



Strong Genetic Correlation Between Interview-Assessed Internalizing Disorders and a Brief Self-Report Symptom Scale

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Self-report scales for symptoms of anxiety and depression are frequently used for screening and research purposes. A moderate phenotypic association between disorders measured by diagnostic interviews and symptoms of anxiety and depression measured by self-report scales has been shown, but little is known about the overlap in these phenotypes' genetic and environmental variance. In the present study, we used twin modeling to identify common genetic and environmental liabilities underlying the phenotypic association between the self-report Symptom Checklist-5 (SCL-5) and lifetime internalizing disorders derived from the Composite International Diagnostic Interview (CIDI). The sample consisted of 7,992 young adult twins from the Norwegian Institute of Public Health Twin Panel (NIPHT), who all responded to a questionnaire. A subset of 2,793 individuals later underwent structured interviews. The best fitting model showed a strong genetic correlation of 0.82 (95% confidence interval; 0.61–1.0) between current self-report symptoms of anxiety and depression, and lifetime internalizing disorders, which suggests an almost complete overlap in genetic liability. The correlation between environmental factors was much lower: 0.16 (0.00–0.34, 95% CI). This implies that brief self-report scales capture genetic variance that is highly overlapping with the genetic variance common to internalizing disorder diagnoses. It thus follows that SCL-5 and similar instruments may be used as screening instruments for genetic risk factors that influence liability to internalizing disorders. In addition, existing data on self-report symptoms of anxiety and depression can be used with increased confidence to specify models including effects from genes coding for internalizing disorders.

■ **Keywords:** classical twin, genetic variance, self-report, internalizing disorders

Structured diagnostic interviews are considered the gold standard for psychiatric epidemiological studies (Segal & Coolidge, 2007). Such interviews are, however, expensive and time consuming. Different types of self-report scales are therefore often applied for screening purposes (Müller, 2009). The association between self-report scales and diagnostic interviews is thus an important subject for both mental health research and for diagnostic and screening purposes in primary health care facilities.

Psychiatric disorders, as classified by the leading classification systems DSM-IV (APA, 2000) and ICD-10 (WHO, 1992), often show an extensive degree of co-

occurrence or comorbidity (Krueger & Markon, 2006). Studies investigating the underlying structure of this comorbidity typically converge on identifying two distinct liability factors influencing two broad groups of disorders, often called internalizing and externalizing (Røysamb et al., in press). Internalizing disorders are characterized by

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internal suffering (Kendler & Prescott, 2006), and include disorders such as major depressive disorder (MDD), generalized anxiety disorder (GAD), and different phobias. Externalizing disorders are characterized by a general liability toward disinhibitory behavior, and include disorders such as substance use disorders and antisocial behavior disorders (Krueger & Markon, 2006). Some studies have found that the internalizing factor tend to bifurcate into two separate liabilities, often called distress and fear (Kendler et al., 2003; Krueger & Markon, 2006; Slade & Watson, 2006). The two-factor structure of psychiatric disorders seems to be driven by genetic and not environmental factors (Kendler et al., 2003).

Short forms of the Symptom Checklist (SCL; Derogatis, Lipman, Rickels, Uhlenhuth, & Covi, 1974) are among the most frequently used self-report scales for internalizing symptoms. A number of studies have investigated the phenotypic association between self-report scales and diagnoses of internalizing disorders based on structured interviews (e.g. Aben et al., 2002; Pedersen & Karterud, 2004; Sandanger et al., 1998). Most find a moderate association, with sensitivity and specificity estimates ranging from 0.50–0.90.

Genetic factors account for a substantial part of the variance of a number of internalizing disorders (Hettema et al., 2001; Sullivan et al., 2000). Typically, heritability estimates range from 0.12–0.65 (Bouchard, 2004; Foley et al., 2001; Kendler et al., 2006; Ørstavik et al., 2007). There is also evidence of shared genetic factors across different anxiety disorders (Tambs et al., 2009a), depressive disorders (Edvardsen et al., 2009), and between depressive and anxiety disorders (Hettema, 2008; Kendler et al., 1993; Middeldorp et al., 2005). Correspondingly, symptoms of anxiety and depression as measured by self-report, have been found to be heritable, with estimates typically ranging from 0.20 to 0.61 (Foley et al., 2001; Nes et al., 2007; Silberg et al., 1990; Tambs & Moum, 1993b). As internalizing disorders are classified based on symptoms of anxiety and depression, it is reasonable to assume that the genetic components may be shared.

However, whilst the phenotypic association between internalizing disorder diagnoses and self-report scales is fairly well established, there is very limited knowledge about how well self-report symptoms of anxiety and depression and interview based internalizing diagnoses capture phenotypes with the same genetic liability. One twin study has reported a substantial genetic correlation of 0.70 (0.57–0.84, 95% CI) between the ten-item SCL depression scale and lifetime MDD among women, when both measures were corrected for measurement error (Foley et al., 2001). However, to what extent this finding is generalizable to a scale designed to capture symptoms of both anxiety and depression and a broader set of internalizing disorders in both males and females, is not known.

Multivariate twin studies typically examine two or more variables and model to what extent their phenotypic overlap is due to shared genetic and/or environmental factors. In the present study, we wanted to examine two variables that are intended to measure related phenotypes assessed by different methods, namely symptoms of anxiety and depression measured by a brief self-report scale and diagnoses of internalizing disorders assessed by a structured diagnostic interview. These phenotypes are only moderately correlated. If, however, the genetic correlation between these measures turns out to be strong, the usefulness of questionnaire data on symptoms of anxiety and depression would be increased for genetic studies. Many twin and family studies do not have diagnostic data on internalizing disorders, but do have self-report measures of symptoms of anxiety and depression. If a brief symptom scale such as SCL is able to capture the genetic factors influencing internalizing disorders, this would permit us to investigate the relationship with genetic factors influencing other variables of interest, such as alcohol and substance abuse, personality disorders, and somatic disorders. In addition, overlapping genetic factors would imply that brief self-report scales could be used as screening instruments for genetic liability towards internalizing disorders in molecular genetic studies.

The aim of the present study was thus to investigate the phenotypic association between a five-item short-form version (SCL-5) of the SCL-25 (Hesbacher et al., 1980) and one or more selected lifetime DSM-IV internalizing disorders diagnosed by a structured interview in a population based sample of young adult males and females. Further, we aimed to partition the phenotypic association into genetic and environmental contributions by the use of twin modeling.

Materials and Methods

Sample

The data for the analyses in the present study come from the Norwegian Institute of Public Health Twin Panel (NIPHTP). The twins are identified through information contained in the national Medical Birth Registry, established January 1, 1967, which receives mandatory notification of all live- and stillbirths of at least 16 weeks of gestation. Two questionnaires have been distributed, the first in 1992 (all twins born between 1967 and 1975), and the second in 1998 (all twins born from 1967 to 1979). The data for the present study come from the second questionnaire, which was sent to 12,700 twin pairs. Responses were received from 8,045 twins after one reminder (3,334 pairs and 1,377 twins whose co-twin did not respond), which gives a response rate of 63%. The 3,334 pairs included 1,052 monozygotic (MZ) male pairs, 794 dizygotic (DZ) male pairs, 1,554 MZ female pairs, 1,310 DZ female pairs, and 1,958 opposite-sex pairs. The 1,377 single responders included 188 MZ males, 274 DZ

males, 159 MZ females, 207 DZ females, and 549 opposite-sex twins. Age in this sample spanned from 18 to 31 years (mean 25.6). Of the 8,045 twins that responded, 7,992 had valid responses that could be used in the analyses of the present study. Invalid questionnaire responses mostly included incomplete data sets.

The present study also use data from a diagnostic interview of Axis I and Axis II psychiatric disorders, conducted between June 1999 and May 2004. Participants were recruited from a sample of 3,153 complete twin pairs from the second questionnaire study who had given consent to be contacted again later. Due to technical problems, 68 twin pairs were drawn directly from the NIPHTP. 2,801 twins were assessed with structured interviews for Axis I and Axis II disorders. Of these 2,801 respondents, 2,793 responses were valid. The sample consisted of 219 MZ male twin pairs, 117 DZ male twin pairs, 446 MZ female twin pairs, 264 DZ female twin pairs, 339 opposite-sex twin pairs and 21 single responders. The response rate was 44% (2,793 out of 6,306). Non-participants consisted of 0.8% pairs not willing or able to participate, 16.2% pairs in which only one twin agreed to participate, and 38.2% pairs in which none responded after reminders. There was a significant sex difference between the group that only has self-report data and the group that has both self-report and interview data. The proportion of women was 54% in the first group and 64% in the latter ($p = .00$). We found no age difference between the two groups (n.s.). Neither did we find any difference between the two groups for SCL-score (n.s.). The attrition from the questionnaire studies to the interview study has been investigated in a previous study (Tambis et al., 2009b), and found not to affect heritability estimates of mental health related variables. Two thousand, five hundred and sixty-two of the interviews were conducted face to face, and for practical reasons 231 were interviewed over the phone. The interviews were mainly conducted by psychology students late in their training and psychiatric nurses who received a standardized training program by teachers certified by the WHO. Members of a pair were assessed by different interviewers that were blind to the information obtained from the co-twin.

Zygosity was initially determined using questionnaire items previously shown to classify correctly more than 97% of the twin pairs (Magnus et al., 1983), and molecular markers for a subgroup of the sample, based on genotyping 24 microsatellite markers. Discrepancy between classification based on the questionnaire and DNA markers implied an expected misclassification rate of 0.67% for the whole sample. The NIPHTP is described thoroughly elsewhere (Harris et al., 2002).

Approval was received from the Regional Ethical Committee and the Norwegian Data Inspectorate, and written informed consent was obtained from the participants after complete description of the study.

Measures

The Symptom Checklist-5 (SCL-5; Tambis & Moum, 1993a) was applied to measure symptoms of anxiety and depression in our sample. This is a shortened version of SCL-25 (Hesbacher et al., 1980), and has been found to correlate 0.92 with the full-scale version (Tambis & Moum, 1993a). SCL-25 is a self-rating scale widely used for assessing internalizing symptoms. It is derived from the anxiety and depression scales in the SCL-90-R (Derogatis, Rickels, & Rock, 1976) and has acceptable reliability and validity as a measure of psychological distress (Hesbacher et al., 1980; Müller, 2009; Strand et al., 2003). The SCL-5 consists of five items addressing how the subject has felt for the last 14 days, responded to on a four-point scale with anchors 1 (*Not at all*) to 4 (*Extremely*). These are: (1) feeling fearful, (2) nervousness or shakiness inside, (3) feeling hopeless about the future, (4) feeling blue, and (5) worrying too much about things. The internal consistency of the SCL-5, measured by Cronbach's alpha, was estimated to 0.83 in the present sample, which is in accordance with previous findings (Strand et al., 2003; Tambis & Moum, 1993a). As recommended by Strand et al. (2003), we used the suggested cut-off for the SCL-5 of 2.0 (≥ 2.0 = mental disorder; Strand et al., 2003). In spite of well-known limitations associated with dichotomizing a variable (MacCallum et al., 2002), preliminary analyses revealed almost identical results whether the SCL-5 was dichotomized or ordinal. We therefore proceeded with one threshold on SCL-5.

For the interview, we applied the Norwegian version of the computerized Munich Composite of International Diagnostic Interview (CIDI; Wittchen & Pfister, 1997). This is a comprehensive structured diagnostic interview developed by the World Health Organization for the assessment of DSM-IV Axis I diagnoses and ICD-10 lifetime diagnoses. The interview has previously shown good test-retest and interrater reliability (Wittchen, 1994; Wittchen et al., 1998). The following lifetime disorders were selected for the present study: MDD, dysthymia, GAD, social phobia, panic disorder, and agoraphobia, as CFA studies have found these disorders to load high on an internalizing factor (Krueger & Markon, 2006; Røysamb et al., in press). The selected lifetime disorders were assigned without diagnostic hierarchical rules in order to examine co-occurrence without exclusions, in accordance with previous studies (Kessler et al., 2005b).

A one-factor structure for the selected internalizing disorders was tested by confirmatory factor analysis (CFA) in Lisrel 8.80 (Jöreskog & Sörbom, 1996). The one-factor structure yielded an excellent fit to the data: $\chi^2 = 180.955$, $df = 9$, GFI = 0.991, CFI = 0.990, RMSEA = 0.083. Factor loadings ranged from 0.58 to 0.88, with a mean loading of 0.77. Cronbach's alfa for the present sample, based on polychoric correlations, was estimated to 0.86. Based on this finding, we collapsed the disorders

into one dichotomized score (no disorder vs. one or more disorders) subsequently labeled 'Internalizing Disorder', and used this as a variable in the analyses.

Statistical Analyses

Odds ratio (OR), calculated by binary logistic regression analysis and corrected for non-independence by the use of generalized estimation equations (GEE) in SPSS 17.0, was used to investigate the phenotypic association between SCL-5 and Internalizing Disorder. In addition, tetrachoric correlations were calculated, as this is a measure of covariation that is better suited for categorical data than Pearson's correlation.

As outlined above, both variables were dichotomized. We assumed that those scoring below and above the threshold reflect different degrees of severity of an underlying continuum of liability to experience symptoms of anxiety and depression, in accordance with a liability threshold model (Falconer, 1965). According to the liability threshold model, mental disorders are caused by the joint effect of a number of risk or liability factors. The underlying liability of a disorder is assumed to be normally distributed, and those with a liability above the threshold express the trait (Plomin et al., 2001). As initial measures of the importance of genetic and environmental influences on the variables, tetrachoric within-twin correlations and cross-twin correlations were calculated.

In classical twin modeling, variation in traits is divided into the additive genetic (A), common environment (C), and individual-specific environment (E) variance components. As MZ twins share all the genetic material, and DZ twins share on average half of their segregating genes, A would tend to make MZ twins correlate twice as high as DZ twins. C is defined as environmental factors that contribute to similarity between twins, and is further assumed to have an equal effect on MZ and DZ twins, in accordance to the Equal Environment Assumption (EEA). E is per definition not shared between twins in a pair, and hence contributes to twin differences. E also contains the measurement error that is inherent in the total variance of the specified model. The influence on each of these variance components on the variables can be estimated using structural equation modeling (SEM; Neale & Maes, 2000). Liability-threshold models were fitted using ML as estimation procedure on raw data in Mx (Neale et al., 2003). The raw data option has several advantages, such as including the variance of single responders, as well as responders on only some variables. The difference in -2 times log likelihood ($\Delta-2LL$) approaches a χ^2 -square distribution, which allows a check for significant deterioration in χ^2 in two nested submodels. In addition to the χ^2 -square difference test, we used the Akaike Information Criterion (AIC) calculated as $\chi^2 - 2df$ (Akaike, 1987). AIC penalizes models that are not parsimonious (Bollen, 1989). The preferred model is reflected by having the lowest AIC-value.

Bivariate model fitting was performed in order to investigate shared genetic and environmental variance between SCL-5 and Internalizing Disorder. A correlated factor model allowing for qualitative and quantitative sex differences was fit to the bivariate data. In this approach, each variable is separately partitioned into its genetic and environmental components, and the correlations between the components are estimated (Loehlin, 1996). We followed the established approach of selecting a saturated ACE-model as the full model, with which nested submodels were compared.

Results

SCL Scores and Lifetime Prevalences of Internalizing Disorders

The prevalence of scoring above cut-off on the SCL-5, and lifetime prevalences for having one or more internalizing disorders are presented in Table 1. Out of the 7,992 individuals in the questionnaire sample, 12.1% scored above cut-off on the SCL-5. Among the 2,793 individuals in the interview sample, 20.1% reported one or more lifetime internalizing disorders. 394 individuals (14.1%) reported MDD, 48 (1.7%) dysthymia, 112 (4%) social phobia, 87 (3.1%) panic disorder, 134 (4.8%) agoraphobia, and 55 (2%) GAD.

Phenotypic Association Between SCL-5 and Internalizing Disorder

The tetrachoric correlation between SCL-5 and Internalizing Disorder was 0.48 (95% CI = 0.41–0.55). The OR of reporting one or more lifetime internalizing disorders if scoring above cut-off on the SCL-5 was 4.75 (95% CI = 3.73–6.04).

Twin Correlations

Tetrachoric twin correlations with 95% confidence intervals were estimated for SCL-5 and Internalizing Disorder. Table 2 displays the cross-twin within-trait correlations for SCL-5 and Internalizing Disorder, and the cross-twin cross-trait correlations by zygosity groups.

The total MZ correlations (combining males and females) were generally high, and more than twice the cor-

TABLE 1

Prevalences for Scoring Above Cut-Off on SCL-5 and to Fulfill the Criteria for One or More Internalizing Disorders (Int) for the Total Sample, and for Males and Females Separately

Model	N	N Above cut-off	% Above cut-off
SCL _{Total}	7,992	968	12.1
SCL _{Male}	3,415	300	8.8
SCL _{Female}	4,577	668	14.6
Int _{Total}	2,793	560	20.1
Int _{Male}	1,019	144	14.1
Int _{Female}	1,774	416	23.4

TABLE 2

Twin Correlations With 95% Confidence Intervals for the SCL-5 and Internalizing Disorder by Gender and Zygosity

	Cross-twin Internalizing	Cross-twin cross-trait	Cross-twin SCL-5
MZ both sexes	0.49 (0.40–0.56)	0.46 (0.37–0.54)	0.40 (0.28–0.52)
DZ both sexes	0.21 (0.14–0.29)	0.15 (0.04–0.25)	0.16 (-0.04–0.32)
MZ males	0.42 (0.15–0.64)	0.46 (0.16–0.70)	0.24 (0.02–0.44)
DZ males	0.28 (-0.07–0.57)	0.23 (-0.23–0.61)	0.07 (-0.24–0.37)
MZ females	0.50 (0.37–0.62)	0.47 (0.31–0.60)	0.40 (0.31–0.48)
DZ females	0.21 (0.05–0.37)	0.37 (0.16–0.55)	0.16 (0.04–0.28)
DZ opposite-sex	0.21 (0.05–0.36)	-0.11 (-0.33–0.11)	0.06 (-0.7–0.19)

responding DZ correlations. Thus there were clear indications of substantial genetic effects on both phenotypes, and on their covariation. No clear indication of common environmental effects was found. This pattern was generally also found for both sexes separately for both SCL-5 and Internalizing Disorder. No indication of qualitative or quantitative sex differences in the correlation structure of the SCL-5 variable was found, as the same-sex and opposite-sex DZ correlations were approximately the same. The negative correlations in the opposite-sex DZ group as opposed to the same-sex DZ groups for Internalizing Disorder may imply qualitative sex differences. The wide and overlapping confidence intervals, however, suggest that this may be random noise.

Model Fitting

The fit statistics for the bivariate modeling are shown in Table 3.

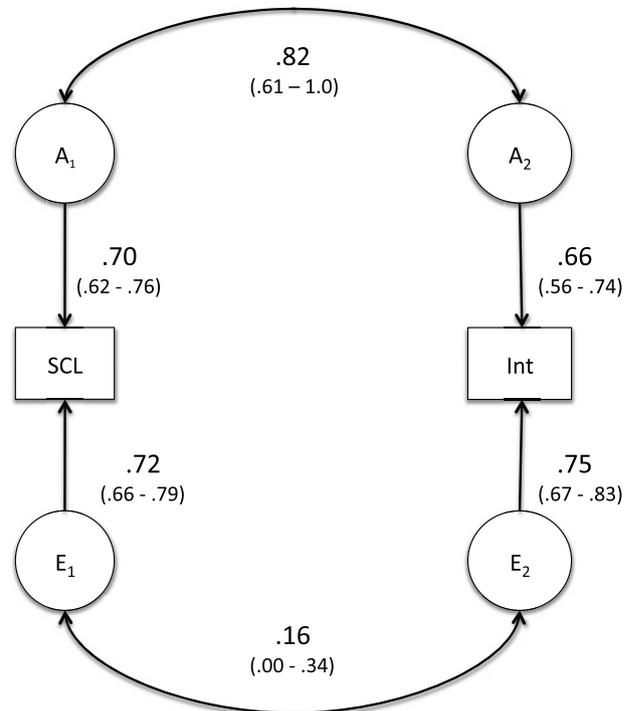
The best-fitting bivariate model was model 4, an AE-model with no sex differences. This model has the lowest AIC value, and does not fit significantly worse than the ACE model under which it is nested ($\Delta\chi^2 = 0$, $\Delta df = 3$, $p = n.s.$, $AIC = -20.552$). The additive genetic contribution to the variance in SCL-5 and Internalizing Disorder is specified by the path coefficients from the variance

TABLE 3

Model Fits for the Bivariate Model Fitting

Model	-2LL	df	p	AIC
Qualitative sex differences				
1 ACE	8,333.606	10,752	—	—
Quantitative sex differences				
2 ACE	8,341.379	10,762	n.s.	-12.227
No sex differences				
3 ACE	8,349.054	10,767	n.s.	-14.552
4 AE	8,349.054	10,770	n.s.	-20.552
5 CE	8,373.808	10,770	0.00	4.202

Note: Best-fitting model in bold type
n.s. = nonsignificant

**FIGURE 1**

Best-fitting correlated factor model.

Note: SCL = Symptom Checklist-5, Int = Internalizing Disorder.

components A_1 and A_2 , respectively (Fig. 1). The heritability of SCL-5 was estimated to be 0.48, and 0.44 for Internalizing Disorder. The bivariate model fitting also revealed that 81% of the phenotypic correlation was explained by genetic effects, and 19% by environmental effects. The genetic correlation between A_1 and A_2 in the best-fitting model was estimated to be 0.82 (0.61–1.0, 95% CI). The environmental correlation (between E_1 and E_2) was estimated to be 0.16 (0.00–0.34).

Discussion

We found both current symptoms of anxiety and depression and lifetime internalizing disorders to be common in our sample, with prevalences comparable to what has been found in other population based studies (Kessler et al., 2005a; Kringlen et al., 2001). The phenotypic association between SCL-5 and Internalizing Disorder was found to be moderate, which is also in accordance with previous studies (Haver, 1997; Sandanger et al., 1998; Williams et al., 2002).

Results from the twin modeling showed moderate heritabilities, both for SCL-5 and for Internalizing Disorder. The estimates were toward the upper limits of what has been found previously (e.g., Bouchard, 2004; Hettema et al., 2001; Nes et al., 2007; Reichborn-Kjennerud et al., 2002; Sullivan et al., 2000). Psychometrically, this is not surprising, as measures of single disorders are more prone

to measurement error and hence unreliability than are measures of several disorders combined. Unreliability of measurement contributes to lower the estimates of heritability. The same tendency was present in a study by Tambs et al. (2009), who, in the same sample as in the present study, found a substantially higher estimate of heritability for the combined anxiety disorders compared to single disorders. Higher heritability estimates for depression has also been found when several depressive disorders were included in the analyses (Edvardson et al., 2009). We found no evidence of common environmental effects for any of the phenotypes, which is in accordance with most twin studies on internalizing disorders (see, e.g., Kendler & Prescott, 2006; Plomin & Daniels, 1987).

Our main finding was the close genetic association between current self-report symptoms of anxiety and depression, and lifetime Internalizing Disorder. The genetic correlation was 0.82, and hence we assume that the genetic risk factors for current symptoms of anxiety and depression, and Internalizing Disorder are highly overlapping. With the exception of the above-mentioned study by Foley et al. (2001), where the genetic association between symptoms of depression and MDD was measured, there are no genetically informative studies on the association between self-report current symptoms of anxiety and depression, and lifetime disorders as measured by diagnostic interviews. The genetic correlation obtained in the present study is in accordance with the finding reported in the study by Foley et al. (0.70). However, in addition to supporting the findings in the study by Foley et al., results from the present study indicate that the overlap in genetic risk includes a number of internalizing disorders. We also found that the genetic overlap applied to males as well as females. Another important difference between the present study and that by Foley et al. is that the latter used measures obtained at two different times, and hence captured stable variance from SCL and MDD, while we only had one point measurement of symptoms of anxiety and depression, and one interview (designed to capture several lifetime internalizing disorders). Still, in the present study, the genetic correlation calculated was very high, and overlapping with that found by Foley et al.

As the timeframes for the two measures in the present study were not the same (internalizing disorders were measured as lifetime disorders, whereas SCL-5 reflects symptoms from the last 14 days), the strong association may seem surprising. However, our finding of a strong association points to SCL-5 as able to capture stable aspects of subject-rated levels of symptomatology, and is supported by several studies (e.g. Duncanjones et al., 1990; Kendler et al., 1995). It is argued that the stable variance in symptom checklists may index genetic factors (Foley et al., 2001). What we seem to have measured then, is the genetic association between basal psychiatric symptoms, and the liability ever in a subject's life to have an internalizing

disorder. If the symptom checklist were in fact a state measure, we would not expect to see such a strong correlation. Our finding is therefore a support to symptom checklists as being able to capture stable aspects of a subject's level of symptomatology. Further, this may imply that if a subject has a liability to developing internalizing disorders, this will be visible from the subject's self-rated level of symptomatology, as we would not expect a subject's symptoms to completely disappear in between episodes of an internalizing disorder.

SCL-5 is based on the SCL-25, which is found to correlate highly with other self-report scales for anxiety and depression (Frojdth et al., 2004; Strand et al., 2003; Williams et al., 2002). It is therefore reasonable to assume that the results from the present study can be generalized to other scales measuring current symptoms of anxiety and depression.

The results of the present study should be interpreted in the context of some potential limitations. First, the mean time from the SCL-5 measure to the interview was 2.5 years (range 1–5). The questionnaire conducted in 1992 also included SCL-5 as a measure, and preliminary analyses in the present study revealed a slightly lower correlation between Internalizing Disorder and the questionnaire conducted in 1992, than between Internalizing Disorder and the questionnaire conducted in 1998. It is therefore reasonable to assume that the phenotypic association would be higher if the measurements were closer in time.

Second, the present study made use of both an interview- and a self-report measure. The different administration modes may be a source of systematic error variance. Social desirability is a response bias that may affect the results of the present study. It has been found that respondents to self-report measures tend to report more symptoms and higher severity than those who undergo interviews, while face-to-face interviews tend to be susceptible to socially desirable responding and hence under-report (Moum, 1998). If social desirability operates mainly on the interview mode, there is reason to assume that the relative genetic and environmental contributions to the phenotypic association would remain unbiased, but the phenotypic association and the heritabilities would be lowered. However, we obtained a genetic correlation close to unity between the measures. This result suggests that although administration mode might influence mean levels and prevalences, the variability of symptoms in our sample has not been affected by systematic error variance stemming from differences in administration mode.

We found neither evidence of qualitative nor quantitative sex differences in the model fitting. However, we have limited statistical power to detect small differences with our sample size, and therefore do not have firm grounds to conclude whether sex differences in the genetic factors are present or not. Future studies should therefore be conducted with sample sizes sufficiently large to detect small

sex differences in the data. Results from earlier investigations on both qualitative and quantitative sex differences in major depression are mixed (Kendler et al., 2006; Middeldorp et al., 2006). Regarding anxiety disorders, substantial sex differences in symptoms reported and prevalence rates have been found across the life span (MacKinaw-Koons & Vasey, 2000). The sources of these sex differences are poorly understood, and they may reflect methodological problems.

Conclusion

Several noteworthy implications can be drawn from our results. Our best fitting model suggests that lifetime diagnostic interviews and brief self-report scales for current symptoms of anxiety and depression are able to capture phenotypes with highly overlapping genetic factors. It follows that in genetically informative studies based on brief self-report scales for anxiety and depression, genetic components detected can be regarded as very close to the genetic factor common to internalizing disorders. Given that many twin studies have collected data on symptoms of anxiety and depression similar to SCL, this means that existing data materials with somewhat increased confidence can specify models including effects from genes coding for internalizing disorders in general. The genetic factor influencing internalizing disorder can thus be modeled based on questionnaire scales. Further, the highly overlapping genetic factors indicates that brief self-report scales could be used as screening instruments for genetic risk for internalizing disorders in molecular genetic studies.

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