

# **A Genome-Wide Scan for Eysenckian Personality Dimensions in Adolescent Twin Sibships: Psychoticism, Extraversion, Neuroticism, and Lie**

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**ABSTRACT** We report the first genome-wide scan of adolescent personality. We conducted a genome-wide scan to detect linkage for measures of adolescent Psychoticism, Extraversion, Neuroticism, and Lie from the Junior Eysenck Personality Questionnaire. Data are based on 1,280 genotyped Australian adolescent twins and their siblings. The highest linkage peaks were found on chromosomes 16 and 19 for Neuroticism, on chromosomes 1, 7, 10, 13 m, and 18 for Psychoticism, and on chromosomes 2 and 3 for Extraversion.

H. J. Eysenck argued that best way to understand behavior is to study human individual differences. In addition to an overview of Eysenck's model, this introduction will review the genetic epidemiology of both adult and adolescent measures of personality. Our focus will be on the genetics of adolescent personality for which much less

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is known. There has been little research to date that has examined, within a developmental framework, the genetic and environmental stability of adolescent personality. Moreover, there have been no attempts to perform tests of genome-wide linkage or association aimed at locating quantitative trait loci responsible for the observed genetic variation in adolescent personality.

Eysenck's chief contribution to psychology was his model of personality, which is based on a quantitative and dimensional representation of human behavior (H. J. Eysenck, 1967, 1971a; H. J. Eysenck & Rachman, 1965). His model includes three orthogonal dimensions: Psychoticism, Extraversion, and Neuroticism. These dimensions are independent of intelligence and have consistently emerged as second-order or superfactors from large-scale factor analytic studies (H. J. Eysenck, 1971b; H. J. Eysenck & M. W. Eysenck, 1985; H. J. Eysenck & S. B. G. Eysenck, 1991). Each superfactor represents a polygenic and hierarchical phenotype that forms a continuum based on a number of first-order traits, which themselves are empirically derived, intercorrelated, and give rise to the superfactors above them (H. J. Eysenck, 1971b; H. J. Eysenck & M. W. Eysenck, 1985; H. J. Eysenck & S. B. G. Eysenck, 1975, 1991).

The construct of *Psychoticism* was first described in detail by H. J. Eysenck and S. B. G. Eysenck (Eysenck & Eysenck, 1968a, 1968b, 1976) and has subsequently been revised to describe and support the idea that high scorers have a greater probability and risk of psychotic illness (H. J. Eysenck, 1995; H. J. Eysenck & S. B. G. Eysenck, 1991). They are best described as solitary, not caring for people, troublesome, having difficulty fitting in, cruel and inhumane, lacking feelings and empathy, and altogether insensitive (H. J. Eysenck & S. B. G. Eysenck, 1991). Despite the scales' intention, evidence suggests that although subjects scoring high on Psychoticism exceed controls on ratings of psychotic like experiences including symptoms of schizotypal and paranoid personality disorder, they are not necessarily at heightened risk for psychosis (Chapman, Chapman, & Kwapil, 1994). Moreover, unlike Extraversion and Neuroticism, the phenotypic factor structure does not appear to have the same genetic structure, suggesting that the scale may be measuring correlated but heterogenous factors or facets (Heath & Martin, 1990).

Similar to Jung's construct with the same name, *Extraversion* is a quantitative trait that more or less defines sociability (H. J. Eysenck, 1953, 1967; H. J. Eysenck & S. B. G. Eysenck, 1991). High scorers

like parties, have many friends, and need to have people to talk to (H. J. Eysenck & S. B. G. Eysenck, 1991). This dimension has been used to differentiate hysterical (extraverted neurotic) from dysthymic (introverted neurotic) neurotic disorders (H. J. Eysenck, 1947, 1957). It has been associated with liability to suicidality, depression, panic, and phobic disorders, schizophrenia (Berenbaum & Fujita, 1994; Bienvenu et al., 2001; Janowsky, 2001; Roy, 1998) and can also differentiate between bi- and unipolar patients (Bagby et al., 1997).

*Neuroticism* was originally conceptualized as a quantitative personality trait defining an individual's vulnerability to various neurotic disorders and psychological distress (H. J. Eysenck, 1953, 1967). Individuals with high Neuroticism are characterized with "emotional instability" and are prone to low self-esteem, feelings of anxiety, depression, and guilt (H. J. Eysenck & S. B. G. Eysenck, 1991). The dimension is also highly significant of a number of clinical mood and affect disorders (Kirk et al., 2000). H. J. Eysenck has argued that there is strong evidence to support the discontinuity between neuroses and psychoses (H. J. Eysenck, 1960, 1970; H. J. Eysenck & S. B. G. Eysenck, 1969, 1976), and so the dimensions were psychometrically designed to reflect this discontinuity (H. J. Eysenck & S. B. G. Eysenck, 1975). Indeed, his personality model can be used to differentiate individuals as normal, neurotic, and psychotic (including persons with schizophrenia and manic depression; H. J. Eysenck & S. B. G. Eysenck, 1991). This does not preclude individuals scoring high on Neuroticism from scoring high (or low) on the other dimensions, and any combination is possible. The revised Eysenck Personality Questionnaire (EPQ-R) also includes a Lie scale, which, in addition to measuring social conformity, can reflect deliberate faking, presentation of an ideal self-concept rather than a candid self-appraisal or an honest but inaccurate self-assessment (H. J. Eysenck & S. B. G. Eysenck, 1991; S. B. G. Eysenck & H. J. Eysenck, 1970; Michaelis & Eysenck, 1971).

### Genetic Epidemiology

Evidence for the genetic contribution to individual differences in adult personality is compelling and comes from a variety of sources: twin pairs reared together (Eaves & Young, 1981; Loehlin & Nichols, 1976; Macaskill, Hopper, White, & Hill, 1994; Rose & Kaprio, 1988; Rose, Kaprio, Williams, Viken, & Obremski, 1990;

Rose, Koskenvuo, Kaprio, Sarna, & Langinvainio, 1988); separated twin pairs (Bouchard, Lykken, McGue, Segal, & Tellegen, 1990; Pedersen, Plomin, McClearn, & Friberg, 1988; Shields, 1962; Tellegen et al., 1988); non-twin adoptees and their biological and adoptive families (Loehlin, 1982, 1985; Loehlin, Horn, & Willerman, 1981; Scarr, Webber, Weinberg, & Wittig, 1981); as well as twin pairs reared together and their relatives, that is, parents, siblings, spouses, adult children (Eaves, 1976; Eaves, Heath, Neale, Hewitt, & Martin, 1998; Lake, Eaves, Maes, Heath, & Martin, 2000; Price, Vandenberg, Iyer, & Williams, 1982). Among the numerous reports based on twin data that have examined the heritability of Neuroticism and Extraversion, nearly all have arrived at genetic estimates in the vicinity of 50% (Eaves & H. J. Eysenck, 1975; Eaves et al., 1999; Eaves et al., 1998; Fanous, Gardner, Prescott, Cancro, & Kendler, 2002; Floderus-Myrhed, Pedersen, & Rasmuson, 1980; Heath et al., 1997; Jang, Livesley, & Vernon, 1996; Jardine, Martin, & Henderson, 1984; Jinks & Fulker, 1970; Keller, Coventry, Heath, & Martin, 2005; Kendler, Neale, Kessler, Heath, & Eaves, 1993; Macaskill et al., 1994; Martin, Eaves, & Fulker, 1979; Pedersen et al., 1988; Rose et al., 1988; Saudino, Pedersen, Lichtenstein, McClearn, & Plomin, 1997; Viken, Rose, Kaprio, & Koskenvuo, 1994). Larger extended twin studies have reported broad heritability estimates for Extraversion, ranging from 43% to 50%, and wider estimates for Neuroticism, ranging from 27% to 61% (Eaves et al., 1999; Keller et al., 2005; Lake, Eaves, Maes, Heath, & Martin, 2000).

Few behavior genetic studies have examined the heritability of Psychoticism and Lie (Eaves, 1976; Eaves et al., 1999; Gillespie, Johnstone, Boyce, Heath, & Martin, 2001; Hay et al., 2001; Heath & Martin, 1990; Keller et al., 2005; Macaskill et al., 1994; Martin et al., 1979). Gillespie and colleagues (Gillespie et al., 2001) analyzed EPQ-R data from 2,943 adult male and female Australian twins and reported that 40% and 44% of the variance in Psychoticism and Lie, respectively, could be explained by additive genetic effects. Keller and colleagues (2005) in their extended adult twin and sibling design ( $N = 12,913$  individuals) reported broad heritability estimates ranging from 28% to 33% for Psychoticism and from 33% to 34% for Lie. Eaves and colleagues' (1999) study of adult twin and family members ( $N = 29,691$  individuals) reported broad heritability estimates ranging from 8% to 29% for Psychoticism and from 29% to 42% for Lie. In all cases, the genetic contribution to adult person-

ality was significant, whereas the contribution of shared environmental or cultural effects was mostly negligible. In other words, the environmental contribution to individual differences in personality was almost entirely limited to aspects of the environment that were unique and unshared between sibling and family members.

Although adult personality appears phenotypically stable, much less is known about its genetic stability. This is because of the lack of longitudinal and genetically informative data sets; most research has been based on data sets that were either longitudinal but genetically uninformative or genetically informative but cross-sectional (Conley, 1984; Eaves, H. J. Eysenck, & Martin, 1989; Ormel & Rijsdijk, 2000; Watson & Clark, 1984). However, several lines of evidence suggest that not only are genetic effects significant but they are also stable over time, at least with respect to Neuroticism and Extraversion (Eaves et al., 1989; Kendler et al., 1993; Viken et al., 1994). Indeed, Eaves and colleagues (1989) have argued that (a) there is little to support the idea that different genes are expressed at different ages in adults, (b) the effects are strongest for Neuroticism and Extraversion, and (c) any apparent changes in adult gene expression are more likely to be a function of reinforcement augmenting earlier inherited personality differences (Eaves et al., 1989). Viken and colleagues (1994) in their analyses based on 15,000 male and female Finnish twins, aged 18 to 53 years, also found that there was little evidence for new genetic contributions to individual differences after age 30, in contrast to significant new environmental effects emerging at every age period. The most recent evidence, based on 20,000 adult individuals who completed the EPQ Neuroticism up to four times over 22 years, reported an average genetic correlation of 0.91, again suggesting a very high degree of genetic stability in the adult measure (Wray, Birley, Sullivan, Visscher, & Martin, 2007).

Similar results of high genetic correlations over time have been found for adolescent personality. Gillespie and colleagues (2004) administered the Junior Eysenck Personality Questionnaire (JEPQ; Eaves et al., 1989; H. J. Eysenck & S. B. G. Eysenck, 1975; S. B. G. Eysenck, 1972) to over 540 twin pairs at ages 12, 14, and 16 years. Multivariate analyses revealed that familial aggregation, with the exception of Lie, was entirely explained by additive genetic effects at each age. Moreover, the genetic factor correlations across time were very high, and after fitting genetic simplex models (see Boomsma, Martin, & Molenaar, 1989; Boomsma & Molenaar, 1987; Eaves,

Long, & Heath, 1986) to the same data, Gillespie and colleagues found that for each dimension, not only were the JEPQ dimensions stable over time but that large proportions of the additive genetic variance observed at ages 16 and 14 could be explained by genetic effects at age 12. Despite evidence for smaller but significant genetic innovations at ages 14 and 16, their results are consistent with a pleiotropic model of gene action whereby the same genes explain variation across different time points within each of the adolescent personality dimensions.

### Aim

Demonstrating heritability is the necessary precursor for locating and identifying quantitative traits loci (QTL), and since Cloninger's first genome wide scan of Harm Avoidance (1998), there has been a growing impetus to locate quantitative traits loci (QTL) for personality (Benjamin, Ebstein, & Lesch, 1998; Boomsma et al., 2000; Dina et al., 2005; Ebstein, 2006; Fullerton et al., 2003; Kirk et al., 2000; Levinson, 2006; Nash et al., 2004; Neale, Sullivan, & Kendler, 2005; Zohar et al., 2003). Although there is some converging evidence for linkage signals from more than one genome scan (Levinson, 2006), all of these studies have been based on adult samples, and nearly all have focused on Neuroticism because of its significant genetic covariance with anxiety and depression (Jardine et al., 1984; Kendler et al., 1993). Yet, despite the evidence for significant heritability and developmental stability in the observed genetic effects for all three dimensions including Lie, no attempts have been made to locate QTLs underpinning variation in adolescent personality. This is largely because the required genotypic information has only until recently become available. The Brisbane Adolescent Twin Study (Wright & Martin, 2004) now includes adolescent twins and siblings with genome-wide linkage and repeated JEPQ measures. These data, although unselected, are ideal for fitting univariate and multivariate linkage models to detect QTLs. Moreover, because several groups have demonstrated that multivariate methods are a powerful means of detecting QTLs that can influence a set of phenotypes pleiotropically (Amos, de Andrade, & Zhu, 2001; Boomsma, 1996; Boomsma & Dolan, 1998; Evans et al., 2004; Martin, Boomsma, & Machin, 1997), the repeated JEPQ measures will provide a unique opportunity to model QTL effects within a developmental framework.

Therefore, the aim of this study is to run genome-wide linkage on measures of adolescent Psychoticism, Extraversion, Neuroticism, and Lie.

## METHOD

### Subjects

Data were collected in three waves as part of ongoing studies into the development of melanocytic naevi (moles) at ages 12 and 14 and of cognition at age 16. The protocols of these studies, which involved in-person testing lasting 2–4 hours, have been described in detail elsewhere (Evans, Frazer, Boomsma, & Martin, 2001; Gillespie, Evans, Wright, & Martin, 2004; McGregor et al., 1999; Wright & Martin, 2004; Wright et al., 2001; Zhu et al., 1999). Briefly, twins and their siblings were enlisted by contacting the principals of primary schools in the greater Brisbane area, by media appeals, and by word of mouth. Informed consent was obtained from all participants and parents prior to testing. The twins were tested as closely as possible to their 12th, 14th, and 16th birthdays. Previous analyses using the same data have shown that this sample is typical of Queensland adolescents with respect to moliness (Zhu et al., 1999) and IQ (Wainwright, Wright, Geffen, Luciano, & Martin, 2005), which, given the project's aims, allayed any concerns that twins with a higher-than-average mole count were being “volunteered” by their parents for participation.

A total of 503 families participated in this study. Although parents were not phenotyped, their genotypes still contributed to identity by descent (IBD) estimation. Parental genotypes where one or both parents participated were obtained from 96 and 358 families, respectively. The sample consisted of 1,280 twins and their siblings from 82 monozygotic (MZ) and 421 dizygotic (DZ) twin pair families each with 0–2 additional siblings. As shown in Table 1, these data generated a total of 922 quasi-independent sib pairs with complete genotypic and phenotypic information for analysis.

### Measures

At each wave twins, co-twins, and their siblings were asked to complete the full 81-item Junior Eysenck Personality Questionnaire (JEPQ; Eaves et al., 1989; H. J. Eysenck & S. B. G. Eysenck, 1975; S. B. G. Eysenck, 1972), which assesses the three major dimensions of personality: Psychoticism (P; 17 items), Extraversion (E; 24 items) and Neuroticism (N; 20 items). In addition, the questionnaire contained the 20-item Lie (L) scale that is a measure of social desirability. All items were scored on a

**Table 1**

**Total Number of Quasi-Independent Sib Pairs (Qisp) Based on Monozygotic (Mz) and Dizygotic (Dz) Twin Pair Families With 0 to 2 Additional Siblings. A Total of 502 Families Generated 922 QISPs**

	Number of Families With Additional Siblings ( <i>N</i> )			QISP <sup>a</sup>
	<i>N</i> = 0	<i>N</i> = 1	<i>N</i> = 2	
MZ twin pair families	1 <sup>b</sup>	69	12	105
DZ twin pair families	274	113	34	817

<sup>a</sup>Total QISP<sub>DZ</sub> = Number of families  $\times$  ( $s - 1$ )/2, Total QISP<sub>MZ</sub> = Families  $\times$  ( $s - 1$ ) ( $s - 2$ )/2, where  $s = N + 2$

<sup>b</sup>Does not contribute QISP

2-point scale (*Yes/No*). In most cases, the JEPQ was administered to siblings once and usually coincident with the first or third interviews when the twins were aged 12 or 16, respectively. The problem for analysis is how best to cope with age effects for siblings who will usually (but not always) be measured at ages different from twins. Some effort, therefore, was made to measure siblings at the same age as the twins, but this was not often possible.

The three dimensions and the Lie scale can be measured reliably by self-report and are highly stable over time (H. J. Eysenck & S. B. G. Eysenck, 1991; Gillespie et al., 2004; Kirk et al., 2000; Ormel & Rijdsdijk, 2000; Watson & Clark, 1984). With the exception of perhaps Psychoticism (see Heath & Martin, 1990), the Neuroticism and Extraversion scales are also extraordinarily robust in terms of the phenotypic (H. J. Eysenck & S. B. G. Eysenck, 1991) as well as the latent genetic and environmental factor structures (Heath & Martin, 1990). Regarding factorial invariance, the dimensions are all identifiable in a diverse range of cultures worldwide and across the socioeconomic spectrum (H. J. Eysenck & S. B. G. Eysenck, 1983). Neuroticism, in particular, has emerged in every model of personality based on questionnaire measurement and analyses of ratings of psychiatric symptoms where anxiety and depression have emerged as general dysphoric or negative effect factor (Zuckerman, 1999; Zuckerman, Kuhlman, Joireman, Teta, & Kraft, 1988).

#### *DNA Collection, Zygoty Diagnosis, and Genotyping*

Blood was collected from twins at 12, 14, and 16 years of age and where possible from parents and siblings for genotyping. DNA was extracted

from buffy coats using a modification of the “salt method” (Miller, Dykes, & Polesky, 1988). For same-sex twin pairs, zygosity was determined by typing nine independent DNA microsatellite polymorphisms plus the X/Y amelogenin marker for sex determination by polymerase chain reaction yielding a probability of concordance for all nine markers in DZ twins of less than  $10^{-4}$  (Nyholt, 2005). The genome scan consisted of 726 highly polymorphic autosomal microsatellite markers and 31 X-linked markers at an average spacing of 5 cM in 539 families (2,360 individuals). The microsatellites consisted of a combination of markers from the ABI-Prism and Weber genotyping sets. Full details of the scan are available in Zhu and colleagues (2004).

### Statistical Analysis

#### *Univariate Analysis*

Our univariate and multivariate analyses are described in detail elsewhere (see Evans et al., 2004). Briefly, multipoint IBD probabilities at each of the autosomal markers were calculated using MERLIN (Abecasis, Cherny, Cookson, & Cardon, 2002), while IBD probabilities at each marker on chromosome X were calculated in MINX<sup>1</sup> Standard methods for maximum likelihood analysis of continuous data using variance components (Neale & Cardon, 1992; Posthuma et al., 2003) were performed in Mx (Neale, 1999). This included modelling the effects of age and sex on the means of each personality dimension. The components of variance, which are hypothesised to account for the correlation in liability between relatives, were parameterized as a function of the variance due to the QTL (Q), to a combined residual polygenic and shared environmental effect (F), and to unique environmental (E) effects. The F effect was estimated by fixing the sib pair correlation to 0.5. In the absence of shared environmental effects, F will largely be an estimate of residual polygenic effects.

The null hypothesis that additive genetic variance caused by a QTL linked to a marker for a given phenotype was zero (i.e.,  $Q = 0$ ) was tested against a model in which Q was estimated. Twice the difference in natural log likelihoods between these models is distributed asymptotically as a 50:50 mixture of  $\chi^2_1$  and a point mass at zero and is consequently designated  $\chi^2_{0.1}$  (Self & Liang, 1987).

#### *Multivariate Analysis*

The advantage of performing a variance components linkage analysis in Mx is that data from three time points can be combined to increase the

1. <http://www.sph.umich.edu/csg/abecasis/Merlin/reference.html>

power to detect linkage. We fitted two multivariate models to test for linkage. In the first, the factor loadings of the QTL on each personality dimension at 12, 14, and 16 were unconstrained, that is,  $q_1 \neq q_2 \neq q_3$  (see Figure 1). Because the true values of some of these parameters under the null hypothesis of no linkage are located on the boundary of the parameter space defined by the alternative hypothesis, the likelihood ratio test statistic is distributed as a complicated mixture of  $\chi^2$  distributions (Self & Liang, 1987). In other words, because the degrees of freedom in multivariate applications may be more complicated than in the univariate case (Marlow et al., 2003), we will retain the conservative convention of degrees of freedom being equal to the difference in nested-model parameters for all analyses.

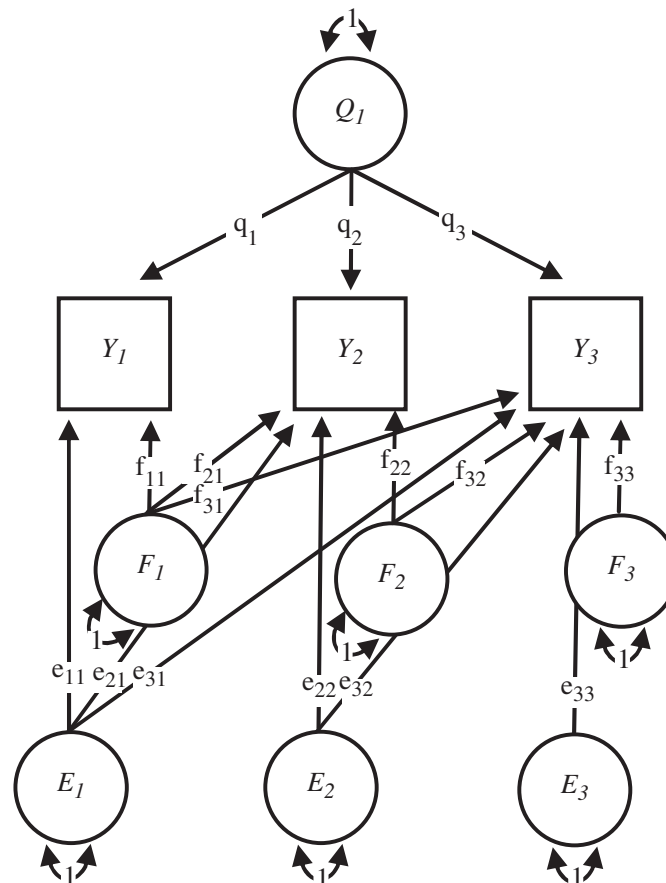
The second test assumes that the QTL is responsible for the same amount of phenotypic variation (unstandardized) at each age by equating the three QTL factor loadings, that is,  $q_1 = q_2 = q_3$ . This was equivalent to testing whether the QTL was responsible for the same amount of phenotypic variation at each age. If this were the case, then the test for linkage was whether the (equated) loadings could then be set to zero. Since only one QTL variance component was estimated, the test statistic was distributed as in the univariate case (i.e., a 50:50 mixture of a point mass at zero and  $\chi^2_1$ ). Note that this test is approximately equal to taking the mean of the phenotypes across the three ages and performing a univariate test of linkage on this statistic (Martin et al., 1997). In both cases we modelled the QTL, F, and E effects under a Cholesky framework.

The univariate variance components linkage analysis is used to test for linkage between each marker loci and each of the personality phenotypes at ages 12, 14, and 16. For univariate analyses, the difference between the two log likelihoods can be converted to a LOD score equivalent to the classical LOD score of parametric linkage analysis (i.e.,  $\Delta - 2LL \div 4.6$ ) (Williams & Blangero, 1999). However, since we wish to compare the univariate and multivariate linkage peaks that do not have a simple LOD score equivalent, our results will be graphed using asymptotic  $p$ -values. We note that the significance levels of the multivariate case are approximate and really ought to be simulated to obtain empirical values, but this is impractical for the multivariate case.

## RESULTS

### Genome-Wide Scan Results

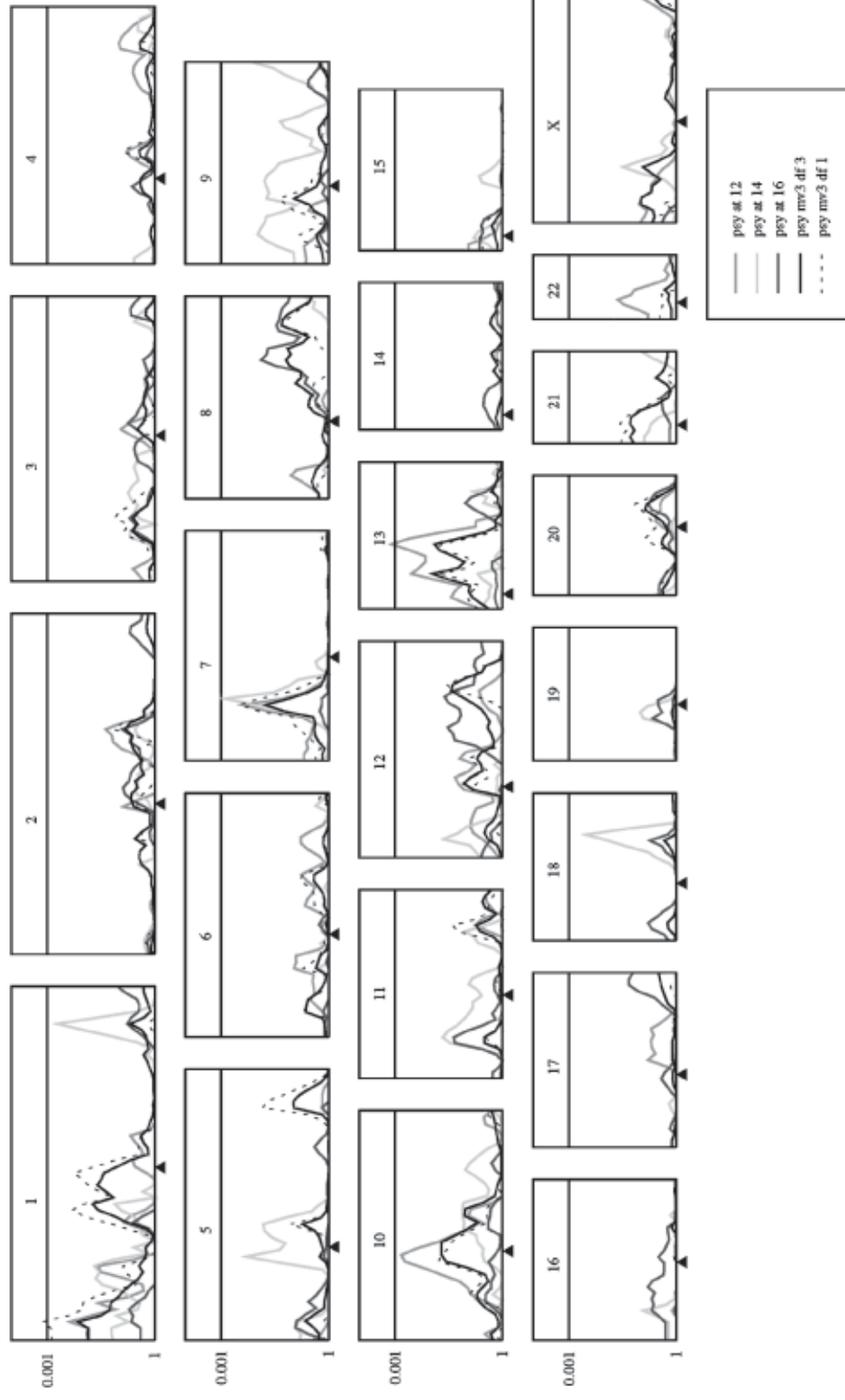
Variance components linkage results based on the combined male and female sample, adjusted for age and sex, are illustrated in Figures



**Figure 1**

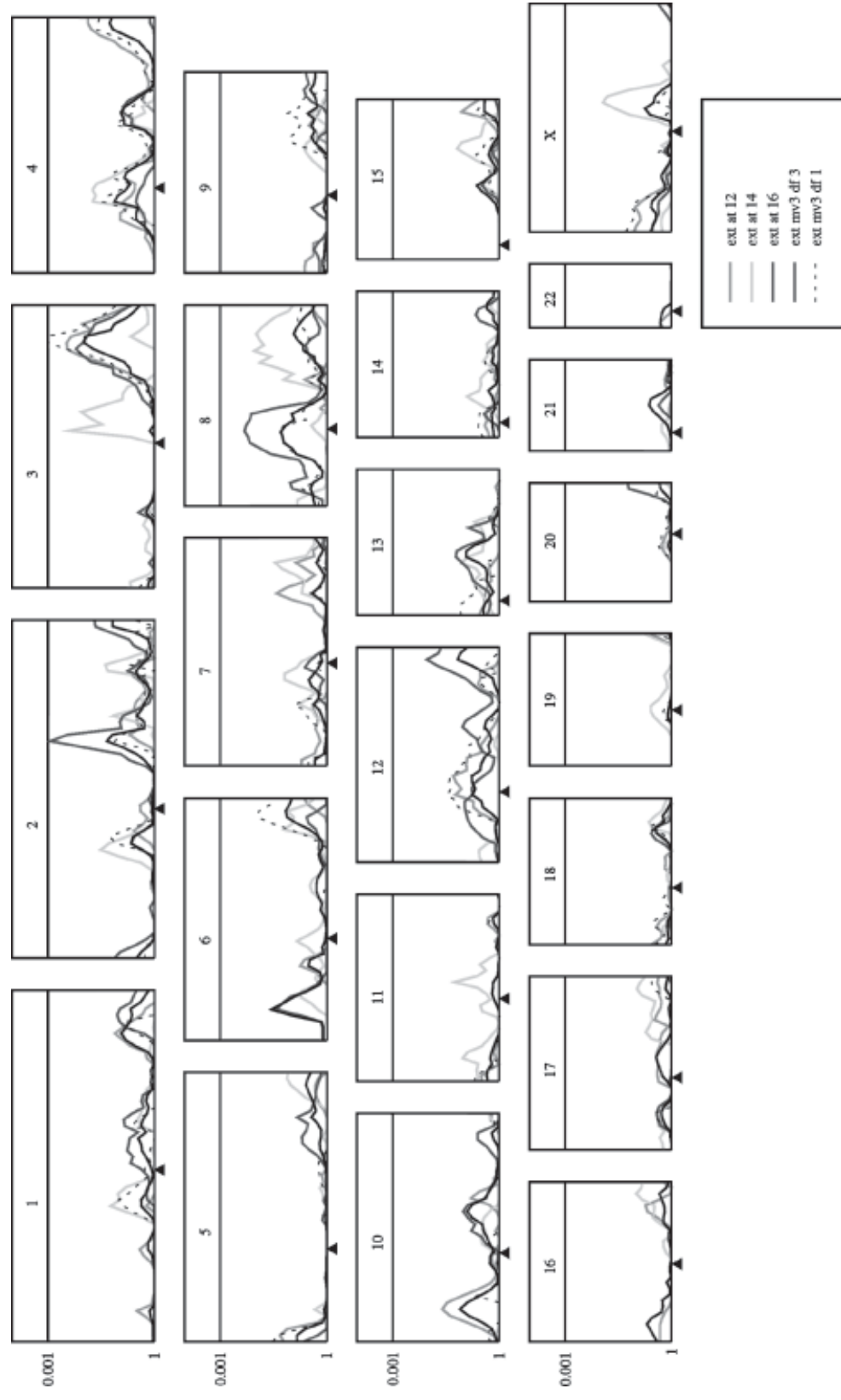
Genetic modelling of personality data. The model includes a Cholesky structure for the familial (F) and nonshared environmental (E) components of variance. The effect of the QTL ( $Q_1$ ) was also modeled within a Cholesky framework under two conditions: The QTL factor loadings were either constrained ( $q_1 = q_2 = q_3$ ) or allowed to vary  $q_1 \neq q_2 \neq q_3$ .

2–5 with a line to denote a nominal  $p$ -value of 0.001 for suggestive linkage. The plots are defined by the linkage curves on the  $y$ -axis and the position of each of the markers along the  $x$ -axis. For the univariate analyses the linkage curves for ages 12, 14, and 16 years are marked red, green, and blue, respectively. This makes it possible to compare the consistency or coincidence of results across measurement occasions. Multivariate 3 $df$  and 1 $df$  linkages are depicted with black and dashed lines, respectively. None of the peaks reached genome-wide significance as defined by Lander and Kruglyak (1995). Based on inspection of the nominal  $p$ -values, the highest peaks ( $p < 0.05$ ) for Psychoticism, Extraversion, Neuroticism, and Lie are summarized in Table 2 through 5, respectively. For Psychoticism, the



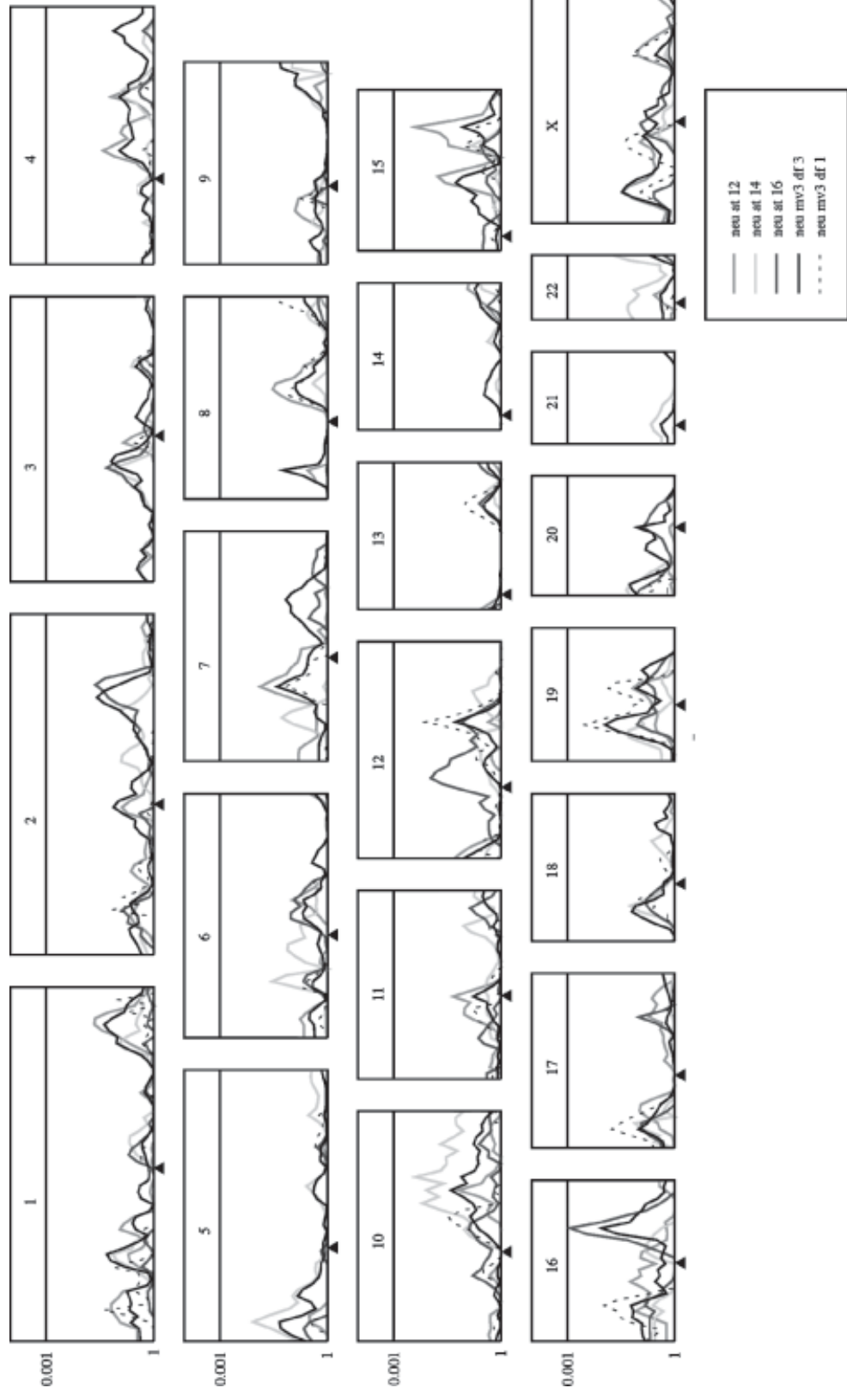
**Figure 2**

Genome-wide scan for JEPQ Psychoticism. The univariate linkage curves for ages 12, 14, and 16 years are marked red, green, and blue, respectively. The multivariate 3df and 1df linkage curves are black and dashed, respectively. ▲ Centromeres.



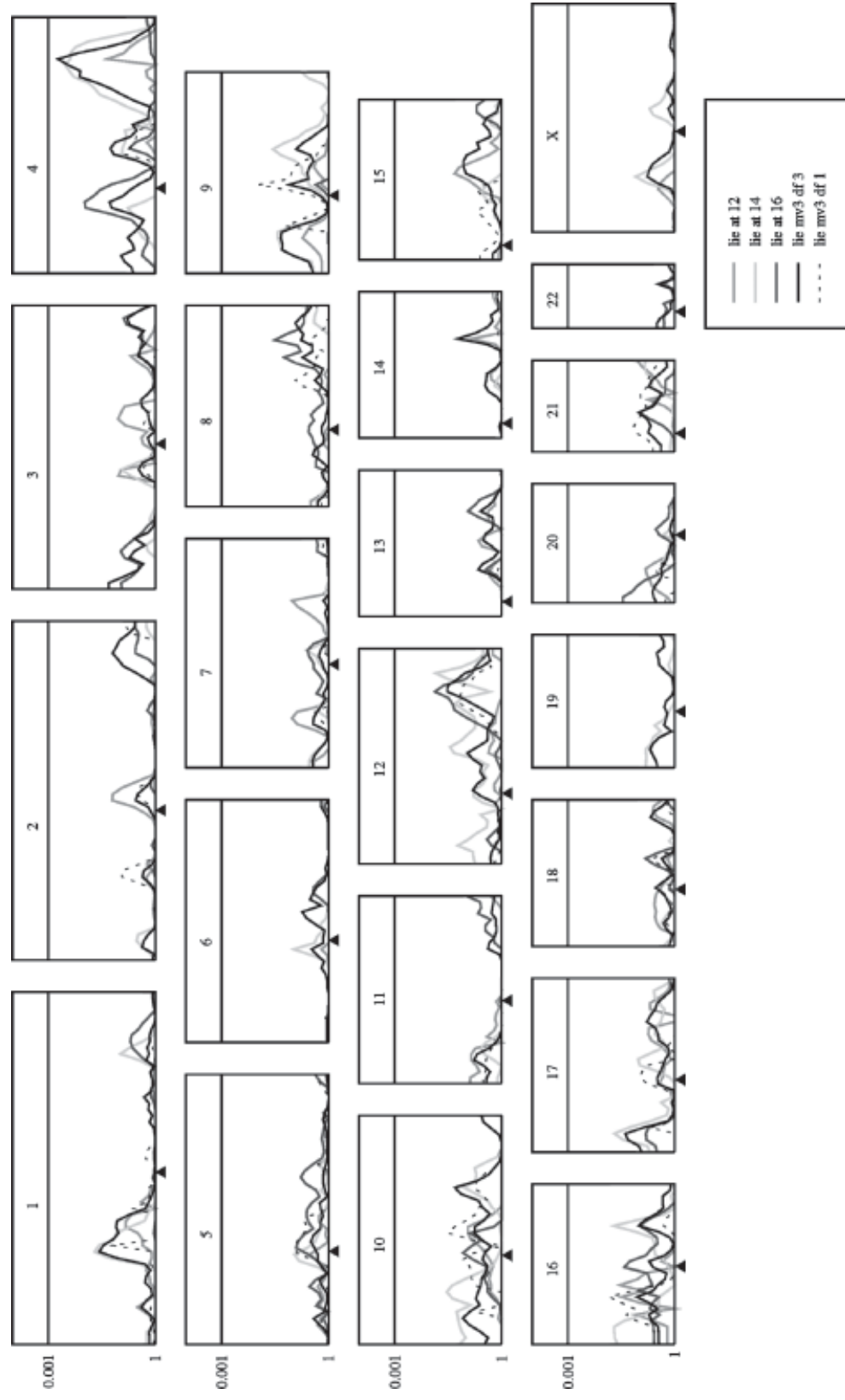
**Figure 3**

Genome-wide scan for JEPQ Extraversion. The univariate linkage curves for ages 12, 14, and 16 years are marked red, green, and blue, respectively. The multivariate 3df and 1df linkage curves are black and dashed, respectively. ▲ Centromeres.



**Figure 4**

Genome-wide scan for JEPQ Neuroticism. The univariate linkage curves for ages 12, 14, and 16 years are marked red, green, and blue, respectively. The multivariate 3df and 1df linkage curves are black and dashed, respectively. ▲ Centromeres.



**Figure 5**

Genome-wide scan for JEPQ Lie. The univariate linkage curves for ages 12, 14, and 16 years are marked red, green, and blue, respectively. The multivariate 3df and 1df linkage curves are black and dashed, respectively. **▲** Centromeres.

highest peaks were on Chromosomes 1, 5, 7, 9, 10, 13, and 18 (see Figure 2). The linkage curve at 12 years on Chromosome 1 at 15 cM is coincident with the 1df and 3df multivariate linkage curves. The region at 45 cM on Chromosome 7 has coincident linkage curves at 12 and 14 years including the 1df and 3df multivariate tests. For Extraversion, the highest peaks were on Chromosomes 2, 3, 8, and 12 (see Figure 3). The region between 190 and 200 cM on Chromosome 3 is the most promising because of the coincident linkage peaks at 12 and 16 years as well as the 1df and 3df multivariate linkage peaks. For Neuroticism, the highest peaks were on Chromosomes 5, 10, 12, 15, 16, and 19 (see Figure 4). Finally, for Lie, the highest peaks were located on Chromosome 4 (see Figure 5).

## DISCUSSION

To our knowledge, this study is the first genome-wide scan that has been used in an attempt to map genes responsible for variation in adolescent Neuroticism, Extraversion, Psychoticism, and Lie. We found no genes of major effect for any of the JEPQ measures in this linkage sample. This is in line with a recent genome-wide association scan of Neuroticism, which failed to find any loci accounting for more than 1% of the variance (Shifman et al., 2007). So, despite the advantage of using multivariate modelling to increase the power to detect QTLs, our findings argue the need for larger samples in order to detect QTLs of small effect. Although none of the peaks reached genome-wide significance as defined by Lander and Kruglyak (1995), the highest linkages were observed on Chromosomes 1, 5, 7, 9, 10, 13, and 18 for Psychoticism; on Chromosomes 2, 3, 8, and 12 for Extraversion; on Chromosomes 5, 10, 12, 15, 16, and 19 for Neuroticism; and on Chromosome 4 for Lie.

We used the Online Mendelian Inheritance in Man<sup>2</sup> to determine whether any of our highest peaks coincided with those found from previous linkage or association studies of related personality traits or correlated behaviors. We recognize that some may be false positives. For Extraversion, none of our highest peaks were in regions previously investigated by other linkage or association studies

2. <http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=OMIM>

**Table 2**  
Summary of Major Genome-Wide Linkage Peaks for Psychoticism

Chromo	Psychoticism			
	cM	Age <sup>1</sup>	$\Delta\chi^2$	p
1	0	1df	10.24	.001
	5	1df	10.41	.001
	10	1df	10.39	.001
	15	12	8.162	.004
	15	3df	12.01	.007
	15	1df	11.34	.001
	20	1df	8.303	.004
	30	1df	6.640	.010
	105	1df	7.841	.005
	130	1df	6.787	.009
	135	1df	7.667	.006
	255	14	9.563	.002
5	65	14	7.854	.005
7	45	12	8.316	.004
	45	14	6.701	.010
	45	1df	8.670	.003
	50	14	10.39	.001
9	170	14	7.281	.007
10	55	12	7.336	.007
	60	12	9.678	.002
	65	12	10.07	.002
	70	12	8.352	.004
	70	12	8.352	.004
13	30	12	8.879	.003
	35	12	7.974	.005
	40	12	7.262	.007
	45	12	7.279	.007
	50	12	9.062	.003
	55	12	11.26	.001
	60	12	9.100	.003
18	90	14	8.826	.003

<sup>1</sup> = ages 12, 14 and 16 as well as multivariate 1df and 3df

$\Delta\chi^2$  = change in chi-square

cM = centimorgan

**Table 3**  
Summary of Major Genome-Wide Linkage Peaks for Extraversion

Chromo	Extraversion			
	cM	Age <sup>1</sup>	$\Delta\chi^2$	p
2	170	16	10.53	.001
	175	16	8.488	.004
3	140	14	6.887	.009
	185	12	7.108	.008
	185	16	6.693	.010
	190	12	8.525	.004
	190	16	7.488	.006
	190	1df	8.815	.003
	195	12	8.556	.003
	195	16	6.705	.010
	195	3df	11.22	.011
	195	1df	10.74	.001
	200	12	8.039	.005
	200	16	6.200	.013
	200	3df	11.14	.011
	200	1df	10.94	.001
	205	1df	7.330	.007
8	55	16	7.326	.007
	60	16	7.534	.006
	65	16	7.938	.005
	70	16	7.759	.005
	75	16	7.312	.007
	80	16	7.141	.008
	135	14	6.794	.009
12	165	16	6.832	.009

<sup>1</sup> = ages 12, 14, and 16 as well as multivariate 1df and 3df

$\Delta\chi^2$  = change in chi-square

cM = centimorgan

focusing on extraversion or related traits (Carmine et al., 2003; Ebstein, 2006; Golimbet, Gritsenko, Alfimova, & Ebstein, 2005; Munafo, Yalcin, Willis-Owen, & Flint, 2007; Ni et al., 2006; Urata et al., 2007). For Psychoticism the linkage peaks between 105 and 135 cM on Chromosome 1 spans the fatty acid amide hydrolase gene

**Table 4**  
Summary of Major Genome-Wide Linkage Peaks for Neuroticism

Chromo	Neuroticism			p
	cM	Age <sup>1</sup>	$\Delta\chi^2$	
5	15	14	6.934	.008
10	105	14	7.495	.006
	115	14	6.963	.008
	125	14	8.225	.004
	110	1df	7.179	.007
15	100	12	8.281	.004
16	90	16	8.655	.003
	95	16	10.52	.001
	95	3df	11.57	.009
	100	16	6.819	.009
19	30	1df	8.782	.003

<sup>1</sup> = ages 12, 14, and 16 as well as multivariate 1df and 3df

$\Delta\chi^2$  = change in chi-square

cM = centimorgan

**Table 5**  
Summary of Major Genome-Wide Linkage Peaks for Lie

Chromo	Lie			p
	cM	Age <sup>1</sup>	$\Delta\chi^2$	
4	165	14	7.767	.005
	165	3df	11.93	.008
	170	14	8.322	.004
	170	3df	11.84	.008
	175	14	8.830	.003
	175	3df	13.54	.004
	180	14	8.255	.004
	180	3df	14.95	.002
	185	14	8.215	.004
	185	3df	12.22	.007
	190	14	7.600	.006

<sup>1</sup> = ages 12, 14, and 16 as well as multivariate 1df and 3df

$\Delta\chi^2$  = change in chi-square

cM = centimorgan

at 1p35-p34. A missense mutation for this gene has previously been associated with adult problem drug use (Sipe, Chiang, Gerber, Beutler, & Cravatt, 2002). The peak on Chromosome 5 at 65 cM is in the region of 5p13 and the ADHD4 gene that has shown a weak association with attention deficit hyperactive disorder when based on a sample of 490 affected children (Ogdie et al., 2004). The linkage peaks on Chromosome 13 between 30 and 60 cM span the HTR2A gene at 13q14-q21, which has been associated in adult samples with schizophrenia (Norton & Owen, 2005), obsessive compulsive disorders (Norton & Owen, 2005), seasonal affective disorders (Levitan et al., 2002), and alcohol dependence (Hill et al., 2002; Himei et al., 2000). Other reports have found no association between the HT2A polymorphisms and personality traits (Tochigi et al., 2005) or any clear link with psychosis (Mata et al., 2004).

Only four genome-wide studies, all based on adult samples, have included measures of Neuroticism (Fullerton et al., 2003; Kuo et al., 2007; Nash et al., 2004; Neale et al., 2005). A number of other papers have examined related phenotypes and not all have used whole genome-wide scans (Abkevich et al., 2003; Camp et al., 2005; Dina et al., 2005; Holmans et al., 2004; Kaabi et al., 2006; Middeldorp et al., 2007; Thorgeirsson et al., 2003). First, none of the highest Neuroticism peaks was located on or near the serotonin neurotransmitter transporter on Chromosome 17. Among the highest peaks for Neuroticism, two coincided with those reported previously for Neuroticism or related phenotypes (Abkevich et al., 2003; Holmans et al., 2004). The peak on Chromosome 12 at 110 cM is within the region of 12q22-q23.2 and the microsatellite markers D12S1300 and D12S1706, which have been associated with major depression (Abkevich et al., 2003) as well as the Neuroticism peak reported by Fullerton and colleagues (2003). The peak on Chromosome 15 at 100 cM is within 15q25.3-q26.2, which is flanked by markers D15S816 and D15S652. This region has been associated with early-onset major depressive disorder (Holmans et al., 2004). Camp and colleagues (2005) have also found linkage in this region at 97.9cM for major depression in men. More recently, Kuo and colleagues (2007) reported suggestive linkage in this region at 124cM based on a sample of 1248 Irish adults. The Kuo study also reported a male-specific suggestive peak on chromosome 16 at 91cM in the same region as our peak for 16-year-olds. Finally, the linkage peaks for Lie between 165 and 190 cM spans the region between 4q32.2

and 4q33 that has been linked to panic (Kaabi et al., 2006) and risk for bipolar disorders (Ginns et al., 1998).

### Limitations

Our results must be interpreted in the context of several important limitations. First, alternate strategies for modeling longitudinal data exist. Previously, we have shown that simplex structures provide an improved fit compared to Cholesky decompositions (Gillespie, Evans, Wright, & Martin, 2004) but because we did not know what the most appropriate model for the QTL effect was, we therefore fitted an atheoretical Cholesky to model the QTL as well as the F and E effects. Although growth models may be more appropriate, these cannot be fitted to data based on only three data points. Despite evidence of longitudinal genetic continuity for the adolescent dimensions of personality (Gillespie et al., 2004), the lack of congruency or coincidence between the univariate and multivariate linkage peaks, with the exception of Extraversion on Chromosome 3, is likely attributable to the fact that the sample was smaller at the second and third waves. And although modelling of the longitudinal data is normally expected to increase statistical power to detect QTLs (Boomsma, 1996; Evans et al., 2004; Martin, Boomsma, & Machin, 1997), the current unselected sample was underpowered to detect loci of even moderate effect. Moreover, increases in power normally associated with multivariate analyses will diminish when traits are highly correlated and when there are large amounts of missing data (see Evans et al., 2004) as was the case for our measures at 14 and 16 years. It is also important to remember that traditional designs in which sib pairs are essentially selected at random provide much less power to detect linkage (Risch & Zhang, 1995), and unless sufficiently large samples can be obtained by way of mailed questionnaires (Kirk et al., 2000; Martin et al., 2000), attempts to detect linkage for complex traits will usually fail if there is only a small phenotypic effect attributable to each locus (Fullerton et al., 2003). Although suggestive linkage peaks are often “tenuous” (see Lander & Kruglyak, 1995), and indeed many of our highest peaks may be false positives, we nevertheless believe these results are worth reporting now since replication of any peaks in future studies will concentrate focus on certain regions. Moreover, our reported *p*-values can be used as part of weighted false discovery approaches (van den

Oord, 2005; van den Oord & Sullivan, 2003) following future whole genome association scans we are currently planning.

## CONCLUSION

To our knowledge, this study is the first to show a genome-wide linkage scan of adolescent personality measures and certainly the first genome-wide scan for the dimensions of Psychoticism, Extraversion, and Lie. Our results are also preliminary, and the sample size and marker density will be substantially increased. Identification of the genes responsible for the genetic variation in adolescent personality would be a major breakthrough in personality research as well as psychiatric genetics insofar as personality is related to mood, affective and psychotic disorders (Battaglia, Przybeck, Bellodi, & Cloninger, 1996; Benjamin et al., 1998; H. J. Eysenck, 1994, 1995; Jardine, et al., 1984; Kendler et al., 1993; Livesley, 2007; Trull, Tragesser, Solhan, & Schwartz-Mette, 2007). Therefore, the first step in this process is replicated linkage followed by whole genome-wide association studies in order to provide a firm foundation for fine mapping and gene identification.

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