**SUPPLEMENTARY MATERIAL**

**Sensitivity analyses**

We then re-analyzed the data after the graphical detection and subsequent removal of a single outlying observation with an FA value of < 0.2, with no effect on any of our significant findings, all of which remained significant. We then adjusted for the effects of antidepressants prescribed at time 1 or time 2 by including this as a term in the regression models. In each case, all of the significant relationships between uncinate FA and depression at time 1 (Right uncinate: standardized beta = -0.14, F = 12.19, p < 0.001; Left uncinate: standardized beta = -0.15, F = 12.32, p < 0.001), depression at time 2 (Right uncinate: standardized beta = -0.12, F = 9.19, p = 0.002; Left uncinate: standardized beta = -0.11, F = 7.32, p = 0.007), neuroticism (Right uncinate: standardized beta = -0.07, F = 3.12, p = 0.08; Left uncinate: standardized beta = -0.11, F = 5.96, p = 0.015) or extraversion (Right uncinate: standardized beta = 0.12, F = 7.52, p = 0.006) were in the same direction as reported for the combined sample. The significant negative relationship between right uncinate FA and neuroticism became a non-significant trend however, when antidepressant treatment was added to the model.

The data were then re-analyzed using cigarette use (never, current, past) as a covariate in the regression analyses. In each case, all of the significant relationships between uncinate FA and depression at time 1 (Right uncinate: standardized beta = -0.14, F = 13.59, p = 0.0002; Left uncinate: standardized beta = -0.15, F = 12.13, p = 0.005), depression at time 2 (Right uncinate: standardized beta = -0.12, F = 10.47, p = 0.001; Left uncinate: standardized beta = -0.11, F = 7.00, p = 0.008), neuroticism (Right uncinate: standardized beta = -0.09, F = 4.42, p = 0.036; Left uncinate: standardized beta = -0.11, F = 6.66, p = 0.01) or extraversion (Right uncinate: standardized beta = 0.13, F = 8.99, p = 0.003) were in the same direction as reported for the combined sample.

We then re-analysed the data after adjustment for self-reported alcohol use (in standard units) at the time of the imaging assessment. All of the significant relationships between uncinate FA and depression at time 1 (Right uncinate: standardized beta = -0.14, F = 11.44, p < 0.001; Left uncinate: standardized beta = -0.15, F = 12.31, p < 0.001), depression at time 2 (Right uncinate: standardized beta = -0.13, F = 9.96, p = 0.002; Left uncinate: standardized beta = -0.11, F = 5.43, p < 0.02). The association between neuroticism and left unccinate FA also remained statistically significant (standardized beta = -0.11, F = 5.28, p = 0.02) although the relationship between neuroticism and right uncinate fractional anisotropy became non-significant on the right (standardized beta = -0.06, F = 2.44, p = 0.12). The relationship between extraversion and FA remained significant bilaterally after the inclusion of alcohol units per week in the model (Right uncinate: standardized beta = 0.12, F = 7.84, p = 0.005; Left uncinate: standardized beta = 0.11, F = 6.04, p = 0.01).

Finally, we adjusted our analysis for the effect of the 48 subjects who recalled a lifetime history of stroke in their clinical interview and questionnaires. Again, in each case, all of the significant relationships between uncinate FA and depression at time 1 (Right uncinate: standardized beta = -0.15, F = 13.42, p < 0.001; Left uncinate: standardized beta = -0.15, F = 12.85, p < 0.001), depression at time 2 (Right uncinate: standardized beta = -0.12, F = 9.88, p = 0.002; Left uncinate: standardized beta = -0.11, F = 7.44, p < 0.001), neuroticism (Right uncinate: standardized beta = -0.09, F = 11.30, p < 0.001; Left uncinate: standardized beta = -0.12, F = 6.94, p = 0.008) or extraversion (Right uncinate: standardized beta = 0.12, F = 8.66, p = 0.004) were in the same direction as reported for the combined sample. Similar results were also obtained if individuals with a history of stroke were removed from the analysis completely, although the association between right uncinate FA and neuroticism became non-significant in this analysis (standardized beta = -0.07, F = 2.38, p=0.12) but with little attenuation in the size of the effect.

**Supplementary Table S1: Association between white matter tract FA and symptoms of anxiety**

|  |  |  |
| --- | --- | --- |
|  | Assessment time 1 | Assessment time 2 |
|  | β | SE(β) | t value | Pr(>|t|) | β | SE(β) | t value | Pr(>|t|) |
| Genu | -0.0007 | 0.0006 | -1.23 | 0.22 | -0.0003 | 0.0005 | -0.49 | 0.63 |
| Splenium | -0.0009 | 0.0009 | -1.06 | 0.28 | -0.0006 | -0.0008 | -0.66 | 0.51 |
| LArc | 3 x 10-5 | 0.0004 | 0.06 | 0.95 | 0.0002 | 0.0005 | 0.31 | 0.75 |
| RArc | 0.0002 | 0.0006 | 0.41 | 0.68 | 0.0003 | 0.0006 | 0.62 | 0.54 |
| LATR | -0.0004 | 0.0006 | -0.82 | 0.41 | -0.0006 | 0.0004 | -1.34 | 0.18 |
| RATR | -0.0007 | 0.0004 | -1.70 | 0.09 | -0.0005 | 0.0004 | -1.16 | 0.25 |
| LCCG | -0.001 | 0.0006 | -2.25 | 0.03 | -0.001 | 0.0006 | -1.70 | 0.09 |
| RCCG | -0.001 | 0.0006 | -1.97 | 0.05 | -0.001 | 0.0005 | -2.10 | 0.04 |
| LUnc | -0.0007 | 0.0004 | -1.72 | 0.08 | -0.0009 | 0.0004 | -1.15 | 0.03 |
| RUnc | -0.0008 | 0.0004 | -2.10 | 0.04 | -0.0007 | 0.0004 | -1.64 | 0.10 |
| LILF | 0.0003 | 0.0006 | 0.47 | 0.64 | 4 x 10-5 | 0.0006 | 0.07 | 0.95 |
| RILF | 0.0001 | 0.0006 | 0.22 | 0.83 | -0.0006 | 0.0006 | -1.15 | 0.25 |

L = left, R = right, Arc = arcuate fasciculus, ATR = anterior thalamic radiation, CCG = cingulum cingulate gyrus, Unc = uncinate fasciculus and ILF = inferior longitudinal fasciculus. None of the findings were significant at PFDR < 0.05.

**Supplementary Table S2: Changes in model fit between depression and fractional anisotropy before and after inclusion of neuroticism in the model**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Before inclusion of neuroticism** | **After inclusion of neuroticism** | **Test for improved model fit** |
| Left uncinate | beta = -0.16 | p < 0.001, R2 = 0.03 | beta = -0.12 | p = 0.004, R2 = 0.15 | F = 73.4, p < 1x10-6 |
| Right uncinate | beta = -0.16 | p < 0.001, R2 = 0.03 | beta = -0.14 | p < 0.001, R2 = 0.15 | F = 78.5, p < 1x10-6 |
|  | **Before inclusion of extraversion** | **After inclusion of extraversion** | **Test for improved model fit** |
| Right uncinate | beta = -0.16 | p < 0.001, R2 = 0.03 | beta = -0.13 | p = 0.002, R2 = 0.14 | F = 75.3, p < 1x10-6  |

\*standardized betas given on identically sized samples with complete data on each measure. Values differ slightly from those given earlier because of necessity to compare model fit using two equally sized samples with complete data.