A Sib-Pair Study of the Temperament and Character Inventory Scales in Major Depression

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Background: Certain aspects of the personality may be associated with the vulnerability to develop depression. A sib-pair method has been used to examine the familiality of the 7 scales of the Temperament and Character Inventory (TCI) and whether this could be related to the genetic vulnerability to develop depression.

Methods: Probands with depression and their nearest-aged siblings from Wales were compared with healthy control probands and their nearest-aged siblings on the TCI and measures of depressed mood.

Results: All 7 scales of the TCI were familial, and scores on 6 of the scales were similar to US population scores. However, the Welsh subjects' scores on the self-transcendence scale were markedly lower than the US mean, suggesting strong cultural or national influences on this measure. Harm avoidance scores were substantially influenced by current and past depression, but this scale also showed stable traitlike characteristics that are likely related to the genetic vulnerability to depression. Novelty seeking and self-directedness were also partly state-dependent and were negatively correlated with low mood; high scorers may be resilient to the development of depression. High reward dependence may also protect against the development of depression and is unrelated to mood state. The cooperativeness, persistence, and self-transcendence scales appear to have a limited relationship with the development of depression.

Conclusions: Harm avoidance, reward dependence, novelty seeking, and self-directedness have traitlike characteristics that are related to the familiality of depression. Cooperativeness, self-transcendence, and persistence are also familial, but this appears to be unrelated to depression.

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In their psychobiological model of the structure and development of personality, Cloninger et al describe 4 dimensions of temperament that are “independently heritable, manifest early in life, and involve preconceptual biases in perceptual memory and habit formation.” These dimensions are harm avoidance, novelty seeking, persistence, and reward dependence. The authors also describe 3 character dimensions: self-directedness, cooperativeness, and self-transcendence. These items are related to “acceptance of the individual self, acceptance of other people and of nature in general.”

Although the differences between individuals according to the temperament dimensions are observable in early childhood and are moderately predictive of adult behavior, character dimensions are defined in terms of “insight learning or reorganization of self-concepts.” Such self-concepts involve the extent to which the individual identifies the self as an autonomous individual (self-directedness), an integral part of society (cooperativeness), or an integral part of the universe as a whole (self-transcendence). The Temperament and Character Inventory (TCI) is a 226-item self-report, true-false questionnaire with 107 questions relating to the 4 temperament dimensions and 119 items for the 3 character dimensions. Scores are summed to provide quantitative scales for each dimension.

The relationship between TCI traits and mood disorders has been examined by several authors. Sato et al showed that the factor structure of the TCI was not disrupted by mild to moderate severity of depression and that this instrument had promise for characterizing the underlying personality structure in depression. Kusunoki et al showed that patients with depression had higher harm avoidance and lower cooperativeness and self-directedness scores than controls. The TCI traits have also been examined during the course of recovery from depression, when it was...
noted that harm avoidance scores remained elevated follow-
ing recovery of mood.

One of the recurrent problems with studies that ex-
amine which aspects of personality are associated with vul-
nerability to depression is that measures of personality traits
may be contaminated by mood state, and the 2 are often
difficult to separate. 3 We used a sib-pair design in the Car-
diff Depression Study6,7 to tackle this problem. The de-
sign facilitates the investigation of both the relationship
between TCI traits and depression and the familiality of
the 7 scales and whether this is related to the genetic vul-
nerability to develop depression. This article discusses the
relationship between the TCI and various depression mea-
sures as well as the familiality of the scales.

The methods of subject selection and evaluation have been
described elsewhere6,7 and were as follows.

**METHODS**

**PROBAND AND SIBLING RECRUITMENT**

One hundred eight probands with depression (D-probands) were
recruited following weekly medical record reviews by 2 psy-
chiatrists (S.S. and A.M.) of admissions to psychiatric facil-
ities (inpatient wards, outpatient clinics, day hospitals, or re-
ferrals to community mental health teams) based in the
neighboring Welsh counties of Gwent and South Glamorgan
and in the adjacent city of Cardiff. They were also recruited from
among those receiving repeated prescriptions for antidepres-
sant medication from 2 family physicians in Cardiff. The pa-
tients were sent letters describing the study via their family phy-
sician (FP) and asked if they would be interested in participation.
Those who replied positively were then contacted directly to
provide further details of the study and determine whether they
fulfilled the following inclusion criteria: All D-probands were
aged 18 to 65 years, fulfilled DSM-IV operational criteria for
major depressive disorder, single or recurrent episode (sec-
section 296.2 or 296.3), and had a sibling (D-sib) willing to par-
ticipate in the study. Subjects with a lifetime-ever history of psy-
chotic or bipolar symptoms were excluded from further study,
as were those for whom it was not possible to recruit their sib-
ling. Thirty-seven D-probands were recruited from inpatient
units, 48 from ambulatory services, and 23 from FP services.

Age- and sex-matched control subjects (C-probands) were
recruited from dental and orthopedic outpatient clinics and from
among the employees of the University Hospital of Wales Na-
tional Health Service Trust (Cardiff). They were recruited if they
had no history of depression and a sibling (C-sib) who was will-
ing to participate in the study. For both D-probands and C-
probands, the sibling nearest in age was recruited whenever pos-
sible. However, if this sibling was unavailable or unwilling, the
sibling next closest in age was asked to participate. Although
most interviews were conducted face-to-face, 18.5% of the D-
sibs and 33.3% of the C-sibs were interviewed by telephone.
The study received approval from the South Glamorgan and
Gwent Research Ethics Committees, and all subjects gave writ-
ten informed consent before participation.

Initially, 119 D-probands and D-sibs and 148 C-probands
and C-sibs were recruited. Information was incomplete for one
or both members of 11 pairs in the depression group and 22 pairs
in the control group. Complete information was obtained for 108
D-proband (38 men and 70 women) and D-sib (50 men and 75
women) pairs and 126 C-proband (44 men and 82 women) and
C-sib (50 men and 76 women) pairs. Because there was a sig-
nificant age difference between the D-probands and C-
probands, which could potentially confound the findings, the

21 youngest control pairs were omitted from the data set. The
final analyses were carried out on 108 D-probands and D-sibs
and 105 C-probands and C-sibs (C-probands: 27 men and 78
women; C-sibs: 42 men and 63 women).

**INTERVIEWS AND SELF-RATING QUESTIONNAIRES**

All subjects were interviewed using the Schedules for Clinical As-
seSSment in Neuropsychiatry They also completed several self-
report questionnaires including the TCI and Beck Depression
Inventory (BDI). Information obtained at the SCAN interview
was entered into the interview’s computerized scoring program
(CATEGOS) to obtain DSM-IV diagnoses. SPSS statistical soft-
ware (SPSS Inc, Chicago, Ill), version 8 for Windows, was used
to create a database and undertake the statistical analyses.
Scores on the cooperativeness and self-directedness scales were significantly positively correlated with age (cooperativeness: Pearson $r = 0.16; P = .002$; self-directedness: Pearson $r = 0.15; P = .002$). Novelty seeking was significantly negatively correlated with age (Pearson $r = -0.32; P < .001$).

Mean±SEM scores for 135 men and 270 women are listed in Table 1, which also provides published means and SEs from a US population sample for comparison. Table 1 shows that cooperativeness, harm avoidance, reward dependence, and self-transcendence were significantly higher in women than men. For cooperativeness, the mean±SEM score was 31.94±0.54 for men and 34.38±0.34 for women, $t_{264.94} = -2.39; P < .001$; 2-tailed test). Harm avoidance ($t_{17.78} = -3.83; P < .001$; 2-tailed test), reward dependence ($t_{16.09} = -6.94; P < .001$; 2-tailed test), and self-transcendence ($t_{16.14} = -2.39; P = .02$; 2-tailed test).

Mean±SEM scores for the 8 D-sibs with depression were removed from the analyses, there were no significant differences for BDI score. There were no significant differences between siblings for sex or analysis of variance with BDI as the outcome variable, and there was no interaction between type of interview and sex.

Table 1. Mean ± SEM Scores on the 7 Scales of the Temperament and Character Inventory for 135 Men and 270 Women, All Subjects Combined, and a US Population Sample*

<table>
<thead>
<tr>
<th>Scale</th>
<th>Men</th>
<th>Women</th>
<th>All Subjects Combined</th>
<th>US Population</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cooperativeness</td>
<td>31.94±0.54</td>
<td>34.38±0.34</td>
<td>33.57±0.29</td>
<td>32.3±0.43</td>
</tr>
<tr>
<td>Harm avoidance</td>
<td>16.24±0.69</td>
<td>18.87±0.61</td>
<td>18.05±0.22</td>
<td>18.62±0.56</td>
</tr>
<tr>
<td>Novelty seeking</td>
<td>16.09±0.63</td>
<td>18.48±0.41</td>
<td>17.26±0.32</td>
<td>17.82±0.39</td>
</tr>
<tr>
<td>Persistence</td>
<td>4.44±0.19</td>
<td>4.43±0.14</td>
<td>4.43±0.11</td>
<td>4.40±0.11</td>
</tr>
<tr>
<td>Reward dependence</td>
<td>13.99±0.35</td>
<td>16.90±0.24</td>
<td>15.93±0.21</td>
<td>15.5±0.25</td>
</tr>
<tr>
<td>Self-directedness</td>
<td>30.59±0.76</td>
<td>29.65±0.50</td>
<td>29.96±0.42</td>
<td>30.7±0.43</td>
</tr>
<tr>
<td>Self-transcendence</td>
<td>11.33±0.62</td>
<td>12.86±0.36</td>
<td>12.35±0.30</td>
<td>19.2±0.36</td>
</tr>
</tbody>
</table>

*Women had significantly higher mean scores than men for cooperativeness ($t_{135.10} = -3.83; P < .001$; 2-tailed test), harm avoidance ($t_{17.78} = -4.26; P < .001$; 2-tailed test), reward dependence ($t_{16.09} = -6.94; P < .001$; 2-tailed test), and self-transcendence ($t_{16.14} = -2.39; P = .02$; 2-tailed test).

**Table 2. Mean ± SEM Scores on the 7 Scales of the Temperament and Character Inventory for the 4 Subject Groups**

<table>
<thead>
<tr>
<th>Subject Group</th>
<th>Cooperativeness</th>
<th>Harm Avoidance</th>
<th>Novelty Seeking</th>
<th>Persistence</th>
<th>Reward Dependence</th>
<th>Self-Directedness</th>
<th>Self-Transcendence</th>
</tr>
</thead>
<tbody>
<tr>
<td>D-probands</td>
<td>31.65±0.69</td>
<td>16.24±0.83</td>
<td>18.99±0.56</td>
<td>4.45±0.27</td>
<td>16.22±0.41</td>
<td>33.57±0.29</td>
<td>12.35±0.30</td>
</tr>
<tr>
<td>D-sibs</td>
<td>33.01±0.58</td>
<td>20.18±0.63</td>
<td>18.48±0.19</td>
<td>16.15±0.47</td>
<td>29.68±0.91</td>
<td>33.60±0.61</td>
<td>11.94±0.50</td>
</tr>
<tr>
<td>C-probands</td>
<td>34.77±0.50</td>
<td>19.63±0.50</td>
<td>4.54±0.20</td>
<td>15.76±0.36</td>
<td>11.94±0.50</td>
<td>34.38±0.34</td>
<td>11.94±0.59</td>
</tr>
<tr>
<td>C-sibs</td>
<td>34.63±0.53</td>
<td>17.59±0.69</td>
<td>20.75±0.65</td>
<td>17.56±0.36</td>
<td>12.19±0.70</td>
<td>33.40±0.53</td>
<td>12.19±0.70</td>
</tr>
</tbody>
</table>

Abbreviations: C-probands, control probands; C-sibs, siblings of control probands; D-probands, depressed probands; D-sibs, siblings of depressed probands.

**Table 2. Mean ± SEM Scores on the 7 Scales of the Temperament and Character Inventory for the 4 Subject Groups**

Scores on the cooperativeness and self-directedness scales were significantly positively correlated with age (cooperativeness: Pearson $r = 0.16; P = .002$; self-directedness: Pearson $r = 0.15; P = .002$). Novelty seeking was significantly negatively correlated with age (Pearson $r = -0.32; P < .001$).

**Table 2. Mean ± SEM Scores on the 7 Scales of the Temperament and Character Inventory for the 4 Subject Groups**

All D-probands fulfilled the DSM-IV criteria for major depressive disorder. Thirty-six (33.3%) of the D-probands were experiencing their first episode of depression, whereas the remaining 72 (66.7%) had also been depressed in the past. Nineteen of the D-sibs reported a past episode of depression causing impairment, and all of these subjects had received treatment for their depression. Nine were depressed at the time of the interview (with 7 subjects reporting this as a first episode). Five of the C-sibs reported previous treated episodes of depression, but none were depressed at the time of the interview. The relative risk for past or current episodes of treated depression in D-sibs compared with C-sibs was 5.42.

Mean scores and SEMs for the 7 TCI scales in the 4 groups of participants are listed in Table 2. Analysis of variance showed significant differences between the 4 groups for harm avoidance ($F_{5,401} = 6.45; P < .001$; post hoc Tukey test: $1 < 2 < 3, 4$), harm avoidance ($F_{5,401} = 87.76; P < .001$; post hoc Tukey test: $1 < 2 < 3, 4$), novelty seeking ($F_{5,401} = 7.47; P < .001$; post hoc Tukey test: $1 < 2 < 3, 4$), and self-directedness ($F_{5,401} = 52.15; P < .001$; post hoc Tukey test: $1 < 2 < 3, 4$).

**TCI Scales and Depression Ratings at Time of Interview**

All D-probands had a large proportion of subjects with depression who had elevated harm avoidance scores. The mean scores for C-probands and C-sibs without depression, listed in Table 2, were similar to those for the US population.
harm avoidance and self-directedness. In addition, the harm avoidance and self-directedness scores of the D-sibs were intermediate between the D-probands and both control groups, and these scores were also significantly different in the D-sibs compared with the C-probands and C-sibs.

Table 3 indicates the correlations between the 7 scales of the TCI and the BDI scores for all 4 groups combined. Scores on the harm avoidance (Pearson $r = 0.67$; $P < .001$) and self-transcendence (Pearson $r = 0.12$; $P = .01$) scales are positively correlated with BDI scores. Scores on the cooperativeness (Pearson $r = -0.23$; $P < .001$), novelty seeking (Pearson $r = -0.18$; $P < .001$), and self-directedness (Pearson $r = -0.65$; $P < .001$) scales are significantly negatively correlated with BDI scores.

**FAMILIARITY OF THE 7 TCI SCALES**

Table 3 also indicates the correlations for sib-pairs with depression and controls combined. All 7 scales are significantly correlated across sib-pairs, with the correlation coefficients ranging from 0.14 for reward dependence to 0.28 for harm avoidance and self-directedness.

**TCI SCALES AND HISTORY OF DEPRESSION**

Nineteen of the D-sibs had had a past episode of depression but were not ill at the time of the interview, whereas 80 D-sibs had never been depressed. Mean scores and SEMs for the 7 TCI scales in these 2 groups of D-sibs are listed in Table 4. The D-sibs who had previously been depressed had significantly higher harm avoidance scores compared with D-sibs with no history of depression ($t_{41.11} = -2.42$; $P = .02$; 2-tailed test). The D-sibs who had never been depressed had significantly higher reward dependence scores compared with D-sibs with a history of depression ($t_{28.09} = 2.59$; $P = .02$; 2-tailed test). For the remaining scales, there were no significant differences between D-sibs with or without a history of depression.

**TCI SCALE SCORES IN NEVER-DEPRESSED D-SIBS AND C-SIBS**

As mentioned, 80 D-sibs reported never having been depressed. These subjects were compared with 100 never-depressed C-sibs on the 7 scales of the TCI; mean scores and SEMs appear in Table 4. Never-depressed D-sibs had significantly higher harm avoidance scores ($t_{151.11} = 2.36$; $P = .02$; 2-tailed test) and significantly lower self-directedness scores ($t_{151.06} = -2.38$; $P = .02$; 2-tailed test) than never-depressed C-sibs. Novelty seeking and reward dependence were also significantly lower in never-depressed D-sibs compared with never-depressed C-sibs (novelty seeking: $t_{173.60} = -1.77$; $P = .04$; 1-tailed test; reward dependence: $t_{159.54} = 1.74$; $P = .04$; 1-tailed test).

**COMMENT**

**SOURCES OF PROBANDS**

The results show that the D-probands who were inpatients when they participated in the study had higher scores on the BDI when compared with the OP and FP groups. This is not surprising, those who require admission to the hospital are likely to have more severe illnesses than those who remain in ambulatory facilities or with their FP for treatment. We have also shown that D-probands recruited from family practices were significantly younger than those recruited via OP or IP sources. Again, this is not surprising because such patients are probably nearer to the onset of their illness course. Nevertheless, the source of recruitment of the probands did not influence the scores on our main measures of interest in this article, the TCI scales. Furthermore, all D-probands fulfilled the same diagnostic criteria.

As we have shown elsewhere, this disorder was substantially familial, with 19 D-sibs reporting past treatment for depression and 8 more who were depressed at the time of the interview. This can be compared with 5 of the C-sibs who reported a history of depression but none of whom were depressed at the time of the interview. The SCAN interview consisted of a comprehensive clinical inquiry about the duration and severity of individual items regarding depressive psychopathologic characteristics. A computerized scoring program was then used to apply the **DSM-IV** diagnoses. However, the interview did not evaluate subclinical or subthreshold symptoms in the subjects, nor were other comorbid disorders evaluated in detail with the exception of the exclusion diagnoses (psychotic symptoms or bipolar disorder).

**AGE, SEX, AND TCI SCALE SCORES**

We found significant sex differences for harm avoidance, reward dependence, cooperativeness, and self-transcendence; women had significantly higher scores than men. These traits are generally considered to be female rather than male characteristics, and similar findings have been noted in previous studies. Cloninger et al reported higher scores for cooperativeness and the “spiritual acceptance” aspect of the self-transcendence scale in women in the general population, whereas Mendelowicz et al found that healthy women had significantly higher reward dependence scores than men. Cloninger et al also reported positive correlations between age and self-directedness and cooperativeness, as found in the Cardiff Depression Study.
D-sibs who had never been depressed had significantly higher reward dependence scores compared with D-sibs who had a history of depression (t141 = −2.42; P < .02; 2-tailed test). D-sibs who had never been depressed had significantly higher reward dependence scores compared with D-sibs who had a history of depression (t141 = −2.42; P < .02; 2-tailed test). Compared with never-depressed C-sibs, never-depressed D-sibs had significantly higher mean scores for harm avoidance (t141 = 2.36; P < .03; 2-tailed test), significantly lower mean scores for novelty seeking (t125 = −1.77; P < .04; 1-tailed test), significantly higher reward dependence scores (t125 = 1.74; P < .02; 1-tailed test), and significantly lower self-directedness scores (t125 = −2.38; P < .02; 2-tailed test).

### Table 4. Mean ± SEM Scores on the 7 Scales of the Temperament and Character Inventory for 19 Siblings of Probands With a Lifetime History of Depression but Who Were Well at the Time of the Interview, 80 Siblings of Probands With Depression, and 100 Siblings of Control Probands Who Had Never Been Depressed

<table>
<thead>
<tr>
<th></th>
<th>Cooperativeness</th>
<th>Harm Avoidance</th>
<th>Novelty Seeking</th>
<th>Persistence</th>
<th>Reward Dependence</th>
<th>Self-directedness</th>
<th>Self-transcendence</th>
</tr>
</thead>
<tbody>
<tr>
<td>D-sibs with history of depression</td>
<td>32.17 ± 1.89</td>
<td>19.28 ± 1.89</td>
<td>18.72 ± 1.36</td>
<td>5.94 ± 0.98</td>
<td>14.28 ± 0.86</td>
<td>29.39 ± 2.02</td>
<td>11.72 ± 1.47</td>
</tr>
<tr>
<td>Never-depressed D-sibs</td>
<td>33.55 ± 0.60</td>
<td>14.26 ± 0.85</td>
<td>19.17 ± 0.65</td>
<td>4.19 ± 0.25</td>
<td>16.79 ± 0.49</td>
<td>30.92 ± 0.99</td>
<td>11.62 ± 0.54</td>
</tr>
<tr>
<td>Never-depressed C-sibs</td>
<td>34.53 ± 0.53</td>
<td>11.75 ± 0.71</td>
<td>20.87 ± 0.67</td>
<td>4.48 ± 0.20</td>
<td>15.71 ± 0.38</td>
<td>33.62 ± 0.54</td>
<td>11.70 ± 0.69</td>
</tr>
</tbody>
</table>

Abbreviations: C-sibs, siblings of control probands; D-sibs, siblings of depressed probands.

### MEAN TCI SCALE SCORES IN US AND WELSH SUBJECTS

Cloninger et al1 have reported mean TCI scores in a US sample obtained from visitors to a shopping mall, and the authors considered that they were representative of the general population. Our subjects were patients or volunteers selected because they had a sibling willing to participate in the study. We have commented elsewhere that our method of control proband selection may have led to the inclusion of particularly altruistic, helpful volunteers and that their scores on the 7 scales of the TCI may have reflected this bias. However, for all but 3 of the scales (harm avoidance, persistence, and self-transcendence), the mean scores for the US sample and the 4 Welsh groups were very similar. For harm avoidance, we suggest that the difference is largely due to the currently depressed subjects contributing to the total for the Welsh group; the mean scores for the healthy control subjects were similar to the US mean scores. Although the mean scores for persistence were only marginally higher in the US compared with the Welsh groups, the mean self-transcendence score for the US population sample was substantially higher than for all 4 Cardiff groups. This may suggest that these US subjects were more religious or spiritual than those from Wales.

The relationship between self-transcendence and personality disorder as conceptualized in the DSM-III-R12 was examined by Svrakic et al,13 who showed that only schizoid personality disorder was significantly (negatively) correlated with self-transcendence scores. The authors concluded that the concepts captured by the self-transcendence scale of the TCI were not incorporated into the traditional personality disorder criteria of the DSM. They suggested that further systematic studies of this scale in other populations would help to clarify its clinical significance. The findings of the Cardiff Depression Study support the view that there may be national or cultural differences in scores on this scale that warrant further investigation, although no differences from US self-transcendence scores have been reported by investigators using the TCI in Swedish14 or Spanish15 populations.

### FAMILIARITY AND HISTORY OF MAJOR DEPRESSION

As we have commented elsewhere,6 the relative risk of reported depression in the D-sibs compared with the C-sibs (5.42) was higher than in most previous studies of major depression.6 This may be attributable in part to the relatively low rates of depression in the C-sibs, who were ascertained via C-probands selected for mental health.

The D-probands had significantly different scores compared with the other 3 groups for cooperativeness, harm avoidance, novelty seeking, and self-directedness. Similar results (higher harm avoidance and lower cooperativeness and self-directedness scores in subjects with depression compared with healthy controls) have been found by others.3,17 Hansenne et al17 found that self-transcendence scores were higher in subjects with depression than healthy controls. Although there were no differences in self-transcendence scores between the 4 subject groups in the Cardiff Depression Study, self-transcendence was significantly, albeit weakly, correlated with BDI score.

Previously, Brown et al18 suggested that higher-order traits such as novelty seeking and reward dependence were relatively independent of mood and anxiety states, whereas harm avoidance reflected changes in mood to a much greater extent. In keeping with these findings, the Cardiff Depression Study has shown highly significant correlations with current mood measures for harm avoidance and has not found any significant differences across the 4 groups of subjects for reward dependence. However, contrary to the suggestion of Brown and colleagues that novelty seeking is independent of current mood, our study found lower novelty-seeking scores in those with depression compared with controls.

The relationship between current mood state and the 7 TCI scales was also reflected in the correlations with BDI. Of the 7 scales, the 4 significantly correlated with BDI were also significantly different for D-probands compared with the other 3 groups. Harm avoidance and self-directedness had high correlations (0.67 and −0.65, respectively), whereas cooperativeness and novelty seeking had more modest correlations with BDI (−0.23 and −0.18, respectively). In addition to these associations with cur-
rent mood measures, all 7 scales of the TCI were familial, as shown by significant sib-pair correlations.

When never-depressed D-sibs were compared with D-sibs who reported a previous episode of depression, there were no significant differences in scores on 5 of the scales. However, scores for harm avoidance remained significantly higher and scores for reward dependence significantly lower in the group with previous depression. This suggests that the cooperativeness, novelty-seeking, and self-directedness scores in subjects with depression return to the normal range following recovery. For harm avoidance and reward dependence, although clinical recovery leads to some improvement in scores, they do not return to a level similar to never-depressed D-sibs. Elevated harm avoidance scores following recovery from depression have also been noted by Richter et al.³

### Vulnerability Traits for Depression

Our results show that several of the TCI scales are sensitive to a history of depression. To attempt to overcome current or past mood state as a possible confounding factor, we examined 2 groups of never-depressed subjects (D-sibs and C-sibs) who were first-degree relatives of subjects with depression or healthy controls. If there were a genetic relationship between a heritable personality trait and depression, the siblings of subjects with depression who had not been depressed themselves, yet who share on average 50% of their genes with their depressed sibling, should have differed on measures of the trait when compared with the never-depressed siblings of healthy individuals. Although the never-depressed D-sibs did not express the phenotype for depression, they should typically have more depression vulnerability genes than individuals (C-sibs) with no such relationship to a D-proband. Consequently, by comparing these 2 groups, it is possible to begin to disentangle state-dependency effects or the effects of prior episodes of depression from potential heritable vulnerability effects. The results showed significant differences between never-depressed D-sibs and C-sibs for harm avoidance, novelty seeking, reward dependence, and self-directedness. Mean scores for never-depressed D-sibs were higher than for never-depressed C-sibs for harm avoidance and reward dependence and lower for novelty seeking and self-directedness. For harm avoidance, novelty seeking, and self-directedness, the mean scores of the never-depressed D-sibs were intermediate between those of the D-probands and never-depressed C-sibs. This suggests that these 3 scales have traitlike characteristics related to a familial vulnerability to depression and are further lowered or elevated when the subject is depressed.

In Table 5, we summarize the relationship between TCI profiles that appear to characterize subjects with present and past depression or a genetic liability to depression. Our results suggest that the 7 scales fall into 4 main types. The first of these consists of the harm avoidance scale. This scale is highly correlated with current depressed mood, and scores do not return to the normal range with recovery. This poses the following question: Are these elevated harm avoidance scores in the group that recovered from depression due to the effect of “scarring” following the depression? Harm avoidance scores were also elevated in those who had an increased genetic loading for depression but had never been depressed, suggesting that harm avoidance is a trait marker of liability to depression.

The second type consists of novelty seeking and self-directedness, both of which were negatively associated with current mood. The D-sibs with a history of depression did not have higher novelty-seeking or self-directedness scores than D-sibs with no history of depression. However, like harm avoidance, scores on both these scales showed some association with familial liability to depression; never-depressed D-sibs had significantly lower scores than never-depressed C-sibs. Reward dependence forms the third scale type. Mean reward dependence scores were significantly higher in the never-depressed D-sibs compared with C-sibs. This is opposite to the direction of the scores found in D-sibs who reported a history of depression. Also, reward dependence scores were not correlated with current mood measures. One interpretation of these findings is that reward dependence is influenced only by recovery from depression. Individuals who have recovered from major depression may become less sentimental, less socially attached, and less dependent on the approval of others, the personality characteristics encompassed by the scale.³ On the other hand, the scale may also measure resilience; that is, the characteristics included in the scale may provide some protection against depression in those who have an increased genetic liability to develop this disorder.

The last scale type consists of cooperativeness, self-transcendence, and persistence. Whereas these scales were familial, the results suggest that this familiality is not related to depression. Although cooperativeness was negatively associated and self-transcendence positively associated with current low mood, neither type of score was

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### Table 5. Summary of Results for the 7 Scales of the Temperament and Character Inventory *

<table>
<thead>
<tr>
<th>Scale Type</th>
<th>Scale(s)</th>
<th>Scores Partly State Dependent</th>
<th>Scores Influenced by History of Depression</th>
<th>Scores Influenced by Genetic Relationship to Proband With Depression</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Harm avoidance</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>2</td>
<td>Novelty seeking, self-directedness</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>3</td>
<td>Reward dependence</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>4</td>
<td>Cooperativeness, self-transcendence, persistence</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
</tr>
</tbody>
</table>

*All scales were familial.
influenced by a history of depression, nor were there differences from control subjects in never-depressed first-degree relatives of subjects with depression.

LIMITATIONS OF THE STUDY

Although we could classify our subjects into groups according to whether they were well, depressed at the time of the interview, or had ever been depressed in the past, we have completed TCI questionnaires only for a single time point. In other words, we have made inferences about the relationship between TCI scores and depression on the basis of cross-sectional data.

Using a sib-pair design allows us to comment on familial rather than genetic risk factors. However, a recent clinically based twin study and several population based studies (described by Sullivan et al) found no evidence of shared environmental effects in depression, and genetic studies of personality have been virtually unanimous in finding only nonfamilial environmental effects. Therefore, most or all of our observed sibling similarities likely reflect shared genes, not shared environment.

The number of subjects included in the analyses is quite small when divided according to the presence or absence of past depression. Furthermore, we used an exploratory approach to data analysis with the attendant risk of multiple testing. Nevertheless, we found some fairly large group differences and a general pattern of results that is in keeping with broad predictions about TCI scales and their relationship with the familial basis of depression.

We have examined the 7 TCI scales in the 4 subject groups who participated in the Cardiff Depression Study. The study has shown that all 7 scales are familial, which supports the proposal of Cloninger et al that the TCI measures enduring and heritable aspects of personality. However, 1 of the scales, self-transcendence, showed a marked difference between our Welsh sample and the published US population scores, suggesting strong cultural effects. Consequently, the self-transcendence scale may have cultural or national variations in healthy populations, and this requires further investigation. For all other scales, the mean scores for our Welsh cohort were highly similar to the published US means.

Harm avoidance scores were substantially influenced by current and past depressed state. The scale also showed traitlike characteristics that are probably related to a genetic vulnerability to depression because the D sibs, even those who had never had depression, scored highly. Novelty seeking and self-directedness were negatively correlated with current low mood. Both of these scales also have traitlike characteristics; low scores are related to an increased risk of depression, whereas high scores could be associated with protection against the development of depression. Although reward dependence is not influenced by current mood, these scores are lowered in those with a history of depression and elevated in individuals with a genetic predisposition to depression but who have never been depressed. Consequently, high scores for reward dependence may play a protective role against the development of depression. Finally, the cooperativeness, persistence, and self-transcendence scales appear to have only a limited relationship to the familiality of depression. Future strategies for further examining vulnerability factors for depression could include prospective or longitudinal studies of the siblings of depressed probands who have not yet developed the disorder.

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CONCLUSIONS

We have examined the 7 TCI scales in the 4 subject groups who participated in the Cardiff Depression Study. The study has shown that all 7 scales are familial, which supports the proposal of Cloninger et al that the TCI measures enduring and heritable aspects of personality. However, 1 of the scales, self-transcendence, showed a marked difference between our Welsh sample and the published US population scores, suggesting strong cultural effects. Consequently, the self-transcendence scale may have cultural or national variations in healthy populations, and this requires further investigation. For all other scales, the mean scores for our Welsh cohort were highly similar to the published US means.

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REFERENCES