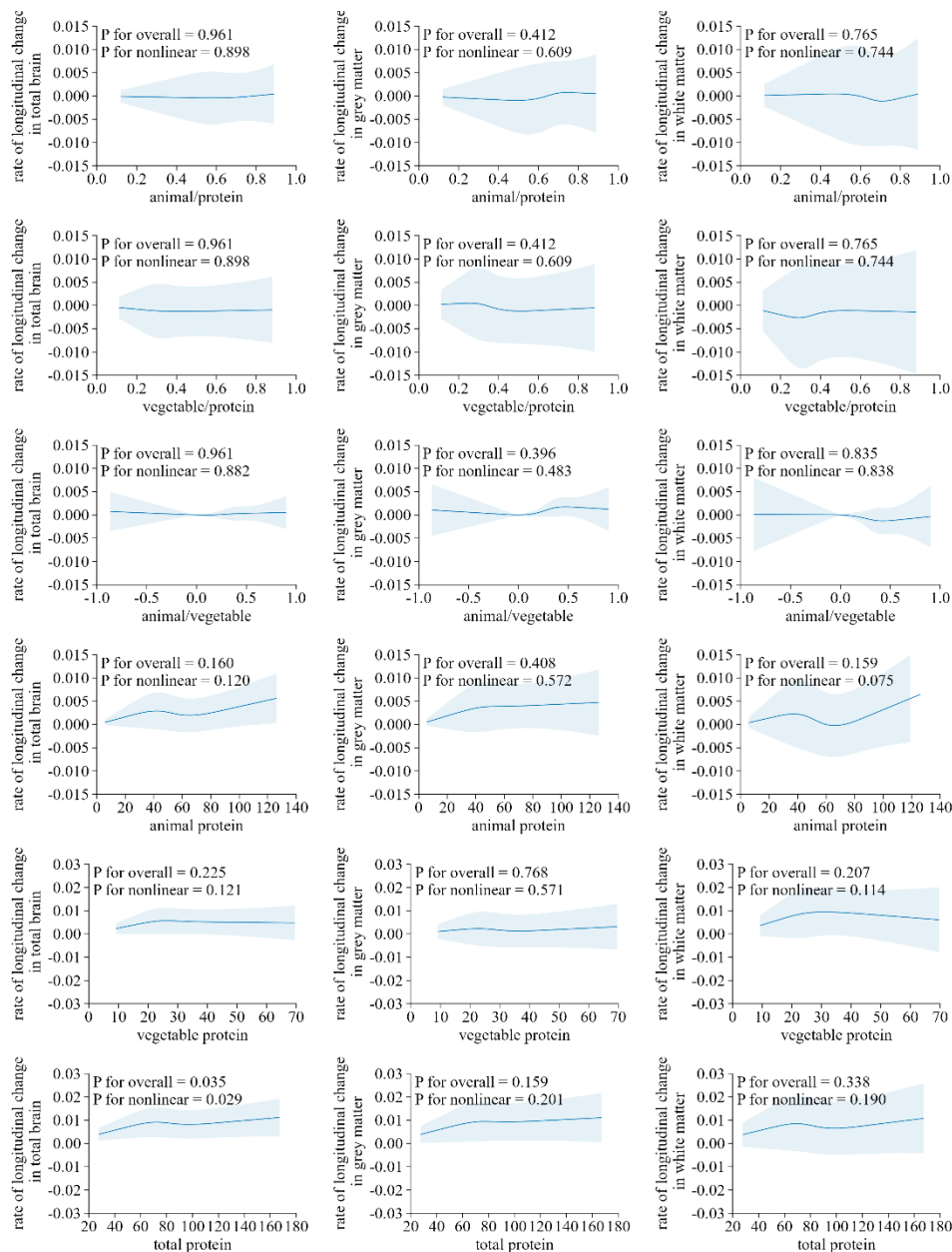
Supplemental Table S4 Association between dietary protein intake and longitudinal change rate of white matter hyperintensities(N=2679)

| | white matter hyperintensities | |
|-------------------|-------------------------------|-------|
| | β (SE) | P |
| total protein | | |
| model1 | 1.644e-04 (2.247e-04) | 0.464 |
| model2 | 9.480e-05(3.183e-04) | 0.766 |
| model3 | 9.494e-05 (3.186e-04) | 0.766 |
| animal/protein | | |
| model1 | 9.985e-03(4.235e-02) | 0.814 |
| model2 | 1.788e-02(4.286e-02) | 0.677 |
| model3 | 1.827e-02 (4.289e-02) | 0.670 |
| vegetable/protein | | |
| model1 | -9.984e-03 (4.235e-02) | 0.814 |
| model2 | -1.788e-02(4.286e-02) | 0.677 |
| model3 | -1.827e-02 (4.289e-02) | 0.670 |
| vegetable protein | | |
| model1 | -3.084e-04 (5.294e-04) | 0.560 |
| model2 | 3.275e-04(6.934e-04) | 0.637 |
| model3 | 3.339e-04(6.940e-04) | 0.631 |
| animal protein | | |
| model1 | -1.369e-04 (2.519e-04) | 0.587 |
| model2 | 2.149e-05(2.907e-04) | 0.941 |
| model3 | 2.051e-05(2.908e-04) | 0.944 |
| animal/vegetable | | |
| model1 | -5.569e-03 (2.084e-02) | 0.789 |
| model2 | -9.557e-03(2.110e-02) | 0.651 |
| model3 | -9.910e-03(2.111e-02) | 0.639 |

Model 1 was adjusted for age, and sex.

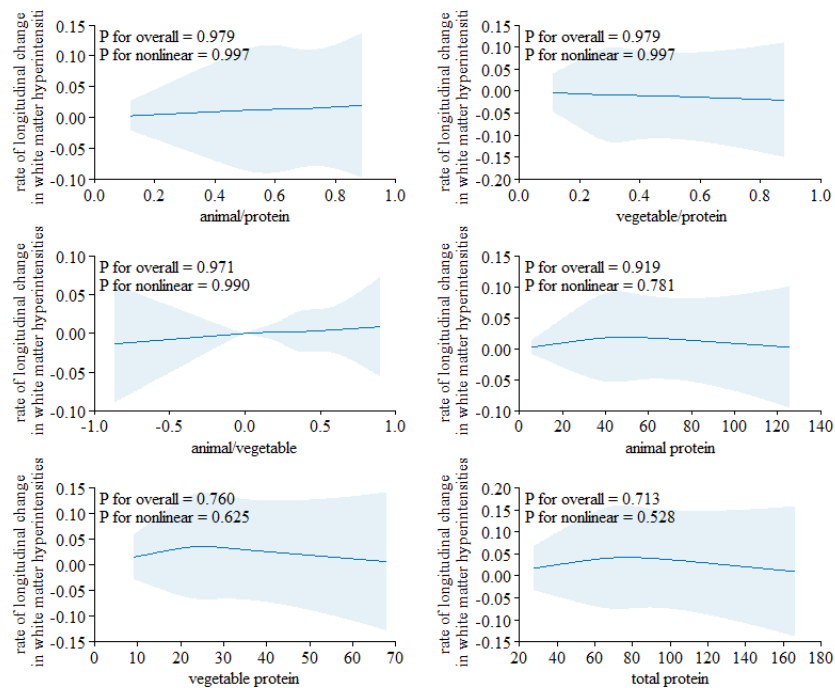
Model 2 was based on model 1 and additionally adjusted for Townsend Deprivation Index, total energy intake, education level, physical activity, smoking, alcohol intake, race, body weight status. Model 3 was based on model 2 and further adjusted for baseline cancer, CVDs, hypertension, and diabetes.

Supplemental Figure S1 Non-linear associations of dietary protein with the longitudinal change rate of brain structure markers Using a Restricted Cubic Spline Regression Model (N= 2723)



Note: The model was adjusted for age, sex, ethnicity, Townsend deprivation index, education level, physical activity, smoking, body weight status, total energy intake, baseline cancer, CVDs, hypertension, and diabetes.

Supplemental Figure S2 Non-linear associations of dietary protein with the longitudinal change rate of white matter hyperintensities Using a Restricted Cubic Spline Regression Model (N= 2679)



Note: The model was adjusted for age, sex, ethnicity, Townsend deprivation index, education level, physical activity, smoking, body weight status, total energy intake, baseline cancer, CVDs, hypertension, and diabetes.

Supplemental Table S5 Association between dietary protein sources with the longitudinal change rate of hippocampus volume (N=2723)

| | | total | | | hippocampus(left) | | | hippocampus(right) | | |
|----------------|---------------|------------|----------|--------|-------------------|----------|--------|--------------------|----------|--------|
| | | β | SE | P | β | SE | P | β | SE | P |
| Red meat | 0 | reference | | | reference | | | reference | | |
| | lower intake | 0.001289 | 0.001885 | 0.4944 | 0.001584 | 0.002794 | 0.571 | 0.001028 | 0.002504 | 0.681 |
| | higher intake | 0.003206 | 0.002171 | 0.1398 | 0.004333 | 0.003217 | 0.178 | 0.003177 | 0.002883 | 0.271 |
| processed meat | 0 | reference | | | Reference | | | reference | | |
| | lower intake | 0.001934 | 0.001985 | 0.3298 | 0.002031 | 0.00294 | 0.490 | 0.002854 | 0.002636 | 0.279 |
| | higher intake | -0.001909 | 0.002023 | 0.3452 | -0.004362 | 0.002997 | 0.146 | -0.000308 | 0.002686 | 0.909 |
| poultry | 0 | reference | | | reference | | | reference | | |
| | lower intake | 0.001441 | 0.001834 | 0.4322 | -0.0008925 | 0.002718 | 0.7427 | 0.003271 | 0.002435 | 0.179 |
| | higher intake | 0.001641 | 0.002389 | 0.4922 | 0.003167 | 0.00354 | 0.371 | 0.00224 | 0.003171 | 0.48 |
| eggs | 0 | reference | | | reference | | | reference | | |
| | lower intake | -0.002186 | 0.002069 | 0.2907 | 0.00005471 | 0.003068 | 0.986 | -0.003451 | 0.002745 | 0.2088 |
| | higher intake | 0.002897 | 0.002182 | 0.1845 | -0.0002213 | 0.003236 | 0.946 | 0.005598 | 0.002896 | 0.0534 |
| cheese | 0 | reference | | | reference | | | reference | | |
| | lower intake | 0.003776 | 0.002095 | 0.0716 | 0.007097 | 0.003104 | 0.0223 | 0.00152 | 0.002784 | 0.585 |
| | higher intake | 0.002528 | 0.002121 | 0.2334 | 0.004368 | 0.003142 | 0.1646 | 0.001013 | 0.002818 | 0.719 |
| nuts | 0 | reference | | | reference | | | reference | | |
| | lower intake | 0.004524 | 0.002004 | 0.0241 | 0.005238 | 0.00297 | 0.0778 | 0.004435 | 0.002663 | 0.096 |
| | higher intake | -0.0009412 | 0.002097 | 0.6536 | -0.004306 | 0.003107 | 0.166 | 0.002172 | 0.002787 | 0.436 |
| yogurt | 0 | reference | | | reference | | | reference | | |
| | lower intake | 0.0008537 | 0.00202 | 0.6727 | -0.0006831 | 0.002994 | 0.8195 | 0.002399 | 0.002682 | 0.371 |
| | higher intake | 0.0006205 | 0.002032 | 0.7601 | 0.00179 | 0.003011 | 0.5521 | 0.0002294 | 0.002698 | 0.932 |
| whole grains | 0 | reference | | | reference | | | reference | | |
| | lower intake | -0.001092 | 0.002405 | 0.6497 | -0.001267 | 0.003562 | 0.722 | -0.001545 | 0.003194 | 0.628 |
| | higher intake | 0.001324 | 0.002444 | 0.5881 | 0.003501 | 0.003621 | 0.3336 | -0.000328 | 0.003246 | 0.92 |
| legumes | 0 | reference | | | reference | | | reference | | |
| | lower intake | 0.0001805 | 0.001972 | 0.9271 | 3.061e-06 | 0.002923 | 0.9992 | 0.001017 | 0.002619 | 0.698 |

| | | | | | | | | | | |
|----------|---------------|-----------|----------|--------|-----------|----------|--------|-----------|----------|--------|
| milk | higher intake | 0.0005184 | 0.001974 | 0.7929 | 0.0006546 | 0.002925 | 0.8229 | 0.0007969 | 0.002621 | 0.761 |
| | 0 | reference | | | reference | | | reference | | |
| | lower intake | 0.0004236 | 0.003044 | 0.8893 | -0.003624 | 0.00451 | 0.4218 | 0.003652 | 0.004042 | 0.366 |
| sea food | higher intake | 0.001149 | 0.003077 | 0.7089 | -0.001162 | 0.004559 | 0.7989 | 0.002848 | 0.004085 | 0.486 |
| | 0 | reference | | | reference | | | reference | | |
| | lower intake | 0.00233 | 0.001966 | 0.2361 | 0.0004649 | 0.002916 | 0.8733 | 0.00468 | 0.002611 | 0.0732 |
| | higher intake | 0.004514 | 0.002095 | 0.0313 | 0.003269 | 0.003107 | 0.2929 | 0.005527 | 0.002782 | 0.047 |

Supplemental Table S6 Association between dietary protein intake with the longitudinal change rate of hippocampus volume in male(N=1337)

| | hippocampus(left) | | | hippocampus(right) | | | hippocampus(total) | | |
|-------------------|-------------------|-----------|--------|--------------------|-----------|-------|--------------------|-----------|-------|
| | β | SE | P | β | SE | P | β | SE | P |
| total protein | | | | | | | | | |
| model1 | -7.47E-05 | 7.934E-05 | 0.347 | 7.540E-05 | 6.83E-05 | 0.270 | -1.47E-05 | 5.15E-05 | 0.776 |
| model2 | 6.86E-05 | 1.173E-04 | 0.559 | 8.441E-05 | 1.01E-04 | 0.400 | 5.51E-05 | 7.61E-05 | 0.470 |
| model3 | 6.55E-05 | 1.176E-04 | 0.577 | 8.303E-05 | 1.01E-04 | 0.413 | 5.33E-05 | 7.63E-05 | 0.485 |
| animal/protein | | | | | | | | | |
| model1 | 0.0267957 | 1.719E-02 | 0.119 | 2.697E-02 | 1.480E-02 | 0.069 | 2.33E-02 | 1.13E-02 | 0.040 |
| model2 | 2.625E-02 | 1.744E-02 | 0.132 | 2.628E-02 | 1.50E-02 | 0.081 | 2.37E-02 | 1.13E-02 | 0.036 |
| model3 | 2.58E-02 | 1.749E-02 | 0.140 | 2.568E-02 | 1.51E-02 | 0.089 | 2.465E-02 | 1.115E-02 | 0.027 |
| vegetable/protein | | | | | | | | | |
| model1 | -2.680E-02 | 1.719E-02 | 0.119 | -2.697E-02 | 1.480E-02 | 0.069 | -2.465E-02 | 1.115E-02 | 0.027 |
| model2 | -2.625E-02 | 1.744E-02 | 0.132 | -2.630E-02 | 1.50E-02 | 0.081 | -2.37E-02 | 1.13E-02 | 0.036 |
| model3 | -2.581E-02 | 1.749E-02 | 0.140 | -2.570E-02 | 1.51E-02 | 0.089 | -2.33E-02 | 1.13E-02 | 0.040 |
| vegetable protein | | | | | | | | | |
| model1 | -5.298E-04 | 1.951E-04 | 0.007 | 7.880E-05 | 1.68E-04 | 0.640 | -2.987E-04 | 0.0001267 | 0.019 |
| model2 | -5.399E-04 | 2.636E-04 | 0.0408 | 2.650E-04 | 2.28E-04 | 0.244 | -3.66E-04 | 1.71E-04 | 0.033 |
| model3 | -5.381E-04 | 2.642E-04 | 0.0419 | 2.590E-04 | 2.28E-04 | 0.257 | -3.63E-04 | 1.71E-04 | 0.035 |
| animal protein | | | | | | | | | |
| model1 | 1.657E-05 | 9.127E-05 | 0.856 | 1.169E-04 | 7.85E-05 | 0.137 | 4.56E-05 | 5.92E-05 | 0.441 |
| model2 | 1.507E-04 | 1.087E-04 | 0.166 | 1.18E-04 | 9.38E-05 | 0.210 | 1.10E-04 | 7.06E-05 | 0.121 |
| model3 | 1.479E-04 | 1.090E-04 | 0.175 | 1.15E-04 | 9.40E-05 | 0.220 | 1.08E-04 | 7.07E-05 | 0.129 |
| animal/vegetable | | | | | | | | | |
| model1 | 1.446E-02 | 8.428E-03 | 0.086 | 1.336E-02 | 7.254E-03 | 0.066 | 1.287E-02 | 5.465E-03 | 0.019 |
| model2 | 1.390E-02 | 8.552E-03 | 0.104 | 1.300E-02 | 7.37E-03 | 0.078 | 1.226E-02 | 5.546E-03 | 0.027 |
| model3 | 1.369E-02 | 8.575E-03 | 0.111 | 1.280E-02 | 7.39E-03 | 0.084 | 1.208E-02 | 5.560E-03 | 0.030 |

Supplemental Table S7 Association between dietary protein intake with the longitudinal change rate of hippocampus volume in female(N=1386)

| | hippocampus(left) | | | hippocampus(right) | | | hippocampus(total) | | |
|-------------------|-------------------|-----------|-------|--------------------|----------|----------|--------------------|-----------|----------|
| | β | SE | P | β | SE | P | β | SE | P |
| total protein | | | | | | | | | |
| model1 | 1.19E-04 | 7.105E-05 | 0.095 | 4.250E-05 | 6.75E-05 | 0.52914 | 3.44E-05 | 5.08E-05 | 0.4987 |
| model2 | 1.37E-04 | 9.695E-05 | 0.159 | 4.44E-05 | 9.22E-05 | 0.62983 | 9.03E-05 | 6.93E-05 | 0.1924 |
| model3 | 1.42E-04 | 9.716E-05 | 0.145 | 4.607E-05 | 9.21E-05 | 0.61682 | 9.22E-05 | 6.94E-05 | 0.184 |
| animal/protein | | | | | | | | | |
| model1 | 2.467E-02 | 1.160E-02 | 0.034 | 0.0212083 | 0.011016 | 0.0544 | 0.0229959 | 0.0082765 | 0.00553 |
| model2 | 2.433E-02 | 1.178E-02 | 0.039 | 2.35E-02 | 1.12E-02 | 0.03598 | 2.41E-02 | 8.40E-03 | 0.00422 |
| model3 | 2.426E-02 | 1.180E-02 | 0.040 | 2.33E-02 | 1.12E-02 | 0.0373 | 2.40E-02 | 8.42E-03 | 0.00442 |
| vegetable/protein | | | | | | | | | |
| model1 | -2.467E-02 | 1.160E-02 | 0.034 | -0.0212083 | 0.011016 | 0.0544 | -0.0229958 | 0.0082765 | 0.005535 |
| model2 | -2.433E-02 | 1.178E-02 | 0.039 | -2.35E-02 | 1.12E-02 | 0.03598 | -2.41E-02 | 8.40E-03 | 0.00422 |
| model3 | -2.426E-02 | 1.180E-02 | 0.040 | -2.33E-02 | 1.12E-02 | 0.0373 | -2.40E-02 | 8.42E-03 | 0.00442 |
| vegetable protein | | | | | | | | | |
| model1 | -0.0001899 | 1.126E-04 | 0.092 | -9.58E-05 | 1.58E-04 | 0.543494 | -0.0002648 | 0.0001496 | 0.07693 |
| model2 | -2.67E-04 | 1.435E-04 | 0.063 | -2.56E-04 | 2.01E-04 | 0.20283 | -2.60E-04 | 1.91E-04 | 0.17373 |
| model3 | -2.64E-04 | 1.438E-04 | 0.067 | -2.51E-04 | 2.02E-04 | 0.21351 | -2.58E-04 | 1.91E-04 | 0.17657 |
| animal protein | | | | | | | | | |
| model1 | 1.63E-04 | 7.725E-05 | 0.035 | 1.34E-05 | 7.35E-05 | 0.85516 | 8.64E-05 | 5.52E-05 | 0.118 |
| model2 | 1.57E-04 | 8.677E-05 | 0.070 | 8.54E-05 | 8.24E-05 | 0.3004 | 1.22E-04 | 6.20E-05 | 0.0488 |
| model3 | 1.60E-04 | 8.692E-05 | 0.066 | 8.37E-05 | 8.25E-05 | 0.31025 | 1.23E-04 | 6.21E-05 | 0.0478 |
| animal/vegetable | | | | | | | | | |
| model1 | 1.186E-04 | 7.105E-05 | 0.095 | 4.25E-05 | 6.75E-05 | 0.52914 | 3.437E-05 | 5.080E-05 | 0.4987 |
| model2 | 1.366E-04 | 9.695E-05 | 0.159 | 4.61E-05 | 9.21E-05 | 0.61682 | 9.034E-05 | 6.927E-05 | 0.1924 |
| model3 | 1.415E-04 | 9.716E-05 | 0.145 | 4.44E-05 | 9.22E-05 | 0.62983 | 9.217E-05 | 6.941E-05 | 0.184 |

Supplemental Table S8 Association between dietary protein intake with the longitudinal change rate of hippocampus volume adjusted for AD-PRS(N=1386)

| | hippocampus(left) | | | hippocampus(total) | | | hippocampus(right) | | |
|-------------------|-------------------|----------|----------|--------------------|----------|----------|--------------------|----------|---------|
| | β | SE | P | β | SE | P | β | SE | P |
| total protein | 9.31E-05 | 7.71E-05 | 0.2273 | 6.59E-05 | 5.19E-05 | 0.2046 | 6.21E-05 | 6.88E-05 | 0.36724 |
| animal/protein | 2.53E-02 | 1.04E-02 | 0.0149 | 2.36E-02 | 6.97E-03 | 0.000724 | 2.40E-02 | 9.25E-03 | 0.00954 |
| vegetable/protein | -2.36E-02 | 6.97E-03 | 0.000724 | -2.53E-02 | 1.04E-02 | 0.0149 | -2.40E-02 | 9.25E-03 | 0.00954 |
| vegetable protein | -3.06E-04 | 1.12E-04 | 0.00644 | -3.91E-04 | 1.67E-04 | 0.0195 | -2.50E-04 | 1.49E-04 | 0.09411 |
| animal protein | 1.10E-04 | 4.75E-05 | 0.0209 | 1.48E-04 | 7.05E-05 | 0.0365 | 9.64E-05 | 6.30E-05 | 0.12566 |
| animal/vegetable | 1.13E-02 | 3.44E-03 | 0.000976 | 1.24E-02 | 5.11E-03 | 0.015 | 1.13E-02 | 4.56E-03 | 0.01356 |

The analyses were based on Model 3 in the main analysis (adjusted for age, sex, ethnicity, Townsend deprivation index, education level, physical activity, smoking, body weight status, total energy intake, baseline cancer, CVDs, hypertension, and diabetes) with additional adjustment for polygenic risk scores of Alzheimer's diseases (AD-PRS).

Supplemental Table S9 Association between dietary protein intake with the longitudinal change rate of hippocampus volume among participants with at least two waves of dietary data (N=2009)

| | hippocampus(left) | | | hippocampus(total) | | | hippocampus(right) | | |
|-------------------|-------------------|----------|-------|--------------------|----------|-------|--------------------|----------|-------|
| | β | SE | P | β | SE | P | β | SE | P |
| total protein | 1.88E-04 | 1.03E-04 | 0.067 | 1.18E-04 | 6.92E-05 | 0.089 | 8.67E-05 | 9.15E-05 | 0.344 |
| animal/protein | 3.00E-02 | 1.29E-02 | 0.020 | 2.80E-02 | 8.69E-03 | 0.001 | 2.91E-02 | 1.15E-02 | 0.011 |
| vegetable/protein | -3.00E-02 | 1.29E-02 | 0.020 | -2.80E-02 | 8.69E-03 | 0.001 | -2.91E-02 | 1.15E-02 | 0.011 |
| vegetable protein | -4.51E-04 | 2.09E-04 | 0.031 | -3.81E-04 | 1.41E-04 | 0.007 | -3.57E-04 | 1.87E-04 | 0.056 |
| animal protein | 2.37E-04 | 9.17E-05 | 0.010 | 1.67E-04 | 6.18E-05 | 0.007 | 1.38E-04 | 8.18E-05 | 0.092 |
| animal/vegetable | 1.42E-02 | 6.38E-03 | 0.026 | 1.32E-02 | 4.30E-03 | 0.002 | 1.37E-02 | 5.68E-03 | 0.016 |

The model was adjusted for age, sex, ethnicity, Townsend deprivation index, education level, physical activity, smoking, body weight status, total energy intake, baseline cancer, CVDs, hypertension, and diabetes among participants with at least two waves of dietary data.

Supplemental Table S10 Association between dietary protein intake with the longitudinal change rate of hippocampus volume with excluding baseline neuropsychiatric disorders (N=2398)

| | hippocampus(left) | | | hippocampus(total) | | | hippocampus(right) | | |
|-------------------|-------------------|-----------|-------|--------------------|-----------|-------|--------------------|-----------|-------|
| | β | SE | P | β | SE | P | β | SE | P |
| total protein | 9.466E-05 | 8.092E-05 | 0.242 | 5.457E-05 | 5.276E-05 | 0.301 | 7.757E-05 | 6.838E-05 | 0.257 |
| animal/protein | 2.399E-02 | 1.125E-02 | 0.038 | 1.899E-02 | 7.329E-03 | 0.010 | 2.552E-02 | 9.277E-03 | 0.001 |
| vegetable/protein | -2.339E-02 | 1.125E-02 | 0.038 | -1.899E-02 | 7.329E-03 | 0.010 | -2.552E-02 | 9.277E-03 | 0.001 |
| vegetable protein | -3.701E-04 | 1.821E-04 | 0.042 | -2.394E-04 | 1.188E-04 | 0.044 | -2.651E-04 | 1.508E-04 | 0.001 |
| animal protein | 1.407E-04 | 7.410E-05 | 0.050 | 8.542E-05 | 4.832E-05 | 0.077 | 1.107E-04 | 6.258E-05 | 0.077 |
| animal/vegetable | 1.169E-02 | 5.564E-03 | 0.036 | 9.216E-03 | 3.626E-03 | 0.011 | -1.222E-02 | 4.607E-03 | 0.008 |

The analyses were based on Model 3 in the main analysis (adjusted for age, sex, ethnicity, Townsend deprivation index, education level, physical activity, smoking, body weight status, total energy intake, baseline cancer, CVDs, hypertension, and diabetes) with excluding baseline neuropsychiatric disorders.

Supplemental Table S11 Association between dietary protein intake with the longitudinal change

rate of hippocampus volume in female adjusted for oral contraceptive (N=1386)

| | hippocampus(left) | | | hippocampus(total) | | | hippocampus(right) | | |
|-------------------|-------------------|-----------|-------|--------------------|-----------|-------|--------------------|-----------|-------|
| | β | SE | P | β | SE | P | β | SE | P |
| total protein | 9.779E-05 | 7.585E-05 | 0.197 | 7.617E-05 | 5.118E-05 | 0.137 | 7.763E-05 | 6.799E-05 | 0.254 |
| animal/protein | 2.509E-02 | 1.021E-02 | 0.014 | 2.443E-02 | 6.885E-03 | 0.001 | 2.570E-02 | 9.153E-03 | 0.005 |
| vegetable/protein | -2.509E-02 | 1.021E-02 | 0.014 | -2.443E-02 | 6.885E-03 | 0.001 | -2.570E-02 | 9.153E-03 | 0.005 |
| vegetable protein | -3.906E-04 | 1.648E-04 | 0.018 | -3.179E-04 | 1.112E-04 | 0.004 | -2.703E-04 | 1.478E-04 | 0.068 |
| animal protein | 1.506E-04 | 6.925E-05 | 0.030 | 1.197E-04 | 4.672E-05 | 0.011 | 1.125E-04 | 6.209E-05 | 0.070 |
| animal/vegetable | 1.243E-02 | 5.033E-03 | 0.014 | 1.176E-02 | 3.393E-03 | 0.001 | 1.204E-02 | 4.510E-03 | 0.008 |

The analyses were based on Model 3 in the main analysis (adjusted for age, sex, ethnicity, Townsend deprivation index, education level, physical activity, smoking, body weight status, total energy intake, baseline cancer, CVDs, hypertension, and diabetes) with additional adjustment for oral contraceptive.