Sex Differences in the Genetic Architecture of Optimism and Health and Their Interrelation: A Study of Australian and Swedish Twins

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Optimism has a positive influence on mental and somatic health throughout lifetime and into old age. This association is mainly due to shared genetic influences, with some indication of sex differences in the heritability of these and related traits (e.g., depression and subjective wellbeing). Here we extend our initial study of Australian twins by combining with data available from Swedish twins, in order to increase the power to explore potential sex differences in the genetic architecture of optimism, mental and self-rated health and their covariation. Optimism, mental, and self-rated health were measured in 3053 Australian (501 identical female (MZf), 153 identical male (MZm), 274 non-identical female (DZf), 77 non-identical male (DZm), and 242 non-identical opposite-sex twin pairs, and 561 single twins; mean age 60.97 ± 8.76), and 812 Swedish (71 MZf, 53 MZm, 93 DZf and 67 DZm twin pairs, and 244 single twins; mean age 60 ± 14.3) twin individuals using the Life Orientation Test (LOT), the General Health Questionnaire (GHQ) and a single-item self-rating of overall health, respectively. In females all three traits were moderately heritable (.27–.47), whereas in males heritability was substantially lower (.08–.19), but genetic modeling showed that sex differences were not significant. The absence of significant sex differences, despite the consistent trend across the two cohorts, is likely due to a lack of power, raising the importance for future studies, on the same or similar traits, to utilize large samples and to keep the possibility of sex differences in mind when conducting their analyses.

Keywords: optimism, self-rated health, mental health, twins

Research on the relationship between wellbeing and health has received increased attention in the last few years (e.g., Roysamb et al., 2003). Positive affect such as optimism has been shown to serve as a protective factor for future mental and somatic health problems (Atienza et al., 2002; Giltay et al., 2004, 2006; Kubzansky et al., 2001; Maruta et al., 2002) and may increase the ability to cope with a diagnosis or treatment of a severe or fatal disorder; for example, cancer, acquired immunodeficiency syndrome (AIDS), or heart disease (Carver et al., 2005; Maruta et al., 2000; Matthews et al., 2004; Nes & Segerstrom, 2006; Park & Gutchess, 2006; Rasmussen et al., 2006; Trunzo & Pinto, 2003). Furthermore, pessimism has been associated with adverse effects on disease progression (Antoni & Goodkin, 1988).

In a recent study, we explored the heritability of optimism, mental, and self-rated health, as well as the genetic influences on the relationship between these traits in an older adult twin sample. We demonstrated that not only approximately half of the variance in optimism, but also the association between optimism and health (mental and self-rated) can be explained by genetic influences (Mosing et al., 2009), in accord with findings from three earlier twin studies on optimism (Caprara et al., 2009; Plomin et al., 1992; Schulman et al., 1993). Interestingly, though not significant, we found some indication of a possible sex difference, such that in females genetic influences may account for a much larger part of the variation in, and covariation between the variables, as compared to males where shared environmental rather than genetic influences may be more important. However, our sample was comprised of a much smaller number of male compared to female twin pairs, which may explain the nonsignificant sex differences we found, as the power may have been too low to detect significant shared environmental effects. The three previous

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studies investigating heritability of optimism and (two of these) the covariation with mental health have used even smaller sample sizes (Caprara et al., 2009; Plomin et al., 1992; Schulman et al., 1993) and therefore could not investigate sex differences. However, two studies have identified potential sex differences in SRH (Lichtenstein & Pedersen, 1995; Svedberg et al., 2001), similar to those suggested in our study, and the heritability estimate for SRH for males (Romeis, et al., 2000) has been found to be much lower (h^2 = 39.6%) than that derived from a female sample (h^2 = 64%; Leinonen et al., 2005). Also, similar sex differences have been reported for related traits such as depression, anxiety, aggression, and subjective wellbeing in a number of studies (Bierut et al., 1997; McGue & Christensen, 1997; Roysamb et al., 2002; Tambs et al., 1995; Vierikko et al., 2003).

Here we combined data from our study of Australian twins (Mosing et al., 2009) with that available on 284 same-sex twin pairs from the Swedish twin registry (Plomin et al., 1992), in order to increase the power to detect possible sex differences in the heritability of optimism, mental and self-rated health and covariation in these traits. This increased the sample by approximately one-third of the original sample size.

Materials and Methods

Participants

Combined sample. The final sample consisted of 572 MZ female, 206 MZ male, 367 DZ female, and 144 DZ male twin pairs, 242 DZ opposite-sex twin pairs, and 805 single twins (without the co-twin participating) with a mean age of 60.98 ± 10.2.

Australian sample: As described in Mosing et al. (2009), the community-based sample was derived from the Australian Twin Registry (ATR; Hopper, 2002) and consisted of 3,053 twin individuals including 501 monozygotic (MZ) female, 153 MZ male, 274 dizygotic (DZ) female, 77 DZ male, and 242 DZ opposite-sex twin pairs, as well as 561 single twins ranging from 50 to 94 years of age (M = 61 ± 8.8). Data were derived as part of a multi-wave mail-out survey conducted between 1993 and 1995 and the survey was approved by the Queensland Institute of Medical Research Human Research Ethics Committee. Details of the survey, the sampling methods, and zygosity determination are described elsewhere (Bucholz et al., 1998; Mosing et al., 2009).

Swedish sample: The Swedish cohort consisted of twins participating in the second wave of the Swedish Adoption/Twin Study of Aging (SATSA; Pedersen et al., 1991) administered in 1987. Here, only those SATSA twins reared together have been included comprising 71 MZ female, 53 MZ male, 93 DZ female and 67 DZ male twin pairs and 244 single twins; mean age 60 ± 14.3 (range 26–91). Note that optimism but not the other two traits have been explored previously in this sample (Plomin et al., 1992). For full details on the sample and zygosity determination see Pedersen et al. (1991) and Plomin et al. (1992).

Measures

The Life Orientation test (LOT) of optimism and pessimism. The LOT consists of eight items (plus filler items) measuring generalized outcome expectancies characteristic of optimism and pessimism, each of which is assessed by four of the items (Sheier and Carver 1985). For the Swedish cohort, the items were translated into Swedish and back-translated into English to ensure efficient translation. One item of the optimism scale did not make sense when literally translated, therefore, 'Every cloud has a silver lining' was replaced with a Swedish saying 'I believe in the proverb that there is nothing evil that does not have any good about it'. The two extreme scores at each end of the 5-point Likert scale used in the Swedish cohort were merged for reasons of consistency with the Australian sample where a 3-point Likert scale was used. The scale score was derived by adding the item scores, with a low score indicating optimism and a high score pessimism. Since self-rated health is an ordinal variable, the final LOT score was converted into the following four categories: participants with a score below 9 were assigned to category one, scores between 10–12 were assigned to category two, scores between 13–15 were assigned to category three, and finally scores above 16 were assigned to category four.

Mental health. In the Australian cohort, psychological distress was measured with the short version of the General Health Questionnaire (GHQ-12; Goldberg & Williams, 1988). In the Swedish sample the GHQ was not administered so identical or very similar items from the Center for Epidemiologic Studies Depression (CES-D) scale (Radloff, 1977) plus one item from the EAS Temperament Survey (EAS; Buss & Plomin, 1975) were used to derive a mental health score (a list of the matched items is displayed in Appendix A). Consistency between the Australian and Swedish scales for mental health was confirmed by a factor analysis, which showed both questionnaires measured the same construct. Participants rated their psychological distress on a 4-point Likert scale. The item scores were added up in accordance with GHQ-guidelines in order to derive the total scale score (ranging between 0 and 36) with scores above 15 indicating distress and above 20 suggesting severe psychological problems. The final score then was converted to an ordinal variable: scores ranging between 0–6 were assigned to category 0, scores ranging between 7–8 were assigned to category 1, and scores ranging between 9–13 and 14–37 were assigned to category 2 and 3 respectively.

Self-rated health (SrH). Health was assessed with a single-item question asking the participants to rate their current health status. It has been shown that a single SRH-question is a valid and reliable measure of overall health and a good predictor of mortality (Leinonen et al., 2005; Lundberg & Manderbacka,

1996). Wording of this item differed slightly between the Australian ('How would you describe your health at present?') and the Swedish survey ('How would you rate your general health status?'). Also in the Australian sample, the item was rated on a five-point Likert scale (1 = *Very good*; 2 = *Good*; 3 = *Fair*; 4 = *Poor*; 5 = *Very poor*), whereas Swedish participants rated their health on a 3-point scale *Good* (3), *Reasonable* (2), and *Bad* (1). However, scores in both samples were distributed similarly with most participants indicating to have a rather good health and only few participants in both surveys rating their health as *Fair*, *Poor*, or *Very poor*. Therefore, categories 3, 4, and 5 (in the Australian sample) were merged. Finally, before merging the two samples, the scores of the Swedish cohort were reversed so that a higher health score indicated worse health.

In order to maximize the available number of twin pairs for genetic analysis, missing item responses for the LOT and the mental health measure were imputed utilizing PRELIS 2.30 (Jöreskog & Sörbom, 1999). In this procedure missing values are replaced with values from other cases (without missing values) with similar response patterns. Items were only imputed if individuals had only one item missing and if there were similar response patterns existing in other cases. By imputing 278 item responses (.31% of the total item responses), the total number of available scale scores for the optimism and mental health measures increased from 7323 to 7601, a gain of 3.8%.

Statistical Analysis

The underlying traits measured are assumed to be distributed normally in the population and the variance in these traits is influenced independently by genetic (A) and environmental (shared, C, and nonshared, E) effects. The classical twin design allows partitioning of the variance in the traits and the covariances between the traits into that due to genetic and environmental influences, as the A, C, and E influences each predict different patterns of monozygotic (MZ) and dizygotic (DZ) twin correlations. Fundamental assumptions of the classical twin design are that, while MZ twins share all their genes, DZ twins share only half of their genes on average and that trait-relevant environments are similar for both MZ and DZ twin pairs (Kendler et al., 1993).

With use of structural equation modeling (threshold modeling for ordinal data) utilizing maximum-likelihood (ML) methods in Mx (Neale et al., 2002) the best combination of A, C, and E influences can be determined explaining the observed data. Specific hypotheses regarding the significance of particular parameters can be tested statistically by comparing the goodness-of-fit of more restricted models to the saturated model (estimating all parameters) using the minus two times log-likelihood (–2LL) statistic (distributed as χ^2).

Prior to genetic modeling, each variable was tested for age, sex and sample effects on the thresholds. In order to assess genetic and environmental factors mediating the phenotypic covariation between the three traits (optimism, mental, and self-rated health) a trivariate Cholesky-model was utilized (Neale & Maes, 2004). Initially, a common effects limitation-model was fitted, allowing for quantitative differences in the sources of variation of optimism, mental, and self-rated health between sexes. To test the significance of specific parameters and to determine the most parsimonious model explaining the phenotypic variance of the three variables the model was reduced by dropping the paths with the smallest parameter estimates first. Additionally, univariate modelingg was conducted in order to confirm the accuracy of the trivariate model.

Results

Preliminary Analysis

No significant ($p < .05$) differences were found in the thresholds within twin pairs or across zygosity groups for all variables. There were also no differences in the thresholds for males and females for any of the variables. However, there were significant sample effects on the thresholds, with Swedish twins rating themselves as slightly healthier, and Australians being slightly more optimistic. There was also a significant decrease of (self-rated) health with age. Sample and age were retained as covariates in subsequent modeling.

Correlations

Table 1 shows the phenotypic polychoric correlations between optimism, mental health, and self-rated health for males and females, as well as the twin correlations for each zygosity group and variable separately for the Combined, Australian, and Swedish sample. Phenotypic correlations were similar for males and females in the Combined sample, and for both the Australian and Swedish samples separately (data not shown).

Twin correlations in the Swedish sample were mostly nonsignificant (i.e., confidence intervals were wide and crossed zero), which is due to the small sample size. As expected, despite different scoring, the twin correlations for optimism were similar, though a little lower, to the ones reported previously (on the same sample) by Plomin et al. Also, the twin correlations for mental health in the Swedish cohort are in line with those of the Australian cohort with respect to both the MZ-DZ pattern and magnitude. In the Combined sample, the increase in sample size (by adding the Swedish twins) led to narrower confidence intervals without changing the twin correlations substantially. For females, MZ twin correlations were significantly higher than DZ twin correlations in all variables, indicating genetic mediation. In males MZ and DZ twin correlations did not differ significantly for any of the three variables (Table 1).

Genetic Modeling

In order to explore possible sex differences in the heritability and genetic covariation between the three traits, a common effects sex-limitation model was

fitted first (Table 2). While in females, all three traits were moderately heritable (0.27–0.47), the heritability in males was substantially smaller, ranging between .08–.19. Nevertheless, subsequent modeling (general ACE-model) showed that the proportions of A, C, and E could be constrained equal in males and females, indicating that the sex differences were not significant. Finally, all shared-environmental (C) influences could be dropped from the common ACE model without a significant deterioration of model fit. This indicates that the best fitting model is an AE model with no sex differences in the effects of A, C, and E on the variance in the three measured traits (Figure 1).

Heritability estimates with confidence intervals (based on univariate analysis as confidence intervals could not be derived from the multivariate model) for optimism, mental, and self-rated health were 0.34 (CI: 0.27–0.41), 0.39 (CI: 0.32–0.45), and 0.48 (CI: 0.40–0.55), respectively, and most of the covariation between the three traits was explained by genetic factors.

Discussion

In the present study we investigated possible sex differences in the genetic architecture of optimism, mental, and self-rated health and their covariation. Despite the larger sample size, the sex differences in

Table 1

Phenotypic Polychoric and Twin Correlations with 95% Confidence Intervals for Optimism, Mental and Self-Rated Health Corrected for Age and Sex for Each Zygosity Group and Sample

		Optimism	Mental health	Self-rated health
Phenotypic correlations (males above diagonal and females below diagonal)				
Optimism		1	.36	.15
Mental health		.33	1	.25
Self-rated health		.19	.27	1
Zygosity	*N* pairs (range)	Optimism	Mental health	Self-rated health
Twin correlations for the Combined sample (95% confidence intervals)				
MZ females	(508–530)	0.37 (.28, .45)	0.43 (.34, .51)	0.50 (.41, .58)
MZ males	(192–197)	0.24 (.07, .39)	0.29 (.13, .44)	0.30 (.12, .46)
DZ females	(309–332)	0.16 (.03, .28)	0.18 (.05, .30)	0.21 (.07, .34)
DZ males	(135–138)	0.16 (–.03, .34)	0.31 (.11, .48)	0.15 (–.09, .38)
DZ opposite-sex	(214–227)	–0.01 (–.17, .15)	0.15 (.01, .29)	0.18 (.01, .34)
Twin correlations for the Australian sample (95% confidence intervals)				
MZ females	(416–441)	0.39 (.29, .48)	0.42 (.33, .51)	0.55 (.45, .63)
MZ males	(134–140)	0.26 (.08, .43)	0.27 (.08, .44)	0.36 (.17, .53)
DZ females	(226–240)	0.17 (.03, .31)	0.18 (.03, .31)	0.26 (.11, .40)
DZ males	(65–70)	0.24 (–.01, .46)	0.32 (.05, .54)	0.28 (–.01, .53)
DZ opposite-sex	(210–214)	–0.01 (–.17, .15)	0.15 (.01, .29)	0.18 (.01, .34)
Twin correlations for the Swedish sample (95% confidence intervals)				
MZ females	(53–71)	0.15 (–.13, .40)	0.52 (.26, .71)	0.21(–.15, .51)
MZ males	(49–52)	0.31 (–.01, .57)	0.31 (–.01, .58)	0.19 (–.26, .57)
DZ females	(69–91)	0.04 (–.23, .30)	0.19 (–.12, .47)	0.16 (–.16, .45)
DZ males	(62–67)	0.11 (–.17, .37)	0.27(–.02, .52)	0.05 (–.33, .42)

Table 2

Trivariate Cholesky-Model Fitting Results For Females/Males and Parameter (Percentage of ACE) Estimates With the Best-Fitting Model in Bold

	Optimism			Mental Health			Self-rated Health					
Trivariate model fitting results	A	C	E	A	C	E	A	C	E	Δ–2LL	Δ*df*	*p* value
Common effects sex-limitation model	.27/.08	.08/.14	.65/.78	.41/.04	.01/.27	.58/.69	.47/.19	.02/.10	.51/.71			
General ACE model/ Sex equated	33	.00	.67	.40	.01	.59	.43	.01	.56	15.324	18	0.64
Omnibus drop of all C-factors	**.33**	—	**.67**	**.40**	—	**.60**	**.44**	—	**.56**	**0.282**	**6**	**1.00**
Omnibus drop of all A-factors	—	—	1	—	—	1	—	—	1	251.88	6	0.00

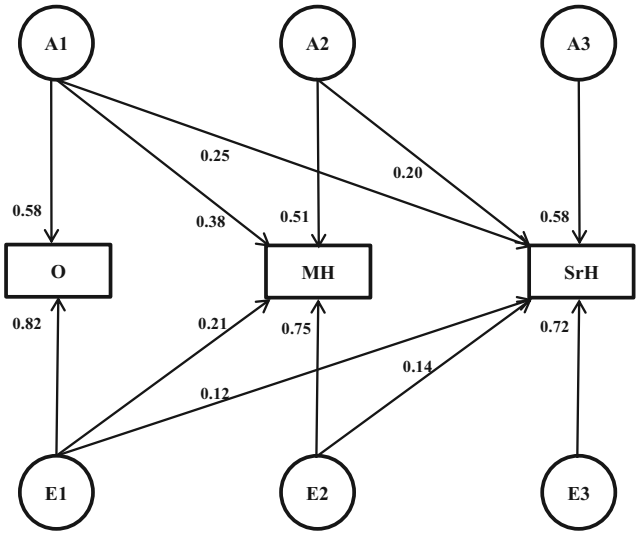

Figure 1

Best-fitting Cholesky-model with standardized path coefficients showing the relationship between optimism (O), mental (MH) and self-rated health (SrH). Path coefficients can be squared to get the percentage of variance accounted for. The Cholesky factors have been decomposed into additive genetic (A) and unshared environmental (E) influences.

heritability and genetic and environmental influences on the covariance between the three traits were not significant. However, though not significant, the twin correlations and parameter estimates (sex-limitation model) for all three variables, strongly suggested that the traits may be more heritable in women than in men, with the MZ twin correlations as well as the difference between MZ and DZ twin correlations consistently being much larger in females than in males. The increase in sample size did not influence the estimates but considerably tightened the confidence intervals, indicating a consistent pattern across the two studies.

Furthermore, previous studies show that, apart from sex differences in self-rated health (Leinonen et al., 2005; Lichtenstein & Pedersen, 1995; Romeis et al., 2000; Svedberg et al., 2001), similar sex differences may be evident in depression and anxiety measurements (highly correlated with our mental health measure), subjective wellbeing (highly correlated with both the health variables used here), and aggression suggesting that these traits also are more heritable in females than in males (Bierut et al., 1997; McGue & Christensen, 1997; Roysamb et al., 2002; Tambs et al., 1995; Vierikko et al., 2003). Our findings in combination with previous studies showing sex-difference in related traits (Bierut et al., 1997; McGue & Christensen, 1997; Roysamb et al., 2002; Tambs et al., 1995) indicate that there indeed may be sex differences in the genetic architecture of optimism, mental and self-rated health, and that even with the larger combined sample we still lack the power to detect significant effects. Future studies on the same or similar traits should keep the possibility of sex differences in mind when conducting their analyses. The potential of sex differences also impacts studies utilizing gene-finding methods; it may be advisable to look at females and males separately as significant hits may be more likely in females.

The final (common AE) model suggested that, as shown in previous research (Caprara et al., 2009; Christensen et al., 1999; Harris et al., 1992; Leinonen et al., 2005; Mosing et al., 2009; Plomin et al., 1992; Rijsdijk et al., 2003; Roysamb et al., 2003; Schulman et al., 1993; Silventoinen et al., 2007), all three traits were moderately heritable with most of the phenotypic correlation between the traits being explained by shared genetic influences, indicating that the genes predisposing to optimism may also increase mental health and both (genes predisposing to optimism and good mental health) in turn increase the self-rating of overall health.

These results cannot be generalized beyond the measures employed and the sample used. For consistency with our previous study (Mosing et al., 2009), optimism (LOT) was treated as a bipolar measurement with a high and a low end, rather than a two-dimensional scale distinguishing optimism and pessimism. Furthermore, there were some item differences between the mental health scales used in the two samples, however, factor analysis as well as the similarity in twin correlations between the samples strongly suggests that these difference were negligible. Finally, the statistical approach used (i.e., the use of a Cholesky model) may lead to some boundary problems; however, to date it is not evident to what extent this concerns the analysis of ordinal variables nor is there a good solution to this potential problem (Carey, 2005).

In conclusion, we found strong indication that the genetic etiology of optimism, mental, and self-rated

health and their interrelations may differ between males and females, with all three traits being more heritable in females than in males. However, these differences did not reach significance.

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Appendix A

GHQ (Item 1–12) Versus CES-D (Italic Underneath Each Item)

1. Been able to concentrate on whatever you are doing?
   I had difficulties keeping concentrated on what I was doing.
2. Lost much sleep over worry?
   I slept poorly.
3. Been feeling unhappy and depressed?
   I felt depressed.
4. Been thinking of yourself as a worthless person?
   I felt that I was worth as much as everyone else?
5. Been feeling reasonably happy all things considered?
   I felt happy.
6. Felt constantly under strain?
   I feel that everything I did was hard and troublesome.
7. Been losing confidence in yourself?
   I often feel insecure (a question of the EAS scale).
8. Felt that you are playing a useful part in things?
   I felt that my life had been a failure.
9. Been able to enjoy your normal day-to-day activities?
   I was satisfied with life.
10. Been able to face up to your problems?
    I felt afraid.
11. Felt you could not overcome your difficulties?
    I felt confidence in the future.
12. Felt capable of making decisions about things?
    I could not get going.