Twin Research (1998) 1, 119–122
© 1998 Stockton Press All rights reserved 1369–0523/98 $12.00
http://www.stockton-press.co.uk/tr

Interaction of marital status and genetic risk for symptoms of depression

Andrew C Heath[1], Lindon J Eaves[2] and Nicholas G Martin[3]

[1]*Department of Psychiatry, Washington University, St Louis*
[2]*Virginia Institute of Psychiatric and Behavioral Genetics, Richmond, USA*
[3]*Queensland Institute of Medical Research, Brisbane, Australia*

Depression scores (DSSI) were available for 1232 MZ and 751 DZ female twin pairs who completed a mailed questionnaire. Pairs were divided into those concordant for being in a marriage-like state, concordant for having no partners, and those discordant. The pattern of twin correlations differed according to marital status. Our results suggest that having a marriage-like relationship acts as a protective factor in reducing the impact of inherited liability to symptoms of depression in the general population.

Keywords: twins, depression, marital status, genotype environment interaction

Most studies of depressive symptoms in the general population have focused exclusively upon the causal role of either environmental experiences (especially stressful life events)[1,2] or genetic predisposition.[3,4] The importance of genotype environment interaction, though recognised in theory,[5–8] has in practice been ignored. In life events research, failure to find a strong overall relationship between stressful life events and depression has led to attempts to identify 'vulnerability' factors, particularly absence of social support, which determine which individuals are most at risk when exposed to stressful life events.[1,9] As reported here, by reanalysing self-report data from 1984 adult female like-sex twin pairs from the Australian NH&MRC twin registry,[3] we have found evidence which suggests that having a marriage-like relationship decreases the impact of *inherited* liability to symptoms of depression. Genetic factors accounted for only 29% of the variance in depression scores in married twins, but for 42% of the variance in young unmarried twins, and 51% of the variance in unmarried individuals aged 31 years or greater. There was no evidence that genetic predisposition to symptoms of depression leads to an increased probability of remaining unmarried.

A health questionnaire was mailed to all 5967 twins pairs aged 18 years and over enrolled in the Australian NH&MRC twin register. The questionnaire included items from the state depression scale of the Delusions-Symptoms-States Inventory (a British scale judged most appropriate for use with an Australian population)[10] and a single item about marital status. Zygosity was diagnosed by two questionnaire items which have been found to give at least 95% agreement with the results of extensive blood-typing.[11,12] Questionnaires were returned by 3810 pairs, giving a 64% pairwise response rate. Analyses reported in this paper focus on the 1233 like-sex identical (MZ) and the 751 like-sex fraternal (DZ) female pairs who responded. Enrolment in the twin register, and participation in the study, were voluntary. For both symptom and personality variables, however, response frequencies did not differ significantly from those observed in studies of representative samples of the Australian population.[4] Ages of respondents ranged from 18 to 88 years, with a mean of 35.66 ± 14.27 for MZs and 35.35 ± 14.27 for DZs.

Twin pairs of each zygosity type were subdivided into older (> 30) and younger ($\leqslant 30$) cohorts, and then into pairs discordant for marital status (married or living in a marriage-like relationship *vs* unmarried), concordant 'married', and concordant unmarried pairs. In discordant pairs, the 'married' twin was always designated the 1st twin, the unmarried twin the 2nd twin. In concordant pairs, identification of a twin as the 1st or 2nd twin was arbitrary. Depression scores were derived by summing DSSI item scores, and then using a log-transformation ($x' = \log_{10}(x + 1)$) to reduce heteroscedasticity.[3] Depression scores were higher in unmarried twins (0.32 ± 0.009) than in married twins (0.23 ± 0.006). However, all cross-correlations between one twin's marital status and the co-twin's depression score were insignificant, with the exception of a single negative correlation ($r = 0.156$, $P < 0.01$) between 1st twin's depression score and co-twin's marital status in young dizygotic twins. The absence of a significant cross-correlation implies that genetic

Correspondence: Dr NG Martin, Queensland Institute of Medical Research, Post Office, Royal Brisbane Hospital, Brisbane 4029, Australia. Fax: +61 7 3362 0101; E-mail: nickM@qimr.edu.au
Received 5 May 1998; accepted 19 May 1998

Table 1 Variance–covariance matrices for log-transformed age-corrected depression score. Twin covariances are given in the lower triangle, correlations in the upper triangle of each matrix

Twin group *(Sample sizes for young; older twins)*	*Young twins*		*Older twins*	
MZF-concordant married	0.1002	0.3824	0.0817	0.3029
(n=177; n=472)	0.0336	0.0769	0.0235	0.0737
MZF-discordant	0.1009	0.3238	0.1993	0.3436
n=139; n=136)	0.0359	0.1198	0.0429	0.1413
MZF-concordant unmarried	0.0968	0.4088	0.0854	0.3873
(n=254; n=53)	0.0381	0.0896	0.0353	0.0971
MZF-concordant married	0.0692	0.0977	0.0772	0.1351
(n=107; n=272)	0.0076	0.0882	0.0117	0.0980
MZF-discordant	0.0694	0.0595	0.1027	0.2507
(n=87; n=102)	0.0050	0.1013	0.0293	0.1326
MZF-concordant unmarried	0.1087	0.2206	0.1092	0.4325
(n=155; n=26)	0.0250	0.1182	0.0543	0.1445

predisposition to depression does not lead to an increased probability of remaining single.

After correcting for the linear and quadratic components of the regression of depression score on age, covariance matrices were computed, giving the variances and covariance of 1st and 2nd twins from each group (Table 1). Sample sizes were small for the older concordant unmarried pairs, for whom we observe a DZ twin correlation which is no smaller than the MZ correlation. However, the discordant pairs also provide information about the importance of genetic and environmental effects in unmarried individuals, when compared with the concordant married pairs. Genetic models were fitted to the full set of covariance matrices by maximum likelihood.[13] Table 2 defines the parameters which we used in model-fitting, and gives expectations for the variances and covariances of twin pairs, conditional upon marital status. It should be noted that in data on twin pairs reared together, the effects of family environment and dominance are confounded, so that for a given condition of environmental exposure, we can estimate either, but not both, of these effects.

Table 2 Expected variances and covariances of twin pairs, conditional upon marital status, under genotype × environment interaction

	MZ twin pairs	*DZ twin pairs*
Variances		
Married	$h^2+d^2+c^2+e^2$	$h^2+d^2+c^2+e^2$
Unmarried	$h'+d'^2+c'^2+e'^2$	$h'^2+d'^2+c'^2+e'^2$
Covariances		
Concordant married	$h^2+d^2+c^2$	$1/2\ h^2+1/4\ d^2+c^2$
Discordant	$hh'+dd'+cc'$	$1/2\ hh'+1/4\ dd'+cc'$
Concordant unmarried	$h'^2+d'^2+c'^2$	$1/2\ h'^2+1/4\ d'^2+c'^2$

Parameters: h, h′: partial regression of depression score on additive genetic deviation in married, unmarried individuals; d, d′: partial regression on dominance deviation; c, c′: partial regression on familial environmental deviation; e, e′: partial regression on non-familial environmental deviation.

The different models which we considered are represented schematically in Figure 1. Model 1 represents the simplest case where there is no interaction of genetic or environmental effects with marital status. In model 2 only those ('non-familial') environmental effects which make one twin different from her co-twin vary. This would arise as an artefact of heteroscedasticity, if mean differences between married and unmarried individuals were associated with differences in error variance even after data transformation. In model 3 only the genetic effects vary as a function of marital status, implying genotype environment interaction. In model 4, both genetic and environmental effects change. This might be a consequence of genotype environment interaction, but it might also result from differences in variability at different points on the depression scale: because of the mean differences between married and unmarried twins, this alone would give rise to differences in both genetic and environmental variances. This could also arise through reciprocal social interaction between spouses,[14] whereby depressive symptoms in a spouse tend to increase the probability that the twin will develop symptoms, and vice versa. Such marital interaction would lead to an increased genetic and even more strongly increased non-familial environmental variance in married individuals.[14]

We conducted two parallel model-fitting analyses. In the first ('joint') analysis, we constrained the genetic and environmental parameters to be the same in both age groups. The second ('separate') analysis allowed the two cohorts to differ in the values of the genetic and environmental parameters. In all cases, a likelihood ratio chi-square[13] was computed to assess the goodness of fit of the model.

Particular hypotheses about the action and interaction of genes and environment may be tested by taking differences between appropriate chi-squares. For example, we may test the heterogeneity of genetic and environmental effects across age cohorts by subtracting the chi-squares from the 'separate' analysis from that for the 'joint' analysis. Subtracting the chi-squares for model 4 from those for models 2 and 3 yields tests of significance for the interaction of marital status with environmental effects and genetic factors respectively.

The results are summarised in Table 3. We tabulate results for models allowing for additive genetic and non-familial environmental effects only, since inclusion of genetic dominance or familial environmental effects did not in any instance lead to a significant improvement in fit. Model 1, which ignores interaction entirely, cannot explain the data. When allowance is made for possible cohort differences, it is clear that the interaction is better explained by a genetic model (model 3) than a purely environmental model (model 2). Furthermore, when we allow for the interaction of marital status and genetic factors, there is no evidence of heterogeneity over age groups. Under the best-fitting model, which assumes homogeneity over age cohorts and allows only genetic effects to interact with marital status (model 3) the parameter estimates were h = 0.158, h' = 0.221, and e = e' = 0.245. A further significant improvement in fit ($\chi^2 = 3.85$, $p = 0.05$) was achieved by allowing the genetic effect in *unmarried* individuals only to change with age, giving: h = 0.158, h' (younger cohort) = 0.209, h' (older cohort) = 0.251 and e = e' = 0.245. This latter model also gave a reasonable fit to the data ($\chi^2_{32} = 42.97$, $p = 0.09$). These results imply that genetic factors are accounting for 29% of the variance in depression scores of married females, 42% of the variance for single females aged 30 years or younger, and 51% of the variance for single females aged 31 years or greater. Allowing for an effect of family environment on the resemblance of older unmarried twins gave a non-significant improvement in fit ($\chi^2_1 = 2.44$, $p = 0.12$), implying that the unexpectedly high

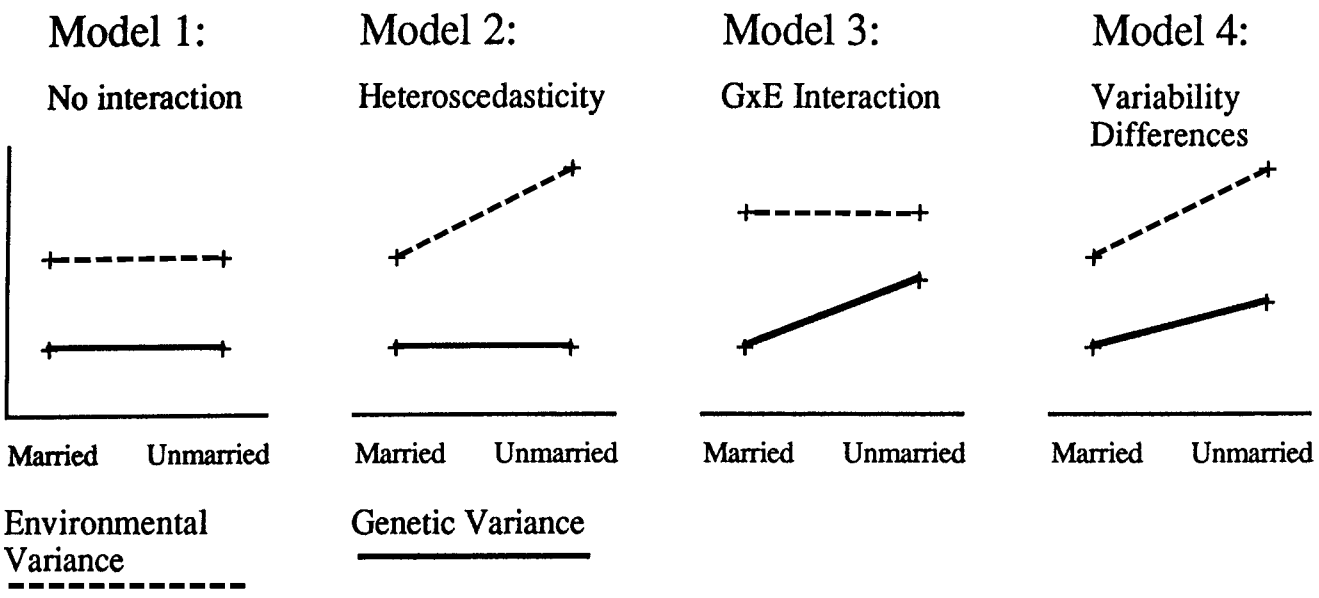

Figure 1 Changes in genetic and environmental variance as a function of marital status predicted under models 1–4

Table 3 Results of model-fitting: likelihood-ratio chi-squares

	Younger cohort			*Older cohort*			*Joint analysis*			*Heterogeneity*		
	d.f.	χ^2	*P*	*d.f.*	χ^2	*P*	*d.f.*	χ^2	*P*	*d.f.*	χ^2	*P*
Model 1	16	26.76	0.04	16	46.80	<0.001	34	74.69	<0.001			
Model 2	15	22.03	0.11	15	27.45	0.03	33	55.31	0.01			
Model 3	15	18.65	0.23	15	24.26	0.06	33	46.82	0.06	3	3.91	0.28
Model 4	14	18.62	0.18	14	23.73	0.05	32	46.36	<0.05			
Model 2 *vs* 4	1	3.41	0.06	1	3.72	0.06	1	8.95	0.001			
Model 3 *vs* 4	1	0.03	0.86	1	0.53	0.47	1	0.46	0.58			

correlation between older concordant unmarried DZ twin pairs can be explained purely by sampling variation.

These results suggest that having a marriage-like relationship acts as an important protective factor in reducing the impact of inherited liability to symptoms of depression in the general population. Other explanations of our findings seem implausible. Any scalar differences in variability associated with mean differences in depression score should lead to differences in environmental as well as genetic variances between groups. Yet we found no significant heterogeneity of environmental variance between married, younger unmarried and older unmarried groups, despite significant differences in genetic variance. Explanations in terms of environmental effects shared by twins can also be excluded. We found no evidence for a significant effect of family background on symptoms. Furthermore, most of the information about genotype/environment interaction in the older cohort is provided by concordant married twin pairs, and discordant twin pairs, who will in each case be living apart. It appears that in the realm of affect, as also in the case of achievement,[15] major effects of environmental variables on human variation are to be found when we look for interactions with genetic differences.

Acknowledgements

Data collection was supported by grants from the Australian National Health and Medical Research Council and the Australian Associated Brewers. Data analysis was supported by grants AA06781 and MH40828. We thank Rosemary Jardine for her role in analysis and Greg Carey, John Hewitt and Ken Kendler for comments on earlier drafts.

References

1 Brown GW, Harris TO. *Social origins of depression*. Tavistock: London, 1978.
2 Henderson AS, Byrne D, Duncan-Jones P. *Neurosis and the social environment*. Academic Press: New York, 1981.
3 Jardine R, Martin NG, Henderson AS. Genetic covariation between neuroticism and the symptoms of anxiety and depression. *Genet Epidemiol* 1984; **1**: 87–107.
4 Kendler KS, Heath AC, Martin NG, Eaves LJ. Symptoms of anxiety and depression in a volunteer twin population. *Arch Gen Psychiatry* 1986; **43**: 213–221.
5 Eaves LJ, Last K, Martin NG, Jinks JL. A progressive approach to non-additivity and genotype–environmental covariance in the analysis of human differences. *Br J Math Stat Psychol* 1977; **30**: 1–42.
6 Eaves LJ. The utility of twins. In: Anderson VE (ed.) *Genetic basis of the epilepsies*, Raven Press: New York, 1982, pp 249–276.
7 Eaves LJ. The resolution of genotype × environment interaction in segregation analysis of nuclear families. *Genet Epidemiol* 1984; **1**: 215–228.
8 Plomin R, De Fries J, Loehlin J. Genotype–environment interaction and correlation in the analysis of human variation. *Psychol Bull* 1977; **84**: 309–322.
9 Kessler RC, Price RH, Wortman CB. Social factors in psychopathology: stress, social support, and coping processes. *Ann Rev Psychol* 1985; **36**: 531–572.
10 Bedford A, Foulds GA, Sheffield BF. A new personal disturbance scale (DSSI/sAD). *Br J Soc Clin Psychol* 1976; **15**: 387–394.
11 Martin NG, Martin PG. The inheritance of scholastic abilities in a sample of twins. I. Ascertainment of the sample and diagnosis of zygosity. *Ann Hum Genet* 1975; **39**: 213–218.
12 Kasriel J, Eaves LJ. A comparison of the accuracy of written questionnaires with blood typing for diagnosing zygosity in twins. *J Biosoc Sci* 1976; **8**: 263–266.
13 Joreskog KG. Structural analysis of covariance and correlation matrices. *Psychometrika* 1978; **43**: 443–477.
14 Heath AC. The analysis of marital interaction in cross-sectional twin data. *Acta Genet Med Gemellol Roma* 1987; **36**: 41–49.
15 Heath AC, Berg K, Eaves LJ, Solaas MH, Corey LA, Sundet J, Magnus P, Nance WE. Education policy and the heritability of educational attainment. *Nature* 1985; **314**: 734–736.