Twin Research and Human Genetics

**Body mass index and depressive symptoms: Testing for adverse and protective associations in two twin cohort studies**

Markus Jokela, Venla Berg, Karri Silventoinen, G. David Batty, Archana Singh-Manoux, Jaakko Kaprio, George Davey Smith, Mika Kivimäki

**Supplementary material**

Appendix 1

Supplementary Table S1

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**Appendix 1.**

**Table S1** shows the intraclass correlations and cross-trait correlations for BMI and depressive symptoms (or negative mood) in both cohorts.

In the Finnish Twin Cohort, univariate analyses indicated that the best-fitting models for BMI included additive genetic component (a2=0.65) and non-shared environmental component (e2=0.35) but no shared environment (χ2=0.0, df=1). The same was true for depressive symptoms (a2=0.36, e2=0.64; χ2=0.0, df=1 for the exclusion of shared environment). Adding non-additive (or dominant) genetic effects (r=1.0 in MZ twins, r=0.25 in DZ twins) to the AE model suggested better fit for the ADE model for depressive symptoms (a2=0.16, d2=0.23, e2=0.61; χ2=6.6, df=1, p=0.01) but not for BMI (χ2=2.0, df=1, p=0.16).

 In the bivariate model fitted with the Finnish Twin Cohort data (excluding individuals with BMI below 20 to take into account the effects of underweight), all shared environmental factors could be omitted without decline in model fit (χ2=0). Omitting non-shared environmental covariance between BMI and depressive symptoms also had no influence (χ2=0). Other paths could not be excluded without significantly decreasing model fit. The final model and its standardized path coefficients are shown in **Figure S1**. Genetic correlation between BMI and depressive symptoms was calculated using the formula

 $r\_{A}=\frac{X\_{11}\* X\_{21}}{\sqrt{X\_{11}^{2}} \* \sqrt{X\_{21}^{2}+ X\_{22}^{2}}}$

where the values are non-standardized path coefficients for the common genetic component of BMI (X11), common genetic component of depressive symptoms (X21), and unique genetic component of depressive symptoms (X22). This indicated a genetic correlation of r=0.12 (95%CI=0.06, 0.17) between BMI and depressive symptoms (r=0.24, CI=-0.02, 0.50 for the additive genetic components only).

Similar results were observed in the MIDUS sample, in which variation in both body mass index (a2= 0.76, e2=0.24) and negative mood (a2=0.42, e2=0.58) were accounted by genetic and non-shared environment with no contribution from shared environment (χ2=0.0, df=1). Including non-additive genetic effects did not improve model fit for BMI (χ2=0.2, df=1, p=0.65) or negative mood (χ2=0.0, df=1). In the bivariate model, omitting all shared environmental factors did not significantly weaken model fit (χ2=0.3, df=3), and the non-shared environmental covariance could also be omitted without significant change in model fit (χ2=0.1, df=1). Other paths could not be excluded withouth significant decrease in model fit. The final model and its standardized path coefficients are shown in **Figure S1**. The genetic correlation between BMI and negative mood was 0.20 (95%CI=0.08, 0.31).

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| **Supplementary Table S1**. Intraclass and cross-trait correlations. |  |  |
|   | **Finnish Twin Cohort** | **MIDUS** |
|   | MZ (n=2846) | DZ (n=5369) | MZ (n=589) | DZ (n=514) |
| Intraclass correlation |   |   |   |   |
|  Body mass index | 0.65 (0.62, 0.68) | 0.29 (0.26, 0.33) | 0.73 (0.68, 0.79) | 0.39 (0.30, 0.50) |
|  Depressive symptoms | 0.40 (0.36, 0.44) | 0.13 (0.09, 0.17) | - | - |
|  Negative mood | - | - | 0.44 (0.36, 0.54) | 0.22 (0.11, 0.34) |
| Cross-trait correlation |  |  |  |  |
|  BMI & Depressive symptoms† | 0.09 (0.05, 0.13) | 0.00 (-0.03, 0.03) | - | - |
|  BMI & Negative mood | - | - | 0.16 (0.08, 0.24) | 0.01 (-0.08, 0.10) |
| † Calculated for twin pairs with BMI>20 to exclude the effects of underweight. |  |

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| **Supplementary Table S2.** Twin-pair analysis of BMI with positive and negative in the MIDUS sample, adjusted for age, sex, education and smoking. |
|   | **Positive Affect** |   |
| Population  | Overall B† (95% CI) | *P-value* | Within-pair B† (95% CI) | *P-value* | Total N (full pairs) |
| MZ twins |   |   |   |   |   |
|  All | -0.12 (-0.3, 0) | 0.08 | 0.08 (-0.2, 0.3) | 0.56 | 594 (293) |
|  BMI >20 | -0.14 (-0.3, 0) | 0.05 | 0.08 (-0.2, 0.3) | 0.57 | 564 (274) |
|  BMI >22 | -0.17 (-0.3, 0) | 0.03 | 0.15 (-0.1, 0.4) | 0.30 | 503 (234) |
| DZ twins |  |  |  |  |  |
|  All | -0.11 (-0.2, 0) | 0.07 | -0.15 (-0.3, 0) | 0.13 | 514 (257) |
|  BMI >20 | -0.12 (-0.3, 0) | 0.06 | -0.14 (-0.3, 0.1) | 0.18 | 489 (233) |
|  BMI >22 | -0.09 (-0.2, 0.1) | 0.23 | -0.15 (-0.4, 0.1) | 0.19 | 431 (190) |
|  |  |  |  |  |  |
|   | **Negative Affect** |   |
| Population  | Overall B† (95% CI) | *P-value* | Within-pair B† (95% CI) | *P-value* | Total N (full pairs) |
| MZ twins |   |   |   |   |   |
|  All | 0.21 (0.1, 0.3) | <0.001 | 0 (-0.2, 0.2) | 0.98 | 589 (293) |
|  BMI >20 | 0.23 (0.1, 0.3) | <0.001 | 0.01 (-0.2, 0.3) | 0.94 | 560 (274) |
|  BMI >22 | 0.27 (0.1, 0.4) | <0.001 | 0.02 (-0.2, 0.3) | 0.87 | 500 (234) |
| DZ twins |  |  |  |  |  |
|  All | 0.04 (-0.1, 0.1) | 0.42 | 0.05 (-0.1, 0.2) | 0.52 | 514 (257) |
|  BMI >20 | 0.04 (-0.1, 0.1) | 0.45 | 0.06 (-0.1, 0.2) | 0.50 | 489 (233) |
|  BMI >22 | 0.00 (-0.1, 0.1) | 0.97 | 0.06 (-0.1, 0.2) | 0.53 | 431 (190) |
| † B for 10-unit increase in BMI with positive and negative affect scores as the outcomes. Overall regressions are fitted with random-intercept models, within-pair regression are fitted using fixed-effect estimator to compare sibling-pairs with each other. Only pairs with full data for each member of sibling pair are included in the within-pair analysis. |





**Figure S1**. Best-fitting Cholesky decomposition models of the association between BMI and mental health in the Finnish Twin Cohort (n=1,136 MZ pairs; n=2,132 DZ pairs, including only twin pairs with BMI≥20) and MIDUS twin sample (n=274 MZ pairs; n=233 DZ pairs). Values are standardized path coefficients (and their standard errors), all associations are statistically significant at the p<0.05 level except for the additive genetic component in Finnish twins (p=0.06).



**Figure S2**. Cholesky decomposition of the association of body mass index (BMI) with positive affect and negative affect into pathways mediated by genetic factors, shared environment, and non-shared environment in the MIDUS twin sample. Values are standardized regression coefficients (SD=1), statistically significant pathways are marked with an asterisk (\* p<0.05). n=293 MZ twin pairs, n=257 DZ pairs.