



Published in final edited form as:

J Anxiety Disord. 2008 May ; 22(4): 635–641. doi:10.1016/j.janxdis.2007.06.002.

The relationship between separation anxiety and impairment

Debra L Foley, PhD^a, Richard Rowe, PhD^b, Hermine Maes, PhD^a, Judy Silberg, PhD^a, Lindon Eaves, PhD^a, and Andrew Pickles, PhD^c

^a Virginia Institute for Psychiatric and Behavioral Genetics, Medical College of Virginia Commonwealth University, USA

^b MRC Social, Genetic, and Developmental Psychiatry Center, Institute of Psychiatry, King's College London, UK

^c School of Epidemiology and Health Science, University of Manchester, Stopford Building Oxford Road, Manchester M13 9PT, UK

Abstract

The goal of this study was to characterize the contemporaneous and prognostic relationship between symptoms of separation anxiety disorder (SAD) and associated functional impairment. The sample comprised $n=2067$ 8–16 year-old twins from a community-based registry. Juvenile subjects and their parents completed a personal interview on two occasions, separated by an average follow-up period of 18 months, about the subject's current history of SAD and associated functional impairment. Results showed that SAD symptoms typically caused very little impairment but demonstrated significant continuity over time. Older youth had significantly more persistent symptoms than younger children. Prior symptom level independently predicted future symptom level and diagnostic symptom threshold, with and without impairment. Neither diagnostic threshold nor severity of impairment independently predicted outcomes after taking account of prior symptom levels. The results indicate that impairment may index current treatment need but symptom levels provide the best information about severity and prognosis.

Keywords

separation anxiety; disorders; anxiety; DSM-IV; impairment; clinical significance criterion

INTRODUCTION

Clinically significant impairment or distress was added to the diagnostic criteria for many psychiatric disorders in the DSM-IV (American Psychiatric Association, 1994). This criterion was introduced to help “establish the threshold for the diagnosis of a disorder in those situations in which the symptomatic presentation by itself (particularly in its milder

Direct reprint requests to Debra Foley dfoley@unimelb.edu.au.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

forms) is not inherently pathological and may be encountered in individuals for who a diagnosis of “mental disorder” would be inappropriate” (American Psychiatric Association, 1994, p7 Use of the Manual).

Despite the widespread adoption of these criteria, especially the impairment criterion, rather little is known about the relationship between impairment and juvenile anxiety disorders in community settings. There is a substantial reduction in the estimated rate of individual or aggregate juvenile anxiety disorders when impairment is required for a diagnosis (Canino, Shrout, Rubio-Stipec, Bird, Bravo, Ramirez et al., 2004; Costello, Egger & Angold, 2004; Romano Tremblay, Viaro, Zoccolillo & Pagani 2001; Essau, Conrath & Peterman 2000; Simonoff, Pickles, Meyer, Silberg, Maes, Loeber et al., 1997), consistent with expectations (Wakefield & Spitzer, 2002). The utility of diagnostic thresholds for identifying impaired youth in need of services cannot, however, be inferred from these data. Youth with sub-threshold symptoms or NOS disorders may also be significantly impaired (Angold, Costello, Farmer, Burns & Erkanli, 1999).

The severity of impairing childhood emotional disorder (anxiety or depression) was prognostic for adolescent disorder (Costello, Angold & Keeler, 1999) but does not clarify whether impairment ratings capture prognostic information independent of symptom or syndrome severity or if there is any heterogeneity in the symptom-impairment relationship within the emotional disorders. Pickles, Rowe, Simonoff, Foley, Rutter & Silberg (2001) found that juvenile depression and oppositional-defiant disorder symptoms were highly impairing whereas conduct disorder symptoms were not. Impairment related to conduct and oppositional symptoms predicted future symptoms and impairment independent of symptom load but impairment related to depression did not. This led to the suggestion (Pickles, Simonoff, Foley, Rutter & Silberg, 2001) that impairment may be an epiphenomenon of depression symptoms. Do results for juvenile depression generalize to all juvenile emotional disorders or do anxiety disorders have a distinct symptom-impairment relationship?

The aim of this study was to characterize the relationship between a common juvenile anxiety disorder, separation anxiety disorder, and associated functional impairment in a large community based sample of youth aged between 8 and 16 years. We report the temporal and prognostic relationship between separation anxiety disorder symptom levels, diagnostic symptom threshold, and functional impairment, by age and sex.

METHOD

Subjects were participants in The Virginia Twin Study for Adolescent Behavioral Development (VTSABD) (Eaves, Silberg, Meyer, Maes, Simonoff, Pickles et al., 1997; Hewitt, Silberg, Rutter, Simonoff, Meyer, Maes et al., 1997; Simonoff, Pickles, Meyer, Silberg, Maes, Loeber et al., 1997), a longitudinal community-based family study of Caucasian twins born between 1974 and 1983. Twins were recruited through the public and private school systems in the state of Virginia and through state-wide publicity. From a target population of 1892 families, 1412 families (75%) agreed to participate in the study at time 1 (Meyer, Silberg, Simonoff, Kendler & Hewitt, 1996). The eligible sample for this report completed an interview about their history of separation anxiety disorder at entry to

the study when they were aged between 8–16 years (N=2652 individual twins; N=1231 boys, N=1421 girls). Of these, N=1924 children were also interviewed 18.6 months (SD=4.7) later at time 2.

Trained field workers interviewed subjects and their parents about the subject's current (past 3 months) history of separation anxiety disorder at time 1 and time 2 using the Child and Adolescent Psychiatric Assessment (CAPA) (Angold, Prendergast, Cox, Harrington, Simonoff & Rutter, 1995; Angold & Costello, 2000). The protocol for the VTSABD was implemented prior to the release of the DSM-IV and symptoms of separation anxiety disorder and the diagnostic symptom threshold were therefore assessed following the DSM-III-R (American Psychiatric Association, 1987). The symptomatic threshold for separation anxiety disorder was defined by 3/9 symptoms in the DSM-III-R and 3/8 symptoms in the DSM-IV. Recurrent excessive distress about anticipated or actual separation was collapsed into one symptom in DSM-IV but in all other respects the symptom criteria were unchanged.

The CAPA included a detailed assessment of impairment associated with each symptom area (Ezpeleta, Keeler, Erkanli, Costello & Angold, 2001; Angold, Prendergast, Cox, Harrington, Simonoff & Rutter, 1995). Disability was rated in reference to parent relationships, sibling relationships, self-care, homework and chores, leaving the house, school performance, school suspension, teacher relationships, school peer relationships, spare time activities, non-school adult relationships, non-school peer relationships, employment, treatment and placement. Each area of disability was rated on a three point scale, for no, partial or severe impairment. A total score of 2 or higher was used to define the presence of clinically significant impairment (Simonoff, Pickles, Meyer, Silberg, Maes, Loeber et al., 1997; Pickles, Rowe, Simonoff, Foley, Rutter, Silberg, 2001). A symptom or symptom-related impairment was rated as present if it was endorsed at either the child or parent interview (Bird, Gould, Staghezza, 1992).

Symptom related impairment was assessed for all children with 2 or more symptoms of separation anxiety and was, by definition, 0 for children without symptoms. Children with just one symptom of separation anxiety were therefore coded as missing for impairment in the data analyses described below. For cross-sectional analyses, there were n=4,811 CAPA assessments of separation anxiety symptoms across time 1 and time 2 of which n=4,380 had an associated impairment rating. The pattern of missing data was not a problem for analyses that included the number of time 1 symptoms because the missing impairment data was then covariate dependent (Little, 1993). Missing data biases would, however, be expected for statistics that are not calculated conditional on symptom score, such as prevalence of impairment among sub-threshold separation anxiety disorder cases. For longitudinal analyses, there were n=2067 CAPA assessments of separation anxiety symptoms at *both* time 1 and time 2 and of these impairment scores were known for n=1864 at time 1 and n=1715 at time 1 and time 2.

Data analysis

Ordinary linear regression was used to test the linearity of the relationship between the number of symptoms of separation anxiety disorder and the level of associated impairment. Possible curvature in the relationship between symptoms and impairment was tested by

estimating the fit of fractional polynomials (Royston & Altman, 1994). Proportional odds ordinal logistic regression was used to assess the relative predictive value of time 1 symptoms, time 1 diagnostic symptom threshold and time 1 impairment on time 2 symptom count (Clayton, 1976; Stram & Wei, 1987). The estimated proportional odds ratio (POR) is the odds at time 2 of having one or more (1+) symptoms versus 0 symptoms, or 2+ versus 0–1 symptoms, or 3+ versus 0–2 symptoms and so on. The coefficients from this model were also used to estimate the odds ratio (OR) of a future diagnosis, defined by being above or below the DSM (three-symptom) threshold. If the proportionality assumption holds, then the POR model delivers an estimate of the OR for diagnosis but more efficiently than that obtained by the use of the more familiar binary logistic regression (Maughan, Collishaw, Pickles, 1998; Pickles, Rowe, Simonoff, Foley, Rutter, Silberg, 2001).

Proportional odds ordinal logistic regression was also used to assess the relative predictive value of time 1 symptoms, time 1 diagnostic symptom threshold and time 1 impairment on time 2 impairment. However, given the pattern of missing impairment data (i.e., for children with only 1 symptom of separation anxiety), we present descriptive rather than formal results for the prediction of impairment.

The POR estimates were standardized because the scale of the symptom and impairment ratings was arbitrary and standardization permitted a direct comparison of the relative prognostic importance of prior symptoms and impairment across different diagnostic areas (*cf.* Pickles, Rowe, Simonoff, Foley, Rutter, Silberg, 2001). Estimates were standardized by the observed variance of the time 1 symptom and impairment ratings. This meant that the standardized POR associated with time 1 symptoms reflected the odds of time 2 symptoms (i.e., 1+ vs. 0, 2+ vs. 0–1, and so on) associated with a 1 SD change in the symptom count at time 1. Similarly, the standardized POR associated with time 1 impairment reflected the odds of time 2 symptoms associated with a 1 SD change in the impairment score at time 1.

Since we analyze two waves of data from twins we use the robust (Huber, 1967) or survey covariance matrix estimator (Binder, 1983) to adjust for the familial and temporal correlations among observations. This approach also provides standard errors, confidence intervals and p-values for means and linear regression coefficients that are corrected for the heteroscedasticity commonly found for symptom counts in community samples. All analyses were conducted in Stata 8 (StataCorp, 2004).

As a check for possible biases associated with sample attrition all analyses were repeated using weighted wave 2 data, where the weights were calculated as the inverse of the wave 2 response probabilities obtained from a logit model with wave 1 symptom count, diagnostic symptom threshold, impairment score and the age and sex of the subject as covariates. Estimates were little changed and inferential conclusions remained unaltered. For simplicity we present the un-weighted analyses.

RESULTS

Contemporaneous Relationship Between Separation Anxiety and Impairment

Nineteen percent (53/281) of children who met the (3+) diagnostic symptom threshold and 5% (13/248) of children with (2) sub-threshold symptoms had clinically significant impairment.

The distribution of subjects by the number of separation anxiety symptoms and associated impairment scores is given in Figure 1. Data points are randomly perturbed to distinguish otherwise coincident points and subdivided into the four categories defined by the diagnostic symptom and impairment thresholds. The fractional polynomial trend line shows a shallow but increasing trend. The average linear trend was highly significant ($p < .001$) and implied that each additional symptom was associated with a 0.18 increase (CI 0.14, 0.22) in the symptom score. There was no significant increase in impairment associated with the 3-symptom diagnostic cut-point once account had been taken of this linear trend (using regression or ordinal logit). However, addition of a quadratic symptom count term was significant ($p < .001$). Dividing the trend up into two linear sections with a lower slope below and a steeper slope above some cut-point gave significant improvement in fit, a similar improvement being obtained for cut-points at three (diagnostic), four and five symptoms. Although the prevalence of separation anxiety disorder differed by sex (male 3.2% v female 6.8%, $p < 0.001$), the presence of impairment in boys (17%, 16/92) and girls (19%, 37/190) above the symptom threshold was very similar. The prevalence of separation anxiety disorder also varied substantially with age (<14 years 6.5% versus 14–16 years 2.9%, $p < 0.001$) but again the presence of impairment in younger (16%) and older youth (22%) above the symptom threshold was very similar. For neither sex nor age did these differences approach significance.

Longitudinal Relationship Between Separation Anxiety and Impairment

Eighteen percent (27/148) of children with separation anxiety disorder at time 1 had separation anxiety disorder at time 2. Eight percent (2/26) of children with a diagnosis of separation anxiety disorder with impairment at time 1 had a diagnosis of separation anxiety disorder with impairment at time 2. Time 1 symptoms were strongly associated with time 2 symptoms, time 2 diagnosis and time 2 diagnosis with impairment (all $p < 0.001$). There was no additional prognostic information associated with diagnostic symptom threshold or impairment after controlling for the total number of symptoms (Table 1).

The standardized POR for time 2 symptoms associated with time 1 symptoms was 1.71 (CI=1.54, 1.91; $p < 0.001$) after controlling for impairment. This meant that for each 1 SD increase in separation anxiety symptoms at time 1 there was a 71% increase in the odds of separation anxiety symptoms at time 2. The standardized POR for time 2 separation anxiety symptoms associated with time 1 impairment was very small 1.06 (CI 0.95, 1.17; $p = 0.3$) and non-significant after controlling for time 1 symptoms. The prognostic power of time 1 symptoms did not differ significantly by sex (regression coefficient for the interaction between sex and time 1 symptoms $p = 0.1$; ordinal logistic $p = 0.7$). Similar tests for an effect of age-group (regression $p = 0.02$; ordinal logistic $p < 0.001$) suggested that symptoms were

more persistent among older than younger children, the unstandardized POR being 1.48 for boys and 1.93 for girls.

Table 2 shows the outcomes at time 2 for children subdivided into the four categories defined by diagnostic symptom threshold and associated impairment at time 1. At time 2 few children were impaired by either threshold or sub-threshold separation anxiety symptoms. The major pattern relates to the elevation of time 2 rates associated with time 1 symptoms rather than time 1 impairment.

Summary of Results

The typical degree of impairment associated with separation anxiety disorder symptoms was low. Most youth both above and below the diagnostic symptom threshold were not significantly impaired. There was, however, a clear trend for increasing symptom levels to be associated with increasingly severe impairment. Boys and girls did not differ in the degree to which they were impaired by their symptoms. Prior symptom level was the only independent predictor of future separation anxiety disorder symptoms, of symptoms being above diagnostic threshold or symptoms being above diagnostic threshold with impairment. Neither diagnostic threshold nor severity of impairment predicted time 2 outcomes after taking account of prior symptom levels. Older youth had significantly more persistent symptoms than younger children.

DISCUSSION

Symptoms of separation anxiety disorder were typically associated with relatively low levels of functional impairment but symptoms appeared to be more impairing among youth with higher symptom levels. There was little evidence that the diagnostic symptom threshold identified any critical point on the symptom scale with respect to expected impairment, consistent with findings for other, more impairing, juvenile psychiatric syndromes (Pickles, Rowe, Simonoff, Foley, Rutter, Silberg, 2001). Using impairment as one of the criteria to define the presence of separation anxiety disorder in community surveys will therefore substantially reduce the estimated prevalence of this disorder but the diagnostic symptom threshold will not identify all youth who are significantly impaired by their symptoms. Moreover, there is little evidence to suggest that in the mid-term represented by the 18-month follow-up examined here, that the extent of impairment arising from symptoms is of prognostic value over and above the symptoms themselves.

To argue that impairment related to separation anxiety is not prognostic in community settings is not to say that impairment may not possess some distinctive etiological elements. Impairment may possess distinctive correlates but these do not appear to influence the course of separation anxiety to any substantial degree within the age-range of our community based sample. It has been argued that prognosis is one key criterion against which diagnostic criteria should be evaluated, that is to say that diagnostic criteria should offer unique information about course, outcomes, response to treatment or other replicable correlates of disorders (Kendell & Jablensky 2003; Robins & Guze, 1970). Others have gone so far as to claim that diagnosis *is* prognosis (Goodwin & Guze, 1974). In practice, diagnostic criteria serve a multiplicity of aims (First, Pincus, Levine, Williams, Ustun &

Peele, 2004) and only some of these are concerned with prognosis. Impairment associated with separation anxiety disorder may be useful for evaluating current treatment needs and functioning but it is not prognostically informative once symptom levels have been taken into account. The utility of using impairment to diagnose separation anxiety disorder will therefore depend on the aim of the investigator.

The low prognostic significance of impairment related to separation anxiety disorder is consistent with previous findings with respect to depressive disorder, but not those for disruptive disorders (Pickles, Rowe, Simonoff, Foley, Rutter, Silberg, 2001). One possible explanation for this lies in the fact that, in contrast to disruptive disorders, for many affective symptoms a level of distress is already a necessary criterion. The data show that many children experience distress associated with separation anxiety with little or no impairment to their functioning. Although impairment may not be independently prognostic, distress may well be contributing to persistence or recurrence of anxiety provoking patterns of thought. What is clear is that application of the impairment criterion will differentially impact on the developmental epidemiology of DSM-IV emotional versus disruptive behavior disorders in youth. Future editions of the DSM will therefore need to reconcile the variable relationship between symptoms and impairment across different juvenile syndromes.

Systematic review suggests that cognitive behavior therapy is an effective treatment for anxiety in older children when compared to no treatment (Cartwright-Hatton, Roberts, Chitsabesan, Fothergill, & Harrington, 2004). In general the tested treatment protocols have been developed without distinction as to whether the target is to reduce specifically symptomatology or associated impairment, and the criterion outcomes have involved some combination of the two, commonly a formal diagnosis. Our findings suggest that while therapy targeted at reducing impairment may be of immediate value, such treatment may not influence the longer-term course of the anxiety. Therapy targeted at symptom reduction can be expected to improve both functioning and course. This may also bring broader psychiatric benefits since there is evidence for persistent anxiety symptoms being a risk factor for later depression (Foley, Pickles, Maes, Silberg & Eaves, 2004). One impetus for requiring significant impairment to diagnose a case was concern about the projected cost of treating all individuals who would otherwise meet criteria for psychiatric disorders in community settings. But diagnosis and treatment need are not the same (Spitzer, 1998). While an argument can be made for preferentially treating those with impairment, anxiety symptoms alone are nonetheless prognostic of later pathology and are themselves distressing. Thus an argument can also be made for treating the symptomatic but currently unimpaired. This group of youth will be both numerically and proportionately much larger in community as compared to referred populations given the strong association between impairment and referral (Angold, Costello, Farmer, Burns & Erkanli, 1999). More generally, it has been suggested that decisions regarding treatment should be based on cost effectiveness, not current severity (Kessler, Merikangas, Berglund, Eaton, Koretz & Walters, 2003), not least because treatment of mild cases may prevent a substantial proportion of future serious cases (Kessler, Merikangas, Berglund, Eaton, Koretz & Walters, 2003; Costello, Angold & Keeler 1999).

Limitations

While based on a large epidemiological study and one of the very few studies to measure impairment specific to each symptom area, the sample contained relatively few severely affected individuals. Caution is therefore required in generalizing these results to all clinical cases. We have examined prognosis in middle childhood and adolescence over an average follow-up interval of 18-months. The relative prognostic importance of symptoms and impairment might be different were we to consider a more extended period or other psychiatric or psychosocial outcomes.

Acknowledgments

This research was supported by grants MH-60324 (Debra Foley, PI) and MH-65322 (Michael Neale, PI) from the U.S. National Institute of Mental Health, Bethesda, MD.

The Virginia Twin Study for Adolescent Behavioral Development, now part of the Mid-Atlantic Twin Registry (MATR), ascertained subjects for this study and was supported by grant MH-45268 (Lindon Eaves, PI), the Carman Trust for Scientific Research, Richmond, VA (Judy Silberg, PI) and by a MacArthur Junior Faculty Award (Judy Silberg). The MATR (Judy Silberg, Director), has received support from the National Institutes of Health, the Carman Trust for Scientific Research, the John T and Katherine D MacArthur Fund, the WM Keck, John Templeton and Robert Wood Johnson Foundations.

References

- American Psychiatric Association. Diagnostic and statistical manual of mental disorders. 3. Washington, DC: Author; 1987.
- American Psychiatric Association. Diagnostic and statistical manual of mental disorders. 4. Washington, DC: Author; 1994.
- Angold A, Prendergast M, Cox A, Harrington R, Simonoff E, Rutter M. The Child and Adolescent Psychiatric Assessment (CAPA). *Psychological Medicine*. 1995; 25:739–53. [PubMed: 7480451]
- Angold A, Costello EJ, Farmer EM, Burns BJ, Erkanli A. Impaired but undiagnosed. *Journal of the American Academy of Child and Adolescent Psychiatry*. 1999; 38:129–137. [PubMed: 9951211]
- Angold A, Costello EJ. The Child and Adolescent Psychiatric Assessment (CAPA). *Journal of the American Academy of Child and Adolescent Psychiatry*. 2000; 39:39–48. [PubMed: 10638066]
- Binder DA. On the variances of asymptotically normal estimators from complex surveys. *International Statistical Review*. 1983; 51:279–292.
- Bird HR, Gould MS, Staghezza B. Aggregating data from multiple informants in child psychiatry epidemiological research. *Journal of the American Academy of Child and Adolescent Psychiatry*. 1992; 31:78–85. [PubMed: 1537785]
- Canino G, Shrout PE, Rubio-Stipec M, Bird HR, Bravo M, Ramirez R, Chavez L, Alegria M, Bauermeister JJ, Hohmann A, Ribera J, Garcia P, Martinez-Taboas A. The DSM-IV rates of child and adolescent disorders in Puerto Rico: prevalence, correlates, service use, and the effects of impairment. *Archives of General Psychiatry*. 2004; 61:85–93. [PubMed: 14706947]
- Cartwright-Hatton S, Roberts C, Chitsabesan P, Fothergill C, Harrington R. Systematic Review of the Efficacy of Cognitive Behaviour Therapies for Childhood and Adolescent Anxiety Disorders. *British Journal of Clinical Psychology*. 2004; 43:421–436. [PubMed: 15530212]
- Clayton DG. An odds-ratio comparison for ordered categorical data with censored observations. *Biometrika*. 1976; 63:405–408.
- Costello EJ, Angold A, Keeler GP. Adolescent outcomes of childhood disorders: the consequences of severity and impairment. *Journal of the American Academy of Child and Adolescent Psychiatry*. 1999; 38:121–128. [PubMed: 9951210]
- Costello, EJ.; Egger, HL.; Angold, A. The developmental epidemiology of anxiety disorders. In: Ollendick, T.; March, J., editors. *Phobic and Anxiety Disorders in Children and Adolescents*. New York: Oxford University Press; 2004. p. 61-91.

- Essau CA, Conradt J, Peterman F. Frequency, comorbidity, and psychosocial impairment of anxiety disorders in German adolescents. *Journal of Anxiety disorders*. 2000; 14:263–279. [PubMed: 10868984]
- Eaves LJ, Silberg JL, Meyer JM, Maes HH, Simonoff E, Pickles A, Rutter M, Neale MC, Reynolds CA, Erikson MT, Heath AC, Loeber R, Truett KR, Hewitt JK. Genetics and developmental psychopathology: 2. The main effects of genes and environment on behavioral problems in the Virginia Twin Study of Adolescent Behavioral Development. *Journal of Child Psychology and Psychiatry*. 1997; 38:965–980. [PubMed: 9413795]
- Ezpeleta L, Keeler G, Erkanli A, Costello EJ, Angold A. Epidemiology of psychiatric disability in childhood and adolescence. *Journal of Child Psychology and Psychiatry*. 2001; 42:901–914. [PubMed: 11693585]
- First MB, Pincus HA, Levine JB, Williams JB, Ustun B, Peele R. Clinical utility as a criterion for revising psychiatric diagnoses. *American Journal of Psychiatry*. 2004; 161:946–954. [PubMed: 15169680]
- Foley DL, Neale MC, Gardner CO, Pickles A, Prescott CA, Kendler KS. Major depression and associated impairment: Same or different genetic and environmental risk factors? *American Journal of Psychiatry*. 2003; 160:2128–2133. [PubMed: 14638582]
- Foley DL, Pickles A, Maes HM, Silberg JL, Eaves LJ. Course and short-term outcomes of separation anxiety disorder in a community sample of twins. *Journal of the American Academy of Child and Adolescent Psychiatry*. 2004; 43:1107–1114. [PubMed: 15322414]
- Goodwin, DW.; Guze, SB. *Psychiatric Diagnosis*. New York: Oxford University Press; 1974. p. ix-xii.
- Hewitt JK, Silberg JL, Rutter M, Simonoff E, Meyer JM, Maes H, Pickles A, Neale MC, Loeber R, Erickson MT, Kendler KS, Heath AC, Truett KR, Reynolds CA, Eaves LJ. Genetics and developmental psychopathology: 1. Phenotypic assessment in the Virginia Twin Study of Adolescent Behavioral Development. *Journal of Child Psychology and Psychiatry*. 1997; 38:943–963. [PubMed: 9413794]
- Hill J, Pickles A, Burnside E, Byatt M, Rollinson L, Davis R, Harvey K. Child sexual abuse, poor parental care and adult depression: evidence for different mechanisms. *British Journal of Psychiatry*. 2001; 179:104–109. [PubMed: 11483470]
- Huber, PJ. The behavior of maximum likelihood estimates under non-standard conditions; *Proceedings of the Fifth Berkeley Symposium on Mathematical Statistics and Probability*; Berkeley, CA: University of California Press; 1967. p. 221-233.
- Kendell R, Jablensky A. Distinguishing between the validity and utility of psychiatric diagnoses. *American Journal of Psychiatry*. 2003; 160:4–12. [PubMed: 12505793]
- Kendler KS, Thornton LM, Gardner CO. Stressful life events and previous episodes in the etiology of major depression in women: an evaluation of the “kindling” hypothesis. *American Journal of Psychiatry*. 2000; 157:1243–1251. [PubMed: 10910786]
- Kessler RC, Merikangas KR, Berglund P, Eaton WW, Koretz DS, Walters EE. Mild disorders should not be eliminated from the DSM-V. *Archives of General Psychiatry*. 2003; 60:1117–1122. [PubMed: 14609887]
- Little RJA. Pattern mixture models for multivariate incomplete data. *Journal of the American Statistical Association*. 1993; 88:125–134.
- Maughan B, Collishaw S, Pickles A. School achievements and adult qualifications among adoptees: a longitudinal study. *Journal of Child Psychology and Psychiatry*. 1998; 39:669–685. [PubMed: 9690931]
- Meyer JM, Silberg JL, Simonoff E, Kendler KS, Hewitt JK. The Virginia Twin-Family Study of Adolescent Behavioral Development: assessing sample biases in demographic correlates of psychopathology. *Psychological Medicine*. 1996; 26:1119–1133. [PubMed: 8931158]
- Pickles A, Rowe R, Simonoff E, Foley D, Rutter M, Silberg J. Child psychiatric symptoms and psychosocial impairment: Relationship and prognostic significance. *British Journal of Psychiatry*. 2001; 179:230–235. [PubMed: 11532800]
- Robins E, Guze SB. Establishment of diagnostic validity in psychiatric illness: its application to schizophrenia. *American Journal of Psychiatry*. 1970; 126:983–987. [PubMed: 5409569]

- Romano E, Tremblay RE, Vitaro F, Zoccolillo M, Pagani L. Prevalence of psychiatric diagnoses and the role of perceived impairment: Findings from an adolescent community sample. *Journal of Child Psychology and Psychiatry*. 2001; 42:451–461. [PubMed: 11383961]
- Royston P, Altman DG. Regression using fractional polynomials of continuous covariates: Parsimonious parametric modeling. *Applied Statistics*. 1994; 43:429–467.
- Simonoff E, Pickles A, Meyer J, Silberg J, Maes H, Loeber R, Rutter M, Hewitt J, Eaves L. Epidemiology of child psychopathology in the Virginia Twin Study of Adolescent Behavioral Development: Influences of age, gender and impairment on rates of disorder. *Archives of General Psychiatry*. 1997; 54:801–808. [PubMed: 9294370]
- Spitzer RL. Diagnosis and need for treatment are not the same. *Archives of General Psychiatry*. 1998; 55:120. [PubMed: 9477924]
- StataCorp. *Stata Statistical Software: Release 8*. College Station TX: Stata Corporation; 2004.
- Stram DO, Wei LJ, Ware JH. Analysis of repeated ordered categorical outcomes with possibly missing observations and time dependent covariates. *Journal of the American Statistical Association*. 1988; 83:631–637.

Table 1
The prognostic importance of separation anxiety disorder symptoms, diagnosis and associated impairment

	Time 2 Outcomes								
	Number of symptoms			Diagnosis (symptom threshold)			Diagnosis with impairment		
Time 1 predictors	POR	95% CI	P value	POR	95% CI	P value	POR	95% CI	P value
N SAD symptoms	1.45	1.22, 1.73	0.001	1.51	1.18, 1.93	0.001	1.66	1.88, 3.11	0.1
SAD diagnosis	1.44	0.66, 3.14	0.4	1.65	0.49, 5.51	0.4	0.87	0.02, 49.6	0.9
SAD impairment	1.12	0.90, 1.40	0.3	0.93	0.67, 1.28	0.6	1.3	0.73, 2.28	0.4

Key to Table 1: POR=proportional odds ratio adjusted for all other time 1 predictors

Table 2

Diagnostic histories of children with a diagnosis of separation anxiety disorder, with and without impairment, at time 2

	Time 2 SAD without impairment		Time 2 SAD with impairment	
	%	n/N	%	n/N
Time 1 no SAD, no impairment	2.5	43/1709	0.3	5/1709
Time 1 no SAD but impaired	0	38/417	0	38/417
Time 1 SAD, no impairment	19	22/116	1.7	2/116
Time 1 SAD and impaired	15.6	5/32	6.3	2/32

Key to Table 2: SAD, separation anxiety disorder; no SAD includes children with 1 or 2 sub-threshold symptoms but impairment was only rated in children with 2+ SAD symptoms