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Gender differences in heritability of depressive symptoms in the elderly

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ABSTRACT

Background. The present study aimed to investigate the relative importance of genetic and environmental influences on depressive symptoms in the elderly.

Method. Depressive symptoms were assessed through the Center for Epidemiological Studies – Depression (CES-D) scale. The CES-D scale was administered to 959 twin pairs (123 female MZs, 90 male MZs, 207 same-sex female DZs, 109 same-sex male DZs and 430 opposite-sex DZs) aged 50 years or older (mean age 72 years). A dichotomous depressed state variable was constructed based on CES-D cut-offs and self-reported use of antidepressant medication. Structural equation models were fitted to the data to dissect genetic and environmental variance components.

Results. The sex-specific heritability estimates for depressive symptoms were 14% for males and 29% for females and 23% when constrained to be equal for men and women. The prevalence of clinically significant depressive symptoms was 16% for men and 24% for women. Heritability estimates for the dichotomous depressed state measure were 7% for males and 49% for females in the full model and 33% when constrained to be equal.

Conclusion. Our results suggest that depressive symptoms in the elderly are moderately heritable, with a higher heritability for women than men, although differences in heritability estimates were not statistically significant.

INTRODUCTION

High levels of depressive symptoms are common among the elderly in western societies, with clinically significant levels reported in 10–20% (Blazer & Williams, 1980; Gurland & Toner, 1983; Lindesay *et al.* 1989; Snowdon, 1990; Haynie *et al.* 2001; Hybels *et al.* 2001). Slightly higher proportions have been reported from southern Europe (Amaducci *et al.* 1998; Zunzunegui *et al.* 1998; Fuhrer *et al.* 1999) and in a recent Italian study of elderly men and women Minicuci *et al.* (2002) found that 58% of the women and 34% of the men reported CES-D scores above a clinically relevant cut-off level for depressive symptoms. Although cultural differences may influence reporting and perception of depressive symptoms, these prevalence rates must be considered as high and the consequences of depressive symptoms among the elderly should be taken seriously. Depressive symptoms as assessed through the CES-D scale are distinct from any clinical diagnosis of affective disorders, such as major depression. Despite this, high scores of depressive symptoms surely reflect a poor health status.

Numerous twin studies of affective disorders have indicated that the concordance for MZ

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twins differs markedly from that of DZ twins. In a meta-analysis of major depression, five twin studies with an average age ranging from 34 to 53 years revealed an overall heritability estimate of 37% (Sullivan *et al.* 2000). Notably, the highest heritability was found in a sample of Swedes who were on average older than the other samples (Kendler *et al.* 1995). There was almost no effect of shared environment, but a substantial effect of the unique environment (Sullivan *et al.* 2000). That genetic factors are involved in the aetiology of depressive symptoms among the elderly has been implicated in three previous twin studies (Gatz *et al.* 1992; McGue & Christensen, 1997; Carmelli *et al.* 2000). These studies of depressive symptom scales in community samples of older adults have reported somewhat lower heritabilities than those for affective disorders; 18–25%, with a small influence of shared environment but a major effect of unique environment (Gatz *et al.* 1992; McGue & Christensen, 1997; Carmelli *et al.* 2000). When a clinical cut-off was applied in the Gatz *et al.* (1992) study, differences between heritability estimates for major depression and for depressive symptoms from self-report scales were diminished. In that study, which included twins aged 60 years and older from the Swedish Adoption/Twin Study of Aging (SATSA), concordance rates for scoring 16 or higher on the CES-D depression scale were 33% in MZ and 12% in DZ pairs (Gatz, 1992). Concordances for affective illness found in a Swedish clinical sample were 45% and 19% for MZ and DZ pairs respectively (Kendler *et al.* 1993).

Apart from the significance and contribution of genetic and environmental factors in the aetiology of depressive symptoms, one unanswered question concerns the importance of these factors for men compared to women. Another unresolved matter regarding the genetic influence is whether the same genes are contributing to liability for depressive symptoms in men and women. A large number of studies have reported higher prevalences of both depressive symptoms and clinical depression in women than in men. If this sex difference in prevalence is not an effect of biased ascertainment, it is possible that the higher prevalence in women reflects a true gender difference in genetic and environmental influences on liability to depressive symptoms. Adoption and twin studies are well suited to decipher the extent to which depressive symptoms are influenced by genetic and environmental factors shared by family members. Furthermore, opposite-sexed dizygotic twin pairs are the most optimal sample to study gender differences in humans. By including opposite-sexed pairs one can evaluate not only whether the magnitude of genetic and environmental effects is equal in men and women, but also whether the same genes influence liability to the disorder in both sexes. There have been several studies that have addressed these issues in major depression using a twin study design (Bertelsen *et al.* 1977; Kendler *et al.* 1995; McGuffin *et al.* 1996; Bierut *et al.* 1999; Kendler *et al.* 2001). The largest of these studies found a higher heritability for major depression in women than in men as well as an indication of separate genes acting on the liability to major depression (Kendler *et al.* 2001). The Danish study on depressive symptoms using twins aged 75 years and older found different heritability estimates for men and women (McGue & Christensen, 1997), however they did not have access to opposite-sex DZ twin pairs and subsequently could not assess any sex-specific gene influences.

The present study was carried out using a population-based sample of elderly Swedish twins (Pedersen *et al.* 1991; McClearn *et al.* 1997; Gold *et al.* 2002; Lichtenstein *et al.* 2002). We utilized a continuous measure of depressive symptoms, the total CES-D scale (Radloff, 1977), and a dichotomous variable based on a cut-off value of 16 or above on the CES-D scale combined with information about treatment with antidepressants as an indication of depressed state. Our main purpose was to quantify the relative importance of genetic and environmental effects on depressive symptoms and depressed state in the elderly and to test whether the heritability is equal in both sexes. Furthermore, we were interested in testing whether heritability estimates would differ for depressive symptoms compared to a depressed state.

SUBJECTS AND MEASURES

Subjects

Our study sample consisted of 959 twin pairs aged 50 years and older with a mean age of

Table 1. *Sample characteristics*

Measure	Women		Men		Unlike-sexed
	MZ	DZ	MZ	DZ	DZ (F/M)
No. of pairs (959)	123	207	90	109	430
Mean age (years)	71·8	70·2	69·3	68·5	73·6
Range	50–93	50–91	50–88	50–87	68–88
S.D.	11·4	11·1	11·4	10·2	4·0
Mean CES-D	11·3	10·3	8·5	8·3	9·6 (8·8/10·4)
S.D.	10·0	9·1	7·8	7·7	7·2 (6·9/7·8)
CES-D < 16 (*n*)	65	94	33	30	155 (91/64)
Prevalence	0·27	0·23	0·19	0·14	0·18 (0·21/0·15)
Depressive state (*n*)	76	104	36	32	167 (98/69)
Prevalence	0·31	0·25	0·20	0·15	0·19 (0·23/0·16)

72 years, taken from three longitudinal studies of ageing. All three studies have been described in detail previously and are subsamples of the population-based Swedish Twin Registry (STR) (Lichtenstein *et al.* 2002): The OCTO-Twin study (McClearn *et al.* 1997), the SATSA (Pedersen *et al.* 1991) and the Gender Study (Gold *et al.* 2002). All participants were Caucasians and born in Sweden. For all three subsamples, individuals participated in at least one in-person testing session in which CES-D questionnaires were administered and the use of antidepressants was gathered. Information from the first occasion of testing that included the CES-D was used. The sample characteristics are presented in Table 1.

For like-sexed pairs, zygosity was initially based on responses to the question, 'During childhood, were you and your twin partner as like as "two peas in a pod" or not more alike than siblings in general?' If both individuals of a pair responded 'alike as two peas in a pod' they were classified as monozygotic (MZ), if both responded 'not alike' they were classified as dizygotic (DZ). This technique has proven to be more than 95% accurate in a number of studies based on the STR (Lichtenstein *et al.* 2002). For all SATSA pairs and those OCTO-Twin pairs not classifiable by this technique, zygosity was determined by serological analyses or comparisons of up to 10 DNA markers. In total, there were 123 female MZ, 90 male MZ, 207 same-sex female DZ, 109 same-sex male DZ and 430 unlike-sex DZ twin pairs.

Measures

Depressive symptoms were measured through the Swedish translation of the 20-item CES-D scale (Radloff, 1977), which has proven to have good psychometric properties in elderly Swedish community samples (Gatz *et al.* 1993). The possible range of the scale goes from zero to 60. If more than two items had missing answers the total score was not computed.

The CES-D scale is not intended for making clinical diagnoses but can be used to identify individuals who are at risk for depression (Lewinsohn *et al.* 1997). Scoring 16 or higher on the CES-D scale was considered as a clinically significant depressive state.

Medication status and use of antidepressants was assessed at the time of in-person testing. Medications were reported in the questionnaires by their 'trade name' and then coded into the ATC system (Anatomical Therapeutic Chemical classification system). All drugs with the ATC code N06A were classified as antidepressive. We created a 'yes or no' variable concerning the use of antidepressants. In this population, 4·8% of all participants used antidepressants. To avoid overlooking individuals who were depressed but had low CES-D scores due to successful antidepressant treatment, we augmented the CES-D information with information on the use of antidepressant medications. Thus, individuals were classified as having a depressive state if they had a CES-D score of 16 or higher, or if they reported use of antidepressant medications. The dichotomous measure of depressive state was included for two reasons. Firstly, some participants were unable to provide self-report symptom data, but information on antidepressants was available. Secondly, for those taking antidepressive medication, symptoms on the CES-D may be less severe, thus underestimating levels of depressive state.

Analysis

We first analysed the continuous measure to estimate the heritability of depressive symptoms and to determine whether the heritability differed between females and males. Secondly, we analysed the dichotomous measure.

In order to avoid bias in the model-fitting due to skewness of scales and age trends, raw scores were first normalized and then standardized to unit variances using standard techniques (Eaves *et al.* 1997). Age effects were regressed out by using the residualized scores (McGue & Bouchard, 1984) and intra-class correlations for all five zygosity groups [monozygotic males (MZM), monozygotic females (MZF), dizygotic males (DZM), dizygotic females (DZF) and dizygotic opposite-sex pairs (DZO)] were calculated separately.

Similarly, probandwise concordances and tetrachoric correlations, were calculated separately for the five different zygosity groups for the dichotomous depressed state variable. Probandwise concordances were defined as the number of affected index siblings of affected individuals divided by the total number of affected individuals. Tetrachoric correlations were calculated from 2×2 contingency tables using SAS software (version 8.02, SAS Institute, Raleigh, NC, USA). In general larger MZ than DZ similarities are taken as an indication that genetic factors influence the trait, because the greater MZ similarity is attributed to a greater genetic similarity of MZ twins compared to DZ twins. Same-sexed DZ twins are expected to share on average 50% of their segregating genes, corresponding to a genetic correlation (r_g) of 0·5. Gender-specific influences are indicated when the intra-class or tetrachoric correlation for same-sexed DZ twins differs from that of opposite-sex pairs. Following quantitative genetic principles, the estimated r_g can vary between 0 and 0·5 for opposite-sexed twin pairs. A value less than 0·5 suggests differences in the nature of genetic effects for men and women.

For depressive symptoms, MZ and DZ variance–covariance matrices were generated using SAS software (version 8.02, SAS Institute). Genetic models were then fitted to these matrices using the structural equation modelling software Mx (Neale, 1994) to dissect genetic and environmental variance components. For the categorical depressed state variable, genetic models were fitted to the 2×2 contingency tables. The liability to develop a depressed state is assumed to have an underlying continuous normal distribution with a threshold above which the subject develops the condition (Falconer & Mackay, 1996). This liability distribution reflects contributions from both genetic and environmental effects. For the categorical data, thresholds for the underlying liability were allowed to differ between men and women, since there are large differences in the population-based prevalences between the sexes.

The full model included additive genetic effects (A), shared environmental effects (C), and non-shared environmental effects (E), which were estimated separately for men and women. Nested models were then fitted that included only additive genetic and non-shared environmental contributions (AE model) or shared and non-shared environmental contributions (CE model). The fit of these models was assessed by a goodness-of-fit χ^2 test. The genetic and environmental parameter estimates and 95% confidence interval (CI) were calculated for all models. After genetic and environmental effects were estimated independently for men and women, parameters were constrained to be equal to test for gender differences in the relative importance of genetic and environmental effects for the phenotypes. Subsequently, we fit models for sex-specific genetic (r_g) and familial–environmental (r_c) effects. The genetic correlation (r_g) for opposite-sexed DZ twin pairs was estimated instead of being fixed to 0·5, and in a separate model the shared environmental correlation (r_c) was estimated rather than being fixed at 1. The estimation of r_g and r_c in separate models allows for detection of qualitative differences, i.e. different genes or shared environments in men compared to women.

RESULTS

Descriptive statistics

CES-D measures were available from both individuals in 959 complete pairs (Table 1). The mean CES-D score of 10·5 for females ($n = 1089$) was greater than the mean value of 8·6 for males ($n = 829$) ($t = 5{\cdot}0$, $p < 0{\cdot}0001$).

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Table 2. *Correlations and concordances*

	Women		Men		Unlike-sexed
	MZ	DZ	MZ	DZ	DZ (F/M)
CES-D score					
Intra-class correlation	0·34	0·12	0·15	0·10	0·12
Depressed state variable					
Probandwise concordance	52	28	24	20	19 (16/23)
Tetrachoric correlation	0·55	0·12	0·14	0·16	0·05
Depressed state (antidep.)					
Probandwise concordance	55	31	22	19	23 (19/28)
Tetrachoric correlation	0·56	0·15	0·06	0·11	0·10

Twin intra-class correlations for depressive symptoms calculated on the total CES-D score (age adjusted and ranked), by sex and twin zygosity. Probandwise concordance rates and tetrachoric correlations calculated for the dichotomous variable.

Depressed state, as measured by the dichotomous variable, was more prevalent in women than men (26% and 17% respectively). The use of antidepressants did not differ significantly between the sexes, but the usage was more prevalent among women than men (5·4% and 3·2% respectively).

Correlations and concordances

Intra-class correlations were calculated for total CES-D scores (Table 2). Female MZ intra-class correlations were greater than the corresponding female DZ correlations, indicating a moderate genetic effect and no shared environment on depressive symptoms in women. The male intra-class correlations were lower and more similar, suggesting that shared environmental effects might be more important for males. The opposite-sexed DZ correlation was similar to the correlations for DZ males and females.

Both probandwise concordances and tetrachoric correlations for the dichotomous depressed state variable displayed a similar pattern, with a greater similarity in the MZ female groups compared to the DZ female group (Table 2). The MZ and DZ male concordance rates are almost equal, indicating no or a modest genetic effect in the phenotype for males. The indicators of similarity for the opposite-sexed pairs were slightly less than those for the DZ same-sexed pairs.

Model fitting

Percentages of total variation with 95% CIs, χ^2, p values and AIC are summarized in Table 3 for the continuous measure. In the full model (Model I) the variance components were estimated freely for both males and females. Consistent with the intra-class correlations, Model I suggests that genetic effects are important for women but not men. The nested AE model (Model II) in which the shared environmental component was dropped did not result in a significant deterioration in fit compared to the full model ($\chi^2 = 0{\cdot}1$, df = 2), and resulted in a lower AIC value indicating a better-fitting model. The nested CE model (Model III) also resulted in a non-significant deterioration of the fit ($\chi^2 = 3{\cdot}8$, df = 2), but the AIC value was not lower than for the full model, demonstrating that Model I is to be preferred to Model III. When the estimates were set equal between the sexes (Model IV) and compared against the full Model I there was no significant worsening of the model fit (I *v.* IV; $\chi^2 = 3{\cdot}1$, df = 3), and Model IV provided a lower AIC value.

Model VI (CE model), nested under Model IV did not show a significant worsening of the model fit (CE *v.* ACE model; $\chi^2 = 2{\cdot}4$, df = 1). The most parsimonious model to explain the data according to AIC, is the AE model with equal estimates for men and women (Model V; AIC = 0·6), however the intra-class correlations do not support equal effects in men and women.

We also ran two series of models in which r_g and r_c were estimated rather than fixed to 0·5 and 1·0 respectively. In Model I r_g was estimated to 0·5 ($\chi^2 = 23{\cdot}5$), i.e. we could not find any evidence of a qualitative difference between men and women. In none of the models where r_g and r_c were estimated was there any divergence from 0·5 and 1 respectively, and no change in the fit of the models if r_g or r_c were estimated compared to fixed (results not shown).

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Table 3. *Estimates of genetic and environmental effects for CES-D scores (normalized and age adjusted data)*

	Parameter estimate						Fit of model				
	Males			Females							
Model	A	C	E	A	C	E	AIC	χ^2	df	p	$\Delta\chi^2$ (df)*
I: ACE	14	2	84	29	1	70	5·5	23·5	9	0·005	
95% CI	(0–29)	(0–22)	(71–96)	(0–42)	(0–20)	(58–85)					
II: AE	16	0	84	30	0	70	1·6	23·6	11	0·015	0·1 (2)
95% CI	(4–29)		(71–96)	(17–42)		(58–83)					
III: CE	0	11	89	0	18	82	5·3	27·3	11	0·004	3·8 (2)
IV: ACE	21	1	77				2·6	26·6	12	0·009	3·1 (3)
95% CI	(0–33)	(0–19)	(68–89)								
V: AE	23	0	77				0·6	26·6	13	0·014	0 (1)
95% CI	(14–32)		(68–86)								
VI: CE	0	15	85				3·0	29·0	13	0·006	2·4 (1)

Note in all models, r_g fixed to 0·5 and r_c to 1·0.

* Models II–IV are compared to Model I whereas Models V and VI are compared to Model IV.

Model I (ACE model): parameters allowed to differ in the two sexes. Model II (AE model): parameters allowed to differ in the two sexes. Model III (CE model): parameters allowed to differ in the two sexes. Model IV (ACE model): estimates the same in both sexes. Model V (AE model): estimates the same in both sexes. Model VI (CE model): estimates the same in both sexes.

Table 4. *Estimates of genetic and environmental effects for the dichotomous depressive state variable*

	Parameter estimate						Fit of model				
	Males			Females							
Model	A	C	E	A	C	E	AIC	χ^2	df	p	$\Delta\chi^2$ (df)*
I: ACE	7	4	89	49	0	51	−10·5	7·5	9	0·59	
95% CI	(0–38)	(0–37)	(59–99)	(0·04–66)	(0–33)	(31–75)					
II: AE	9	0	91	49	0	51	−14·5	7·5	11	0·76	0 (2)
95% CI	(0–38)		(62–99)	(26–69)		(31–74)					
III: CE	0	4	96	0	32	68	−10·2	11·8	11	0·38	4·3 (2)
IV: ACE	33	0	67				−12·6	11·4	12	0·49	3·9 (3)
95% CI	(0–50)	(0–24)	(50–85)								
V: AE	33	0	67				−14·6	11·4	13	0·57	0 (1)
95% CI	(16–50)		(50–85)								
VI: CE	0	20	80				−11·1	14·9	13	0·32	3·5 (1)

Note in all models, r_g fixed to 0·5 and r_c to 1·0.

* Models II–IV are compared to Model I whereas Models V and VI are compared to Model IV.

Model I (ACE model): parameters allowed to differ in the two sexes. Model II (AE model): parameters allowed to differ in the two sexes. Model III (CE model): parameters allowed to differ in the two sexes. Model IV (ACE model): estimates the same in both sexes. Model V (AE model): estimates the same in both sexes. Model VI (CE model): estimates the same in both sexes.

Throughout, all models tested with the continuous measure displayed a lack of statistical precision. Two of the five zygosity groups, opposite-sex DZs and male MZs, contributed to more than half of the total χ^2 value. Opposite-sex pairs showed a lower variance and male MZs a slightly higher variance than expected in the modelling.

In Table 4, model-fitting results for the dichotomous depressed state variable are shown. The best-fitting models were the AE model (Model II) with different estimates for men and women and Model V in which these estimates were equal across the sexes. For women, the genetic variance component (A) for the dichotomous variable was greater than for the continuous measure, but the lack of precision is evident in both instances. When genetic (r_g) and environmental (r_c) correlations were estimated in the depressed state, Model I, r_g did not diverge

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from 0·5. But in Model II r_g was estimated to 0·47 (CI 0–0·5) and in the constrained Model IV r_g was estimated to 0·28 (CI 0–0·5).

DISCUSSION

The aim of the present study was first to investigate the relative importance of genetic and environmental factors for depressive symptoms among the elderly. Secondly, we addressed the question of whether there are any differences between men and women in the magnitude of these effects and whether the same or different genes are acting as risk factors for depressive symptoms in men and women. Finally, we were interested in contrasting the importance of genetic influences for a continuous measure of depressive symptoms with those for a dichotomous measure representing depressed state. To our knowledge, the combination of these issues has not been addressed in the elderly with the use of a relatively large population-based twin sample including opposite-sex DZ twin pairs.

Our results show that heritability is moderate in elderly women, both for depressive symptoms (29%) and depressed state (49%) but limited in elderly men, 14% and 7% respectively. In all models tested, the unique environment was the major source of variance. The heritability for depressive symptoms when constrained to be equal across the sexes (23%) can be compared to Gatz *et al.* (1992), McGue & Christensen (1997) and Carmelli *et al.* (2000), who reported heritability estimates for depressive symptoms of 18%, 34% and 21% respectively. The Danish study (McGue & Christensen, 1997), which included both sexes and had a slightly higher mean age (80 years) than the present study, found a non-significant sex-specific heritability of 41% for women and 21% for men in models where shared environment converged to zero. We found slightly lower estimates in our full model. The Swedish study (Gatz *et al.* 1992), which focused on age differences and included both men and women, found greater heritabilities in twins aged over 60 years than those under 60 years. However, they did not report separate heritability estimates for men and women but concluded that genetic effects appear to be stronger for women than men. It should be noted that the Gatz *et al.* (1992) study is based on a postal questionnaire assessment of the SATSA sample. In the baseline assessment of male twins 59–70 years of age, Carmelli *et al.* (2000) found a heritability of 21%, which is comparable to the results from previous studies. A longitudinal follow-up 10 years later suggested that genetic variance was the greatest contributor to stability. Finally, a study of CES-D scores in younger female twin pairs (Silberg *et al.* 1990) aged 18–52 years reported a heritability of 12·9%. Thus, these studies converge in suggesting that heritability of depressive symptoms is greater in the elderly than in younger populations (under 60 years). Furthermore, heritability appears to be greater among elderly women than elderly men.

Our study differs from previous work because we have opposite-sexed twin pairs, allowing for estimation of the genetic correlation (r_g) and environmental correlation (r_c) between the sexes. Both for depressive symptoms and depressive state we found r_c equal to 1·0 and r_g equal to 0·5 in our full models, indicating that the environments and genes acting on the liability to depressive symptoms or depressive state do not differ in men and women in this study population. Despite the relatively large sample, with close to 1000 pairs of twins (of which 430 are opposite sex), it is possible that different genes could be acting on the liability to depressive symptoms. However, to detect such differences one needs a substantially larger study population.

For women, and in the models constrained to be equal across the sexes, the heritability estimates of depressed state were greater than those for the continuous measure of depressive symptoms. There are two possible interpretations, and both may apply. Firstly, narrow definitions of psychiatric disorders tend to be more familial than broader definitions when evaluated in multiple threshold models (McGuffin *et al.* 1994). The CES-D is more of a 'state' than 'trait' measure, as responses reflect frequency of experiencing a symptom during the last week. Furthermore, a number of findings among the elderly suggest that heritabilities for behaviours within the normal range (e.g. memory performance) are lower than those for pathology (e.g. Alzheimer's disease) (Pedersen, 1996). Secondly, the use of psychiatric medication may obscure symptoms that are heritable, i.e. effective treatment could lower the CES-D score in a fashion

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that affects the categorization of a depressed state within pairs.

Our heritability estimates for the dichotomous depressive state variable are quite similar to the findings on major depression by Bierut *et al*. (1999) and Kendler *et al*. (2001). We found a heritability of 49% among females and 7% among males in our full model, compared to 44% and 24% respectively by Bierut *et al*. (1999). Kendler *et al*. (2001) reported slightly higher heritabilities of 57% for women and 44% for men in their best-fitting AE model. Furthermore, they found evidence that different genes might be acting between the sexes for the DSM-III-R criteria of major depression. These comparisons should be considered with caution, however, as there is no way of knowing whether the individuals in the present study fulfil DSM criteria for major depression.

There are several limitations in the present study and the results should be interpreted with this in mind. The subsamples were recruited from different perspectives, although all are within the STR and all CES-D information has been assessed by self-report questionnaires. The focus of SATSA was normal ageing and took advantage of the age structure of the sample of separated twins. OCTO-Twin focused on the oldest old, while the focus of the Gender Study was on sex differences in the elderly. Nevertheless, there were no significant differences in prevalence within the sexes across samples, indicating that the initial purposes and selection strategies do not bias the results. We used antidepressive medications as an indication of depressed state, through which we identified a small number of extra cases. Antidepressants could be prescribed for medical conditions other than mood disorders and thus provide some false cases. However, at the time these data were collected, prescription of these medications was relatively restrictive. Parameter estimates from models run on the CES-D cut-off of 16 (i.e. excluding the extra cases identified through use of medications) did not differ substantially from those for the depressive state measure (results not shown). Nevertheless, effective treatment could lower the CES-D score and thereby underestimate the prevalence of depressed state, no matter what medical reason led to antidepressive treatment. Our sample might be undersized for analysing the dichotomous variable, as the use of a dichotomous variable will require a far larger sample size than a continuous measure (Martin *et al*. 1987; Neale *et al*. 1994). Another limiting factor is the number of opposite-sex pairs for detecting genetic differences (r_g) between the sexes. The most parsimonious model based on AIC criteria constrained heritability to be equal in both sexes with no shared environmental effect. However, this conclusion is not supported by the intra-class correlations and concordances. It should be noted that the AIC value is not always preferable for selecting a favoured model, especially for discrete traits, since it has a tendency to reject the true model, particularly when true A and C are relatively small and the sample limited in size (Sullivan & Eaves, 2002).

Our findings have generated further evidence concerning the genetic influences on depressive symptoms in the elderly. Although not significant, we feel the data suggest that genetic effects for both depressive symptoms and liability to depressive state are more important for elderly women than for elderly men. There are no qualitative differences in genetic influences for men and women (i.e. the 'same genes' are of importance). Furthermore, heritability may be somewhat greater for depressive state than for depressive symptoms in the elderly. In agreement with previous studies there is no doubt that non-shared environmental factors are the major source of variance in depressive symptoms in elderly populations.

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