*Twin Research and Human Genetics*

The Genetic and Environmental Relationship Between Childhood Behavioral Inhibition

and Pre-Adolescent Anxiety

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**Supplemental Tables**

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| Supplemental Table S1. Factor structure fit indices from studies exploring the psychometrics of the original BIQ and retrospective version of the BIQ (current study) |
| Study | *χ2* | *df* | *χ2*/*df* | *p* | *RMSEA* | *CFI* | *TLI/NFI* | N |
| Previous Studies |
| Bishop et al., 2003 | 1835 | 390 | -- | <0.001 | 0.08 | 0.88 | 0.87 | 613 |
| Broeren & Muris, 2010 | -- |  | 1.74-2.34 |  | 0.07-0.08 | 0.88-0.91 | -- | 531 |
| Kim et al., 2011 | 1382.61 | 390 | -- | <0.001 | 0.08 | 0.90 | -- | 495 |
| Vreeke et al., 2012\* | -- |  | -- | -- | 0.05 | 0.98 | 0.96 | 2,343 |
| Current Study |
| Correlated Factor Model | 4650.86 | 395 | -- | <.001 | 0.12 | 0.88 | 0.87 | 681 |
| \* A short form of the BIQ was used in Vreeke et al. (2012), so this study may not be directly comparable.\*\* Indicates final model in current study |

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| Supplemental Table S2. Pearson correlations between the BIQ and parent measures of child anxiety and child measures of child anxiety (“C” indicates child report; “P” indicates parent report) |
| Measure | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 |
| 1. BIQ | -- |  |  |  |  |  |  |  |  |
| 2. SCARED-C, social anxiety | .26\*\* | -- |  |  |  |  |  |  |  |
| 3. SCARED-C, generalized anxiety | .05 | .40\*\* | -- |  |  |  |  |  |  |
| 4. SCARED-C, separation anxiety | .04 | .43\*\* | .41\*\* | -- |  |  |  |  |  |
| 5. SCARED-C, panic | .04 | .41\*\* | .49\*\* | .51\*\* | -- |  |  |  |  |
| 6. SCARED-P, social anxiety | .67\*\* | .29\*\* | .03 | .05 | .00 | -- |  |  |  |
| 7. SCARED-P, generalized anxiety | .25\*\* | .07 | .20\*\* | .09\* | .08\* | .48\*\* | -- |  |  |
| 8. SCARED-P, separation anxiety | .22\*\* | .05 | .06 | .26\*\* | .08\* | .39\*\* | .59\*\* | -- |  |
| 9. SCARED-P, panic | .19\*\* | .04 | .03 | .05 | .10\* | .43\*\* | .61\*\* | .61\*\* | -- |
| \**p* < .05; \*\**p* < .001 |

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| Supplemental Table S3. Model Fit Statistics from Common Pathway (CP) Analyses Assessing Child and Parent Indicators on Each Anxiety Symptom Cluster |
| Model | Estimated Parameters | -2 LL | DF | AIC | Δ LL | Δ DF | p |
| Social Anxiety |
| Full CP model with child and parent indicators set to be free | 17 | 6651.303 | 1265 | 4121.303 | - | - | - |
| CP model with child and parent indicators constrained to be equal \* | 16 | 6651.465 | 1266 | 4119.465 | .162 | 1 | .687 |
| Generalized Anxiety |
| Full CP model with child and parent indicators set to be free | 17 | 6859.450 | 1265 | 4329.450 | - | - | - |
| CP model with child and parent indicators constrained to be equal \* | 16 | 6859.450 | 1266 | 4327.450 | <.001 | 1 | .999 |
| Separation Anxiety |
| Full CP model with child and parent indicators set to be free | 17 | 6252.353 | 1264 | 3724.353 | - | - | - |
| CP model with child and parent indicators constrained to be equal \* | 16 | 6252.597 | 1265 | 3722.597 | <.001 | 1 | .999 |
| Panic |
| Full CP model with child and parent indicators set to be free \* | 17 | 6421.260 | 1264 | 3893.260 | - | - | - |
| CP model with child and parent indicators constrained to be equal \* | 16 | 6421.260 | 1265 | 3891.260 | .245 | 1 | .621 |
| \* Indicates best-fitting model(s) from that series of nested sub-models |

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| Supplemental Table S4. Cross-Twin, Cross-Trait Genetic Correlations Between BI and Anxiety Symptom Clusters |
| Measure | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
| *MZ Twins* |
| 1. Behavioral Inhibition – Twin 1
 | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- |
| 1. Behavioral Inhibition – Twin 2
 | .81 | -- | -- | -- | -- | -- | -- | -- | -- | -- |
| 1. Social Anxiety – Twin 1
 | .50 | .42 | -- | -- | -- | -- | -- | -- | -- | -- |
| 1. Social Anxiety – Twin 2
 | .44 | .60 | .60 | -- | -- | -- | -- | -- | -- | -- |
| 1. Generalized Anxiety – Twin 1
 | .06 | .04 | .34 | .21 | -- | -- | -- | -- | -- | -- |
| 1. Generalized Anxiety – Twin 2
 | -.09 | .10 | .10 | .42 | .47 | -- | -- | -- | -- | -- |
| 1. Separation Anxiety – Twin 1
 | .10 | .05 | .39 | .32 | .51 | .23 | -- | -- | -- | -- |
| 1. Separation Anxiety – Twin 2
 | -.04 | .04 | .07 | .37 | .33 | .49 | .57 | -- | -- | -- |
| 1. Panic – Twin 1
 | -.07 | -.13 | .24 | .15 | .46 | .27 | .46 | .38 | -- | -- |
| 1. Panic – Twin 2
 | .04 | .13 | .08 | .36 | .25 | .49 | .38 | .58 | .60 | -- |
| *DZ Twins* |
| 1. Behavioral Inhibition – Twin 1
 | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- |
| 1. Behavioral Inhibition – Twin 2
 | .02 | -- | -- | -- | -- | -- | -- | -- | -- | -- |
| 1. Social Anxiety – Twin 1
 | .52 | -.15 | -- | -- | -- | -- | -- | -- | -- | -- |
| 1. Social Anxiety – Twin 2
 | -.06 | .64 | -.02 | -- | -- | -- | -- | -- | -- | -- |
| 1. Generalized Anxiety – Twin 1
 | .14 | .001 | .34 | .12 | -- | -- | -- | -- | -- | -- |
| 1. Generalized Anxiety – Twin 2
 | -.002 | .26 | .05 | .40 | .17 | -- | -- | -- | -- | -- |
| 1. Separation Anxiety – Twin 1
 | .15 | -.05 | .34 | .02 | .43 | .13 | -- | -- | -- | -- |
| 1. Separation Anxiety – Twin 2
 | .05 | .20 | .10 | .31 | 22 | .44 | .35 | -- | -- | -- |
| 1. Panic – Twin 1
 | .14 | .06 | .33 | .12 | .47 | .13 | .46 | .23 | -- | -- |
| 1. Panic – Twin 2
 | -.01 | .18 | .19 | .31 | .26 | .53 | .25 | .49 | .34 | -- |
| \**p* < .05; \*\**p* < .001 |

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| Supplemental Table S5. Model Fit Statistics for from Multivariate Analyses Between BI and Anxiety Symptom Clusters |
| Model | Estimated Parameters | -2 LL | DF | AIC | Δ LL | Δ DF | p |
| Full ACE Parameters |
| Full ACE | 55 | 17200.516 | 3109 | 10982.516 | - | - | - |
| ACE drop all C \* | 40 | 17204.918 | 3124 | 10956.918 | 4.401 | 15 | .996 |
| ACE drop all A | 40 | 17306.158 | 3124 | 11058.158 | 105.642 | 15 | <.001 |
| ACE drop all A and C | 25 | 17498.420 | 3139 | 11220.420 | 297.904 | 30 | <.001 |
| Final Model from Above – Drop Parameters Shared with BI |
| Full AE | 40 | 17204.918 | 3124 | 10956.918 | - | - | - |
| AE drop all shared A | 36 | 17240.292 | 3128 | 10984.292 | 35.374 | 4 | <.001 |
| AE drop all shared E | 36 | 17244.994 | 3128 | 10988.994 | 40.076 | 4 | <.001 |
| AE drop all shared A and E | 32 | 17474.040 | 3132 | 11210.040 | 269.122 | 8 | <.001 |
| AE drop E51 \* | 39 | 17205.620 | 3125 | 10955.620 | .702 | 1 | .402 |
| AE drop A31 \* | 39 | 17206.437 | 3125 | 10956.437 | 1.519 | 1 | .218 |
| AE drop A41 \* | 39 | 17207.393 | 3125 | 10957.393 | 2.475 | 1 | .116 |
| AE drop A51 | 39 | 17209.877 | 3125 | 10959.877 | 4.960 | 1 | .026 |
| AE drop E41 | 39 | 17213.725 | 3125 | 10963.725 | 8.807 | 1 | .003 |
| AE drop E31 | 39 | 17215.306 | 3125 | 10965.306 | 10.388 | 1 | .001 |
| AE drop E21 | 39 | 17255.350 | 3125 | 11005.350 | 50.433 | 1 | <.001 |
| AE drop A21 | 39 | 17237.923 | 3125 | 10987.923 | 33.005 | 1 | <.001 |
| Full AE – Drop Non-Significant Parameters from Above |
| Full AE | 40 | 17204.918 | 3124 | 10956.918 | - | - | - |
| AE drop E51, A31, A41 \*\* | 37 | 17209.341 | 3127 | 10955.341 | 4.422 | 3 | .219 |
| \* Indicates best-fitting model(s) from that series of nested sub-models; \*\* Indicates final best-fitting model overallNotes on path naming: A21/E21 = Shared between BI and social anxiety symptomsA31/E31 = Shared between BI and generalized anxiety symptomsA41/E41 = Shared between BI and separation anxiety symptomsA51/E51 = Shared between BI and panic symptoms |

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| Supplemental Table S6. Variance and Covariance Components for the Best-Fitting Multivariate Model Between Anxiety Symptom Clusters (95% Confidence Intervals) |
| *Social* | *Generalized* | *Separation* | *Panic* |
|  | Additive Genetic (A) Components  |  |
| A11 | A21 | A22 | A31 | A32 | A33 | A51 | A52 | A53 | A54 |
| .49 | .06 | .44 | .06 | .15 | .42 | .09 | .19 | .10 | .30 |
|  | Unique Environment (E) Components  |  |
| E11 | E21 | E22 | E31 | E32 | E33 | E51 | E52 | E53 | E54 |
| .52 | .09 | .41 | .06 | .01 | .29 | .03 | .03 | <.001 | .27 |
| Notes on variance component naming: A11/E11 = Social anxiety symptomsA22/E22 = Generalized anxiety symptomsA33/E33 = Separation anxiety symptomsA44/E55 = Panic symptomsAll other paths represent shared variance between the anxiety symptom clustersNotes: Within each phenotype, these should add up to 1.00 but may not due to rounding error.  |  |

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| Supplemental Table S7. Model Fit Statistics for from the Direction of Causation and Correlated Liabilities Models Between BI and Social Anxiety Symptoms |
| Model | Estimated Parameters | -2 LL | DF | AIC | Δ LL | Δ DF | p |
| Model with Correlated Liabilities (Cross Paths) Between Phenotypes |
| Full AE with A21 and E21 \* | 10 | 8911.565 | 1245 | 6421.565 | -- | -- | -- |
| AE drop A21 | 9 | 8944.554 | 1246 | 6452.554 | 32.989 | 1 | <.001 |
| AE drop E21 | 9 | 8947.257 | 1246 | 6455.257 | 35.691 | 1 | <.001 |
| AE drop A21 and E21 \*\* | 8 | 9172.122 | 1247 | 6678.122 | 260.557 | 2 | <.001 |
| Direction of Causation Model with Causal Beta Paths Between Phenotypes |
| Full AE with β1 and β2 | 10 | 8912.351 | 1245 | 6422.351 | -- | -- | -- |
| AE drop β1  | 9 | 9116.040 | 1246 | 6624.040 | 203.689 | 1 | <.001 |
| AE drop β2 \* | 9 | 8913.621 | 1246 | 6421.621 | 1.270 | 1 | .260 |
| AE drop β1 and β2 \*\* | 8 | 9172.122 | 1247 | 6678.122 | 259.771 | 2 | <.001 |
| Comparing Final Models  |
| Full AE with A21 and E21  | 10 | 8911.565 | 1245 | 6421.565 | - | - | - |
| AE drop β2 \* | 9 | 8913.621 | 1246 | 6421.621 | 2.055 | 1 | .152 |
| \* Indicates best-fitting model(s) from that series of nested sub-models; \*\* Indicates identical modelsNotes on path naming: A21/E21 = Shared between BI and social anxiety symptomsβ1 = Causal path from BI to social anxiety symptomsβ2 = Causal path from social anxiety symptoms to BI |

**Supplemental Text**

There are several possible explanations for the vastly different MZ and DZ correlations for BI and social anxiety symptoms. The first is sibling contrast effects. These can be ruled out because the means and variances for these phenotypes could be constrained to be equal within twin pairs and across zygosity. The second is a violation of the equal environments assumption (EEA). The EEA, upon which all twin studies are predicated (Neale & Cardon, 1992), states that MZ and DZ twins are equally correlated for their exposure to environmental influences that are of etiologic importance to the trait under study. Thus, while most prior investigations of the EEA have supported its validity (Eaves et al., 2003), we cannot rule out the possibility of some level of violation here for BI and social anxiety that is driven by parent report. This could occur if parents of MZ twins inflate similarities of a trait and parents of DZ twins deflate similarities, introducing a pseudo unequal environment across zygosity (Emde et al., 1992). In the current study, this trend is seen for parent-report BI and social anxiety symptoms but not for child self-report measures. Such effects have been noted in a previous study of BI (Smith et al., 2012) and, thus, could present a limitation for any twin study of BI and, possibly, social anxiety. Parent and child measures offer their own unique insights and limitations into underlying psychopathology (Cole et al., 2000), including BI (Muris et al., 2003) yet are often minimally correlated (Birmaher et al., 1997; Muris et al., 2003), so we obtained reports from both types of informants. After testing more complex multi-rater models, we used the average of the parent and child SCARED scores to provide an optimal compromise in the main analyses.

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