Appendix I

Details of the Risk Factor Variables Used in the Model

Genetic Risk was calculated from the number of positive reports from both twins using the FH-RDC criteria for MD (69). Scores ranged from zero to four but high scores were rare so this variable was trichotomized into scores of 0, 1 and 2-4.

Low Parental Warmth was assessed using a modified version of the Parental Bonding Instrument (70). Each twin had four scores: self-report of father's and mother's warmth and cotwin's report of father's and mother's warmth to twin. The measure was scored as a trichotomy with 15% in the low parental warmth category, 37% in the moderate category, and 48% in the high parental warmth category.

Childhood Sexual Abuse (CSA) was taken from a single item in the MF1 interview "Have you ever been sexually abused or molested?" If a positive response was given, the age at which this first occurred was recorded. In this report, childhood sexual abuse was considered present if the age given was prior to 16.

Parental Loss was a binary measure scored 1 if the twin reported that one or more parents left the nuclear home due to death, divorce or parental separation prior to age 17.

Neuroticism was assessed by the Short-Scale (12-item) version from the EPQ-R (71) obtained at MF1. We scored it as a 4 level ordinal measure: 0, 1-3, 4-6, 7+.

Self-Esteem was assessed using the full Rosenberg's self-esteem scale (72)

obtained at MF1, reversed-scored so that higher scores reflected lower self-esteem and ordinalized into four categories with the following %s: 0=36%, 1=47%, 2=9%, and 3=8%.

Early Onset Anxiety Disorder was a binary variable scored 1 for subjects with an onset, prior to age 18, of panic disorder, generalized anxiety disorder or any form of phobia as assessed at the MF2 interview using diagnostic criteria outlined previously (19).

Conduct Disorder was treated as a five category ordinal variable that reflected the number of DSM-IV conduct disorder criteria met prior to age 18 that were endorsed at MF1. The variable had the following distribution: 0=58%, 1=22%, 2=11%, 3=6%, 4=3%.

Years of Education was treated as an ordinal variable as follows: less than high school 10%, completed high school only 20%, some college 26%, college graduate 34%, graduate school 10%.

Lifetime Traumas reflected the number of items reported at the MF1 interview that assessed exposure to combat, life-threatening accident, natural disaster, severe injury, physical assault, and being threatened with weapon. The distribution was skewed so it was treated as an ordinal variable.

Social Support was assessed from the MF1 interview. We examined items reflecting the quality of relationships with spouse, twin, parents, and other relatives which we ordinalized into three categories from high to low: 0=69%, 1=19%, 2=12%.

DSM-III-R alcohol abuse or dependence was assessed at MF1 or MF2. DSM-IV

drug abuse or dependence was assessed at MF2. Nicotine dependence as assessed by a score of ≥7 on the Fagerström Tolerance Questionnaire (73) collected at MF2.

Ever Divorced was a binary measure scored 1 for individuals who reported a lifetime history of divorce or annulment at the MF2 interview.

Prior History of MD was a binary measure reflecting the presence or absence of a lifetime history of DSM-III-R MD, as reported either at the MF1 or MF2 interview, with an onset at least eight years before the MF2 interview.

Last Year Marital Satisfaction was constructed as a three level ordinal variable using 7 items assessing the level of marital satisfaction in the last year at the MM2 interview, obtained from the Social Interaction Scale (74). We generated three classes: 0=married, high satisfaction, 56%, 1=unmarried 29%, and 2=married, low satisfaction 15%

Distal, Dependent Proximal and Independent Proximal SLEs were assessed, using our SLE measures, in the MF2 interview. Each twin was systematically asked about the occurrence, at any time in the preceding 12 months, of 11 "personal" events and 4 classes of "network" events, each event being dated to the nearest month with high inter-rater reliability (75). The dependence of a SLE, reflecting the probability that the respondent's own behavior contributed to the SLE, was rated on a 4-point scale. In these analyses, we dichotomized SLEs into those clearly or probably independent vs. clearly or probably dependent. For an individual with a reported onset of MD in the year preceding their MM2 interview, we counted, separately, the number of dependent and independent proximal life events occurring in that month and the two preceding months

(75). For individuals reporting no depressive onset, a random 3-month window was used to assess the occurrence of SLEs. The number of SLEs was treated as an ordinal variable. Distal SLEs reflected the sum of all SLEs reported at other times during the year prior to the MF2 interview. We created for these variables, the following categories: i) Distal SLEs – 0=25%, 1=24%, 2=21%, 3=13%, 4=8%, 5 or more=9%; ii) Dependent proximal events 0=83%, 1=13%, 2=3%, 3 or more=1% and iii) Independent proximal events 0=69%, 1=23%, 2=6%, 3 or more=2%.

Appendix II

Parameter Estimates

The test of equality across sexes was based on raw path coefficients. However, for ease of interpretation and a consistent measure of effect size, we report standardized path coefficients. Here the raw path estimates are presented first and then, in parentheses, the standardized path coefficients. It is the latter that are depicted in figure 1 and 2. See below for the abbreviations used.

Path to	from	Male	=	Female
n	lpw	-		0.127(0.122)***
n	csa	0.366(0.341)***		0.236(0.226)***
n	pl	0.103(0.096)**		-
lse	lpw	0.091(0.078)***	=	0.091(0.078)***
lse	pl	-		0.100(0.085)**
lse	n	0.531(0.491)***	=	0.531(0.476)***
eoad	fr	0.140(0.126)***	=	0.140(0.130)***
eoad	lpw	-		0.073(0.068)*
eoad	csa	0.241(0.217)***		0.127(0.117)*
eoad	n	0.206(0.199)***	=	0.206(0.199)***
eoad	lse	0.076(0.080)**	=	0.076(0.082)**
cd	lpw	-		0.234(0.213)***
cd	csa	0.464(0.407)***		0.131(0.120)**
cd	pl	0.157(0.138)***	=	0.157(0.143)***
cd	n	0.092(0.086)***	=	0.092(0.087)***
cd	eoad	-		0.100(0.099)**
edu	pl	0.250(0.235)***	=	0.250(0.232)***
edu	lse	0.211(0.231)***	=	0.211(0.229)***
edu	cd	-		0.064(0.065)**
ltr	fr	0.104(0.097)**		-
ltr	csa	0.118(0.110)**		0.216(0.197)***
ltr	eoad	-		0.143(0.141)***
ltr	cd	0.239(0.255)***	=	0.239(0.239)***
dud	csa	0.142(0.126)**	=	0.142(0.119)**
dud	lse	-		0.066(0.065)*
dud	eoad	0.149(0.148)**		-
dud	cd	0.315(0.320)***		0.445(0.411)***
dud	trm	-		0.149(0.138)***

nd	gr	0.071(0.065)*	=	0.071(0.062)*
nd	lpw	0.071(0.065)*		-
nd	n	0.080(0.078)**	=	0.080(0.073)**
nd	cd	0.096(0.100)**	=	0.096(0.092)**
nd	edu	0.283(0.274)***		0.411(0.385)***
nd	ltr	0.162(0.158)***	=	0.162(0.155)***
aud	n	-		0.064(0.057)*
aud	eoad	0.128(0.120)***	=	0.128(0.117)***
aud	cd	0.398(0.386)***	=	0.398(0.370)***
aud	edu	0.079(0.071)**		-
aud	ltr	0.204(0.186)***	=	0.204(0.190)***
div	lpw	-		0.100(0.090)*
div	edu	0.080(0.081)**	=	0.080(0.077)**
div	ltr	0.106(0.108)**		0.266(0.261)***
div	nd	0.224(0.235)***	=	0.224(0.231)***
ph	gr	0.097(0.077)**	=	0.097(0.078)**
ph	lpw	-		0.120(0.097)**
ph	csa	0.149(0.119)**	=	0.149(0.121)**
ph	n	0.210(0.179)***	=	0.210(0.177)***
ph	lse	0.071(0.066)*		-
ph	eoad	0.122(0.108)***	=	0.122(0.107)***
ph	cd	0.115(0.104)**		-
ph	ltr	0.145(0.123)***	=	0.145(0.128)***
ph	dud	0.143(0.127)**		-
ph	aud	-		0.107(0.102)**
ph	div	0.279(0.234)***	=	0.279(0.251)***
lss	lpw	0.386(0.344)***		0.260(0.227)***
lss	csa	-		0.172(0.150)***
lss	n	0.079(0.075)**	=	0.079(0.072)**
lss	lse	0.187(0.194)***	=	0.187(0.190)***
lss	ltr	-		0.090(0.086)*
lss	div	-		0.093(0.091)*
lms	lpw	-		0.084(0.078)*
lms	n	0.116(0.118)***	=	0.116(0.113)***
lms	lse	0.076(0.083)*		-
lms	aud	0.079(0.088)***	=	0.079(0.087)***
lms	div	-		0.104(0.108)**
lms	lss	0.175(0.186)***	=	0.175(0.188)***

dsle	fr	0.106(0.097)***	=	0.106(0.096)***
dsle	csa	-		0.150(0.137)***
dsle	eoad	0.083(0.085)***	=	0.083(0.082)***
dsle	cd	0.151(0.158)***		-
dsle	ltr	0.124(0.122)***	=	0.124(0.124)***
dsle	dud	0.127(0.131)***		-
dsle	aud	-		0.083(0.088)**
dsle	div	-		0.097(0.098)**
dsle	lms	0.127(0.123)***	=	0.127(0.124)***
ipsle	eoad	0.146(0.155)***	=	0.146(0.152)***
ipsle	ltr	0.126(0.129)***		-
ipsle	div	-		0.117(0.126)***
ipsle	ph	0.091(0.110)**		-
ipsle	dsle	-		0.102(0.109)***
dples	fr	-		0.141(0.129)***
dples	pl	-		0.123(0.112)**
dples	n	-		0.160(0.152)***
dples	ltr	0.119(0.117)***	=	0.119(0.119)***
dples	dud	0.145(0.151)**		-
dples	aud	0.097(0.105)**	=	0.097(0.104)**
dples	lms	0.166(0.161)***	=	0.166(0.162)***
dples	dsle	0.100(0.101)**		-
lymd	lpw	0.158(0.114)**		-
lymd	n	0.180(0.141)***	=	0.180(0.140)***
lymd	dud	0.119(0.094)**	=	0.119(0.105)***
lymd	ph	0.173(0.157)***	=	0.173(0.159)***
lymd	lss	-		0.143(0.122)**
lymd	lms	-		0.253(0.201)***
lymd	dpsle	0.114(0.090)*		-
lymd	ipsle	0.314(0.236)***	=	0.314(0.242)***
lymd	dles	0.468(0.366)***		0.293(0.239)***

- Value of zero
= raw path coefficients equal in males and females
Abbreviations: fr – familial risk, lpw – low parental warmth, csa – childhood sexual abuse, pl – parental loss, n – neuroticism, lse –low self-esteem, eoad – early onset anxiety disorder, cd- conduct disorder, edu – educational attainment, ltr – lifetime traumas, dud – drug use disorder, nd – nicotine dependence, aud – alcohol use disorder, div – history of divorce, ph-past history of major depression, lss – low social support, lms – low marital satisfaction, dpsle – distal stressful life events, ipsle – independent proximal stressful life events, dpsle - dependent proximal stressful life events, lymd – last year major depression