|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Male-male pairs** | **Male-female pairs** | **Female-female pairs** | **Female-male pairs** |
| **Relation to proband** | **Concordant pairs** | **Matched OR (95% CI)** | **Concordant pairs** | **Matched OR (95% CI)** | **Concordant pairs** | **Matched OR (95% CI)** | **Concordant pairs** | **Matched OR (95% CI)** |
| **First-degree relatives** | 　 | 　 | 　 | 　 | 　 | 　 | 　 | 　 |
|  Full siblings  | 120 | 5.91(4.66-7.48) | 104 | 4.88(3.95-6.01) | 144 | 5.14(4.13-6.40) | 103 | 4.44(3.60-5.49) |
|  Parents | 22 | 3.52(2.27-5.45) | 46 | 4.81(3.53-6.55) | 62 | 4.33(3.33-5.64) | 31 | 4.59(3.12-6.74) |
|  Offspring | 22 | 4.27(2.76-6.60) | 31 | 4.23(2.89-6.20) | 62 | 5.01(3.83-6.57) | 46 | 3.92(2.88-5.35) |
|  *Total* | 164 | 5.15(4.20-6.31) | 181 | 4.73(4.02-5.57) | 268 | 4.92(4.17-5.80) | 180 | 4.31(3.65-5.09) |
| **Second-degree relatives** | 　 | 　 | 　 | 　 | 　 | 　 | 　 | 　 |
|  Maternal half-siblings | 14 | 1.65(0.75-3.64) | 16 | 2.06(1.23-3.43) | 23 | 2.18(1.19-4.00) | 16 | 2.06(1.24-3.43) |
|  Paternal half-siblings | 18 | 1.71(0.93-3.13) | 11 | 1.70(0.95-3.02) | 21 | 1.95(1.06-3.59) | 11 | 1.75(0.95-3.24) |
|  Uncles or aunts | 51 | 3.04(2.24-4.15) | 39 | 2.78(2.02-3.83) | 38 | 1.90(1.37-2.64) | 46 | 2.41(1.80-3.22) |
|  Nephews or nieces | 51 | 2.85(2.07-3.92) | 46 | 2.40(1.79-3.22) | 37 | 1.96(1.40-2.73) | 39 | 2.21(1.60-3.06) |
|  Grandparents | 0 | - | 1 | 1.12(0.15-8.39) | 1 | 0.63(0.10-3.98) | 2 | 2.50(0.60-10.49) |
|  Grandchildren  | 0 | - | 2 | 3.34(0.80-13.88) | 1 | 0.56(0.08-3.95) | 1 | 0.62(0.09-4.56) |
|  *Total* | 134 | 2.54(1.95-3.30) | 115 | 2.36(1.95-2.86) | 121 | 2.00(1.56-2.58) | 115 | 2.18(1.80-2.65) |
| **Third-degree relatives** | 　 | 　 | 　 | 　 | 　 | 　 | 　 | 　 |
|  First cousins  | 150 | 2.27(1.79-2.88) | 116 | 1.69(1.41-2.02) | 126 | 1.43(1.13-1.82) | 116 | 1.59(1.32-1.91) |

**Supplementary Table S1**. Gender effects: Odds ratios (with 95% confidence intervals) for the risk of Social Anxiety Disorder in relatives of probands diagnosed with Social Anxiety Disorder, compared to the relatives of unaffected individuals.

Footnotes: Heritability estimates based on Tetrachoric correlations are: Male-male pairs: 0.67, Female-female pairs: 0.50, Male-female or Female-male pairs: 0.55.

**Supplementary Table S2.** Risks of Social Anxiety Disorder (SAD) and Avoidant Personality Disorder (AVPD) in relatives of probands with AVPD only (N=1,994), compared with relatives of unaffected individuals.

|  |  |  |  |
| --- | --- | --- | --- |
|  |  | **SAD in relatives of AVPD-only probands** | **AVPD in relatives of AVPD-only probands** |
| **Relation to proband** | **Average degree of genetic similarity** | **Concordant pairs** | **Matched odds ratio****(95% CI)** | **Concordant pairs** | **Matched odds ratio****(95% CI)** |
| **First-degree relatives (total)** | 50% | 45 | 3.50(2.51-4.89) | 12 | 4.37(1.98-9.65) |
| **Second-degree relatives (total)** | 25% | 43 | 1.93(1.35-2.75) | 4 | 2.11(0.52-8.56) |
| **Third-degree relatives** | 12.5% | 42 | 1.64(1.18-2.29) | 7 | 1.76(0.73-4.25) |
| **Non-biological relativesa** | 0% | 10 | 3.87(1.96-7.65) | 0 | -- |

a Individuals who have at least one child together with the proband.

**Supplementary Table S3.** Sensitivity analyses: Risks of Social Anxiety Disorder in relatives of probands diagnosed with Social Anxiety Disorder (N=16,539) compared with relatives of unaffected individuals, after excluding individuals with potentially confounding diagnosesa (N=1,860).

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Relation to proband** | **Average degree of genetic similarity** | **Number of dyads** | **Concordant pairs** | **Matched odds ratio****(95% CI)** | **Tetrachoric correlation** |
| **First-degree relatives** | 　 | 　 | 　 | 　 | 　 |
|  Full siblings  | 50% | 238,612 | 387 | 5.33(4.67-6.08) | 0.27 |
|  Parents | 50% | 290,558 | 140 | 4.83(4.05-5.77) | 0.16 |
|  Offspring | 50% | 165,588 | 140 | 4.35(3.65-5.19) | 0.16 |
|  *Total* | *50%* | 694,758 | 667 | 4.97(4.45-5.55) | 0.20 |
| **Second-degree relatives** | 　 | 　 | 　 | 　 | 　 |
|  Maternal half-siblings | 25% | 45,324 | 57 | 2.12(1.48-3.06) | 0.13 |
|  Paternal half-siblings | 25% | 52,854 | 49 | 1.98(1.35-2.91) | 0.10 |
|  Uncles or aunts | 25% | 375,893 | 140 | 2.31(1.93-2.77) | 0.08 |
|  Nephews or nieces | 25% | 297,870 | 139 | 2.24(1.86-2.70) | 0.08 |
|  Grandparents | 25% | 243,726 | 4 | 1.54(0.59-4.04) | -0.07 |
|  Grandchildren  | 25% | 49,358 | 4 | 1.43(0.54-3.79) | -0.07 |
|  *Total* | *25%* | 1,065,025 | 393 | 2.26(1.95-2.63) | 0.08 |
| **Third-degree relatives** | 　 | 　 | 　 | 　 | 　 |
|  First cousins  | 12.5% | 782,316 | 408 | 1.66(1.44-1.91) | 0.08 |
| **Non-biological relatives** | 　 | 　 | 　 | 　 | 　 |
|  Spouses/partnersb | 0% | 95,971 | 85 | 3.87(3.10-4.84) | 0.20 |

a Pervasive Developmental Disorders (F84), Schizophrenia, schizotypal and delusional disorders (F20 to F29), Paranoid personality disorder

 (F60.0) and Schizoid personality disorder (F60.1).

b Individuals who have at least one child together with the proband.