**Supplementary Table 1: Number or missing values of immunometabolic indicators within the analytical sample (N=929)**

|  |  |
| --- | --- |
| **Immunometabolic indicator** | **Number of missings** |
|  | N (%) |
| BMI | 40 (4.3) |
| Waist circumference | 49 (5.3) |
| Systolic blood pressure | 42 (4.5) |
| Diastolic blood pressure | 42 (4.5) |
| Triglycerides level | 83 (8.9) |
| HDL cholesterol level | 75 (8.1) |
| Fasting plasma glucose level | 73 (7.9) |
| IL-6 level | 149 (16.0) |
| TNF- level | 149 (16.0) |
| CRP level | 76 (8.2) |

Abbreviations: BMI, body mass index; CRP, C-reactive protein; HDL, high-density lipid; IL, interleukin; TNF, tumour necrosis factor.

**Supplementary Table 2: Associations between depressive symptom profiles and immunometabolic characteristics within probands**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  |  | **Total depression severity** | **Mood symptoms profile** | **Cognitive symptoms profile** | **Somatic symptoms profile** | **Atypical-like symptoms profile** |
| **BMI** |  (se) | 0.14 (0.06) | 0.07 (0.06) | 0.02 (0.06) | 0.24 (0.06) | 0.19 (0.06) |
| *p* | 0.02 | 0.29 | 0.76 | 1.67E-04 | 2.45E-03 |
| FDR | 0.11 | 0.61 | 0.82 | **2.78E-03** | **1.53E-02** |
| **Waist circumference** |  (se) | 0.13 (0.06) | 0.07 (0.06) | 0.02 (0.06) | 0.21 (0.06) | 0.20 (0.06) |
| *p* | 0.02 | 0.23 | 0.72 | 2.92E-04 | 3.79E-04 |
| FDR | 0.11 | 0.53 | 0.80 | **2.92E-03** | **3.16E-03** |
| **Systolic blood pressure** |  (se) | 0.04 (0.05) | 0.03 (0.06) | -0.02 (0.05) | 0.07 (0.06) | 0.00 (0.05) |
| *p* | 0.49 | 0.63 | 0.67 | 0.21 | 0.99 |
| FDR | 0.79 | 0.79 | 0.80 | 0.53 | 0.99 |
| **Diastolic blood pressure** |  (se) | 0.03 (0.06) | 0.02 (0.06) | -0.06 (0.06) | 0.08 (0.06) | 0.02 (0.06) |
| *p* | 0.59 | 0.72 | 0.33 | 0.19 | 0.72 |
| FDR | 0.79 | 0.80 | 0.62 | 0.53 | 0.80 |
| **Triglycerides level a** |  (se) | 0.05 (0.06) | 0.02 (0.06) | -0.02 (0.06) | 0.10 (0.06) | 0.07 (0.06) |
| *p* | 0.42 | 0.77 | 0.69 | 0.11 | 0.23 |
| FDR | 0.73 | 0.82 | 0.80 | 0.41 | 0.53 |
| **HDL cholesterol level a** |  (se) | -0.03 (0.06) | -0.06 (0.06) | 0.03 (0.06) | -0.04 (0.06) | -0.06 (0.06) |
| *p* | 0.60 | 0.33 | 0.62 | 0.55 | 0.29 |
| FDR | 0.79 | 0.62 | 0.79 | 0.79 | 0.61 |
| **Fasting plasma glucose level a** |  (se) | 0.03 (0.06) | 0.00 (0.06) | -0.03 (0.06) | 0.08 (0.06) | 0.04 (0.06) |
| *p* | 0.60 | 0.99 | 0.57 | 0.20 | 0.50 |
| FDR | 0.79 | 0.99 | 0.79 | 0.53 | 0.79 |
| **IL-6 level a** |  (se) | 0.25 (0.06) | 0.19 (0.06) | 0.22 (0.06) | 0.28 (0.07) | 0.24 (0.06) |
| *p* | 9.82E-05 | 4.71E-03# | 4.73E-04 | 2.77E-05 | 2.78E-04 |
| FDR | **2.45E-03** | **2.61E-02** | **3.38E-03** | **1.38E-03** | **2.92E-03** |
| **TNF- level a** |  (se) | 0.08 (0.06) | 0.05 (0.07) | 0.05 (0.06) | 0.12 (0.07) | 0.09 (0.06) |
| *p* | 0.20 | 0.44 | 0.42 | 0.07 | 0.15 |
| FDR | 0.53 | 0.74 | 0.73 | 0.29 | 0.47 |
| **CRP level a** |  (se) | 0.07 (0.07) | 0.01 (0.07) | 0.04 (0.07) | 0.12 (0.07) | 0.1 (0.07) |
| *p* | 0.32 | 0.92 | 0.59 | 0.07 | 0.14 |
| FDR | 0.62 | 0.96 | 0.79 | 0.29 | 0.47 |

Abbreviations: BMI, body mass index; CRP, C-reactive protein; FDR, False Discovery Rate; HDL, high-density lipid; IL, interleukin; TNF, tumour necrosis factor.

Results obtained from linear models adjusting for age and sex. =standardized regression coefficient, bold values indicate that the association was significant at an FDR<.05. a Tests were performed on log-transformed data. # Threshold for p value corresponding to maximum q value <0.05.

**Supplementary Table 3: Associations between depressive symptom profiles and immunometabolic characteristics within siblings**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  |  | **Total depression severity** | **Mood symptoms profile** | **Cognitive symptoms profile** | **Somatic symptoms profile** | **Atypical-like symptoms profile** |
| **BMI** |  (se) | 0.18 (0.05) | 0.14 (0.05) | 0.14 (0.05) | 0.19 (0.05) | 0.28 (0.05) |
| *p* | 4.03E-04 | 8.55E-03 | 5.78E-03 | 2.59E-04 | 3.57E-08 |
| FDR | **4.03E-03** | **3.05E-02** | **2.22E-02** | **3.24E-03** | **8.94E-07** |
| **Waist circumference** |  (se) | 0.16 (0.05) | 0.11 (0.05) | 0.11 (0.05) | 0.18 (0.05) | 0.27 (0.05) |
| *p* | 8.06E-04 | 2.52E-02 | 1.91E-02 | 1.47E-04 | 5.63E-09 |
| FDR | **5.76E-03** | 6.31E-02 | 5.30E-02 | **2.45E-03** | **2.81E-07** |
| **Systolic blood pressure** |  (se) | 0.07 (0.05) | 0.03 (0.05) | 0.03 (0.05) | 0.08 (0.05) | 0.06 (0.05) |
| *p* | 0.16 | 0.46 | 0.47 | 0.07 | 0.20 |
| FDR | 0.25 | 0.55 | 0.55 | 0.14 | 0.30 |
| **Diastolic blood pressure** |  (se) | 0.08 (0.05) | 0.05 (0.05) | 0.04 (0.05) | 0.10 (0.05) | 0.09 (0.05) |
| *p* | 0.11 | 0.29 | 0.46 | 0.04 | 0.06 |
| FDR | 0.20 | 0.38 | 0.55 | 0.10 | 0.12 |
| **Triglycerides level a** |  (se) | 0.08 (0.05) | 0.05 (0.05) | 0.06 (0.05) | 0.09 (0.05) | 0.11 (0.05) |
| *p* | 0.15 | 0.35 | 0.27 | 0.10 | 0.03 |
| FDR | 0.25 | 0.44 | 0.36 | 0.19 | 0.06 |
| **HDL cholesterol level a** |  (se) | -0.15 (0.05) | -0.12 (0.05) | -0.12 (0.05) | -0.15 (0.05) | -0.15 (0.05) |
| *p* | 2.54E-03 | 1.37E-02# | 1.63E-02 | 1.82E-03 | 2.03E-03 |
| FDR | **1.09E-02** | **4.57E-02** | 5.09E-02 | **1.09E-02** | **1.09E-02** |
| **Fasting plasma glucose level a** |  (se) | 0.16 (0.05) | 0.12 (0.05) | 0.12 (0.05) | 0.16 (0.05) | 0.18 (0.05) |
| *p* | 2.61E-03 | 2.18E-02 | 1.87E-02 | 2.30E-03 | 5.32E-04 |
| FDR | **1.09E-02** | 5.73E-02 | 5.30E-02 | **1.09E-02** | **4.43E-03** |
| **IL-6 level a** |  (se) | 0.03 (0.05) | 0.00 (0.05) | -0.01 (0.05) | 0.06 (0.05) | 0.07 (0.05) |
| *p* | 0.61 | 0.99 | 0.77 | 0.26 | 0.18 |
| FDR | 0.67 | 0.99 | 0.82 | 0.36 | 0.27 |
| **TNF- level a** |  (se) | 0.03 (0.05) | -0.01 (0.05) | -0.03 (0.05) | 0.08 (0.05) | 0.09 (0.05) |
| *p* | 0.55 | 0.82 | 0.57 | 0.13 | 0.07 |
| FDR | 0.63 | 0.86 | 0.63 | 0.22 | 0.14 |
| **CRP level a** |  (se) | -0.04 (0.05) | -0.09 (0.05) | -0.07 (0.05) | 0.01 (0.05) | 0.06 (0.05) |
| *p* | 0.41 | 0.10 | 0.21 | 0.84 | 0.24 |
| FDR | 0.52 | 0.19 | 0.31 | 0.86 | 0.34 |

Abbreviations: BMI, body mass index; CRP, C-reactive protein; FDR, False Discovery Rate; HDL, high-density lipid; IL, interleukin; TNF, tumour necrosis factor. Results obtained from linear mixed models adjusting for age and sex and family structure as random intercept. =standardized regression coefficient, bold values indicate that the association was significant at an FDR<.05. a Tests were performed on log-transformed data. # Threshold for p value corresponding to maximum q value <0.05.

**Supplementary Table 4: Associations between depression symptom profiles of probands and immunometabolic traits in their siblings**

|  |  |  |
| --- | --- | --- |
|  |  | *Depressive symptom profiles in probands* |
| *Immunometabolic outcome in siblings* |  | **Total depression severity** | **Mood symptoms profile** | **Cognitive symptoms profile** | **Somatic symptoms profile** | **Atypical-like symptoms profile** |
| **BMI** |  (se) | 0.036 (0.058) | 0.030 (0.058) | 0.010 (0.059) | 0.044 (0.058) | 0.052 (0.058) |
| *p* | 0.54 | 0.61 | 0.87 | 0.45 | 0.38 |
| **Waist circumference** |  (se) | 0.035 (0.053) | 0.049 (0.052) | 0.026 (0.053) | 0.021 (0.053) | 0.066 (0.053) |
| *p* | 0.50 | 0.35 | 0.62 | 0.69 | 0.21 |
| **Systolic blood pressure** |  (se) | 0.040 (0.048) | 0.009 (0.048) | -0.023 (0.048) | 0.079 (0.048) | 0.054 (0.049) |
| *p* | 0.40 | 0.85 | 0.64 | 0.10 | 0.27 |
| **Diastolic blood pressure** |  (se) | 0.040 (0.051) | 0.001 (0.050) | -0.015 (0.051) | 0.085 (0.051) | 0.100 (0.051) |
| *p* | 0.43 | 0.98 | 0.77 | 0.09 | <.05 \* |
| **Triglycerides level a** |  (se) | -0.040 (0.056) | -0.033 (0.055) | -0.010 (0.056) | -0.051 (0.056) | -0.013 (0.055) |
| *p* | 0.47 | 0.55 | 0.85 | 0.36 | 0.82 |
| **HDL cholesterol level a** |  (se) | -0.065 (0.054) | -0.090 (0.053) | -0.050 (0.054) | -0.038 (0.054) | -0.034 (0.054) |
| *p* | 0.23 | 0.09 | 0.36 | 0.48 | 0.53 |
| **Fasting plasma glucose level a** |  (se) | 0.034 (0.056) | 0.043 (0.056) | 0.005 (0.057) | 0.031 (0.057) | 0.037 (0.056) |
| *p* | 0.55 | 0.44 | 0.93 | 0.58 | 0.51 |
| **IL-6 level a** |  (se) | 0.038 (0.055) | 0.044 (0.055) | -0.004 (0.056) | 0.038 (0.055) | -0.004 (0.055) |
| *p* | 0.50 | 0.42 | 0.94 | 0.49 | 0.94 |
| **TNF- level a** |  (se) | 0.017 (0.055) | 0.016 (0.055) | 0.007 (0.056) | 0.017 (0.055) | -0.009 (0.055) |
| *p* | 0.75 | 0.77 | 0.90 | 0.75 | 0.87 |
| **CRP level a** |  (se) | 0.039 (0.056) | 0.021 (0.056) | -0.022 (0.056) | 0.062 (0.056) | 0.002 (0.056) |
| *p* | 0.49 | 0.70 | 0.69 | 0.26 | 0.97 |

Results of the linear mixed effect models with symptom profiles of the probands as the predictor variable and immunometabolic characteristics in their siblings as the outcome measure, while including age and sex of the siblings as covariates and family structure as the random intercept. Abbreviations: BMI, body mass index; CRP, C-reactive protein; HDL, high-density lipid; IL, interleukin; TNF, tumour necrosis factor. a Tests were performed on log-transformed data, \* nominally significant but did not survive multiple testing penalty, =standardized regression coefficient.

**Supplementary Table 5: Associations between immunometabolic characteristics of probands and depression symptom profiles of their siblings**

|  |  |  |
| --- | --- | --- |
|  |  | *Immunometabolic characteristics in probands* |
| *Depressive symptom profiles of siblings* |  | **BMI** | **Waist circumference** | **Systolic blood pressure** | **Diastolic blood pressure** | **Triglycerides level a** | **HDL cholesterol level a** | **Fasting plasma glucose level a** | **IL-6 level a** | **TNF- level a** | **CRP level a** |
| **Total depression severity** |  (se) | 0.006 (0.011) | 0.049 (0.058) | 0.007 (0.062) | -0.056 (0.056) | 0.040 (0.059) | -0.024 (0.055) | 0.077 (0.056) | 0.024 (0.059) | 0.059 (0.057) | -0.049 (0.058) |
| *p* | 0.62 | 0.40 | 0.92 | 0.32 | 0.51 | 0.66 | 0.17 | 0.68 | 0.30 | 0.40 |
| **Mood symptoms profile** |  (se) | 0.010 (0.011) | 0.052 (0.058) | -0.019 (0.062) | -0.075 (0.056) | 0.029 (0.059) | -0.018 (0.054) | 0.085 (0.057) | 0.031 (0.060) | 0.063 (0.059) | -0.009 (0.060) |
| *p* | 0.39 | 0.37 | 0.76 | 0.18 | 0.63 | 0.74 | 0.14 | 0.61 | 0.28 | 0.88 |
| **Cognitive symptoms profile** |  (se) | 0.003 (0.011) | 0.039 (0.058) | 0.006 (0.062) | -0.052 (0.056) | 0.087 (0.059) | -0.05 (0.055) | 0.079 (0.056) | -0.002 (0.059) | 0.014 (0.058) | -0.012 (0.059) |
| *p* | 0.76 | 0.50 | 0.93 | 0.35 | 0.15 | 0.36 | 0.16 | 0.98 | 0.81 | 0.83 |
| **Somatic symptoms profile** |  (se) | 0.003 (0.011) | 0.041 (0.058) | 0.020 (0.062) | -0.030 (0.056) | 0.025 (0.060) | -0.015 (0.055) | 0.057 (0.057) | 0.028 (0.058) | 0.062 (0.056) | -0.074 (0.057) |
| *p* | 0.81 | 0.48 | 0.75 | 0.60 | 0.67 | 0.78 | 0.32 | 0.62 | 0.28 | 0.20 |
| **Atypical-like symptoms profile** |  (se) | -0.002 (0.011) | 0.028 (0.057) | -0.082 (0.061) | -0.095 (0.055) | 0.001 (0.06) | -0.038 (0.055) | -0.024 (0.056) | 0.003 (0.057) | 0.077 (0.056) | -0.072 (0.057) |
| *p* | 0.87 | 0.63 | 0.19 | 0.09 | 0.99 | 0.49 | 0.67 | 0.96 | 0.17 | 0.21 |

Results of the linear mixed effect models with immunometabolic characteristics in the probands as the predictor variable and depression symptom profiles of their siblings as the outcome measure, while including age and sex of the siblings as covariates and family structure as the random intercept. Abbreviations: BMI, body mass index; CRP, C-reactive protein; HDL, high-density lipid; IL, interleukin; TNF, tumour necrosis factor. a Tests were performed on log-transformed data, =standardized regression coefficient.