

# Genetic and Environmental Contributions to Loneliness in Adults: The Netherlands Twin Register Study

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Heritability estimates based on two small studies in children indicate that the genetic contribution to individual differences in loneliness is approximately 50%. Heritability estimates of complex traits such as loneliness may change across the lifespan, however, as the frequency, duration, and range of exposure to environmental influences accrues, or as the expression of genetic factors changes. We examined data on loneliness from 8,387 young adult and adult Dutch twins who had participated in longitudinal survey studies. A measure of loneliness was developed based on factor analyses of items of the YASR (Achenbach, (1990) *The Young Adult Self Report*, University of Vermont, Department of Psychiatry, Burlington, VT). Variation in loneliness was analyzed with genetic structural equation models. The estimate of genetic contributions to variation in loneliness in adults was 48%, which is similar to the heritability estimates found previously in children. There was no evidence for sex or age differences in genetic architecture. Sex differences in prevalence were significant, but we did not see an association with age or birth cohort. All resemblance between twin relatives was explained by shared genes, without any suggestion of a contribution of shared environmental factors.

**KEY WORDS:** Heritability; loneliness; twins; young adults.

## INTRODUCTION

Aristotle's observation of the importance of positive interpersonal relationships holds for our post-industrial world as well as for the ancient Greeks. The classic work of Harlow and Harlow (1987) demonstrated that positive tactile contact is as strong a determinant of mother–infant attachment in monkeys as feeding, and that deprivation of such contact produces adult animals with behavioral problems different than those resulting from physical restraint or stressors. The human primate is an especially social animal, with social contact, nurturance, and

affiliation important to normal development and a long and happy life (Bowlby, 1988; Cacioppo *et al.*, 2000; House *et al.*, 1988). When one's intimate and social needs are not adequately met, a complex set of feelings termed "loneliness" occurs that motivates one to seek the fulfillment of these needs (Baumeister and Leary, 1995; Weiss, 1973). The core experience of loneliness consists of social isolation and the absence of both relational and collective connectedness (Russell *et al.*, 1980; Hawkey, Browne and Cacioppo, in press). There is now substantial evidence that loneliness is at the heart of a constellation of socio-emotional states, which include self-esteem, mood, anxiety, anger, optimism, fear of negative evaluation, shyness, social skills, social support, dysphoria, and sociability (e.g., see reviews by Berscheid and Reis, 1998; Duck *et al.*, 1994; Ernst and Cacioppo, 1999; Peplau and Perlman, 1982; Rook, 1988; Shaver and Brennan, 1991).

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Although there are gripping states of loneliness that everyone experiences transiently in specific circumstances or interactions, some individuals live in the devastating clutches of loneliness. In a meta-analysis of risk factors for loneliness in adulthood and old age, Pinquart and Sorensen (2003) estimated that approximately 10% of older adults complain of frequent feelings of loneliness. Situational threats to a valued interpersonal relationship ranging from social exclusion, ostracism, rejection, separation and divorce, to bereavement are known to elevate feelings of loneliness. Weiss (1973), for instance, found that a spouse following his or her partner through a series of job transfers may be low in loneliness and well adjusted in one town but lonely and poorly adjusted in another. Nevertheless, loneliness is typically conceptualized as a stable trait, with individual differences in the set-point for feelings of loneliness about which people vacillate depending on the specific circumstances in which they find themselves. Consistent with this reasoning, loneliness has a one-year test-retest reliability of 0.73 (unpublished conference data by Russell, Kao and Cutrona, 1987; cited in Shaver and Brennan, 1991) and levels of loneliness increase little across the adult lifespan until above the age of 80 (Pinquart and Sorensen, 2003).

In a pioneering study of the origins of feelings of loneliness, McGuire and Clifford (2000) examined the heritability in children's loneliness. In their first study, 69 biologically related sibling pairs and 64 unrelated pairs in adoptive families in the Colorado Adoption Project completed an 8-item loneliness scale when they were 9, 10, 11, and 12 years of age. In a second study, 22 monozygotic (MZ) twins, 40 dizygotic (DZ) twins, and 80 full-siblings 8–14 years of age completed a 16 item scale to assess loneliness in relation to their schoolmates. Results revealed a significant genetic ( $h^2 = 55%$  and  $48%$ , respectively, in Studies 1 & 2) contribution to individual differences in loneliness. However, in the adoption study a model that contributed the resemblance between relatives to shared environment also fit the data and could not be distinguished on statistical grounds from a genetic model.

The effects of environmental contributions to variables such as loneliness can accrue over time, or the expression of genetic factors may change across the life span, so that the heritability of loneliness may be different in adults than in children. It is, therefore, important to examine whether the heritability of loneliness in an older sample mirrors what has been found by McGuire and Clifford in children. The

sample sizes in McGuire and Clifford's (2000) studies were small, leading to low statistical power to distinguish different models of familial resemblance. The current study involved 8387 twins (3797 complete and 793 incomplete twin pairs) from The Netherlands. The comparison of resemblance between MZ and DZ twin pairs offers the possibility to decompose the variance of loneliness into genetic and environmental components (Boomsma *et al.*, 2002). An index of loneliness was derived based on longitudinal data from the Young/adult Self Report (Achenbach, 1990).

The sample includes male and female same-sex twin pairs as well as opposite-sex twin pairs. We therefore could investigate sex differences in the genetic architecture of loneliness. Variation in loneliness in adult men may show greater environmental influences than in women. Taylor (2002) found that males tend to respond to threats with a "fight or flight" response but females tend to respond to threats with a "tend and befriend" response. She noted that: "... women who drew effectively on the social group for help may have more successfully dealt with threats than those who did not—hence, the befriending response" (Taylor, 2002, pp. 20–21). In a study of wild savannah baboons, Silk *et al.*, (2003) found evidence that females form close and enduring relationships with other group members, and that individual differences in this capacity are related to infant survival independent of the effects of dominance rank, group membership, and environmental condition. In Western cultures, the differential exposure to experiences outside the family may provide another source for sex differences. Specifically, feelings of social connectedness and loneliness in males may reveal more environmental contributions because males are exposed to a greater range and frequency of environmental influences. All else constant, the broader exposure to significant environmental influences may increase the environmental source of variance, and lower heritability.

## METHODS

### Participants

The Netherlands Twin Register (NTR) collects longitudinal data by mailed surveys every two to three years in adolescent and adult twins and their families. Twin families were recruited through City Councils. In 1990 we asked City Councils in The Netherlands for addresses and names of twins aged

13–20 years. City Councils supplied 6,023 addresses of twin families. Since then, we have also recruited older twins through City Councils, and asked adult twins to register with the NTR in our yearly newsletter (Boomsma *et al.*, 2000, 2002; Vink *et al.*, 2004).

Longitudinal survey studies of lifestyle, personality and psychopathology have taken place in 1991, 1993, 1995, 1997, 2000 and 2002/3. A seventh survey is ongoing. The socioeconomic (SES) distribution of twins who are over 25 years was 22% of low, 41% of middle and 37% of high SES. Smoking behavior of twins and religious background of the participating families (Boomsma *et al.*, 1994; 1999; Koopmans *et al.*, 1999) is comparable to that in the Dutch population. In this paper we use data from all surveys except the 1993 survey, when the YASR was not included. Data are available for 8387 twins (3280 males and 5107 females). Of all twin participants, 2971 had valid data at one time-point, 2386 at two time-points, 1558 at three, 959 at four and 513 at all five time-points. Average age of the twins in 1991 was 17.7 years ( $SD=2.4$ ), in 1995 it was 19.8 years ( $SD=3.2$ ), in 1997 25.5 years ( $SD=9.8$ ), in 2000 30.0 years ( $SD=11.2$ ) and in 2002/3 32.7 years ( $SD=11.2$ ). The increase in age and in standard deviations reflects the recruitment of more adults into the study. For same-sex twin pairs zygosity was determined from questions about physical similarity and confusion of the twins by family members, friends and strangers. For 726 same-sex twin pairs information on zygosity based on DNA polymorphisms was also available. Agreement between zygosity diagnoses from survey and DNA data was 97%.

## Measures

The 1991, 1995, 1997, 2000 and 2002/3 surveys contained the YASR (Achenbach, 1990). We selected 2 items from the Anxious/Depressed subscale, (item 12: I feel lonely, and item 33: Nobody loves me) and 4 items from the Withdrawn subscale (42: I like to be alone, 48: Others don't like me, 67: I lose friends very quickly, and 111: I try to have as little as possible to do with other people), each of which was rated on a scale of 0 = not applicable, 1 = a little or sometimes, and 2 = clearly or often applicable. Polychoric correlations were calculated among these six items from the 1991 wave of data collection ( $n=3270$ ) for submission to factor analysis. A confirmatory factor analysis (RAMONA; Systat, version 10) specified two factors corresponding to the scale source of the items, and an oblique rotation to estimate a correlation between factors (CF-Quartimax

criterion). This analysis revealed a reasonably good fit of the data to the two-factor structure with a root mean square error of approximation (RMSEA) of 0.067 (90% C.I. = 0.057–0.078), and a factor correlation of 0.80.

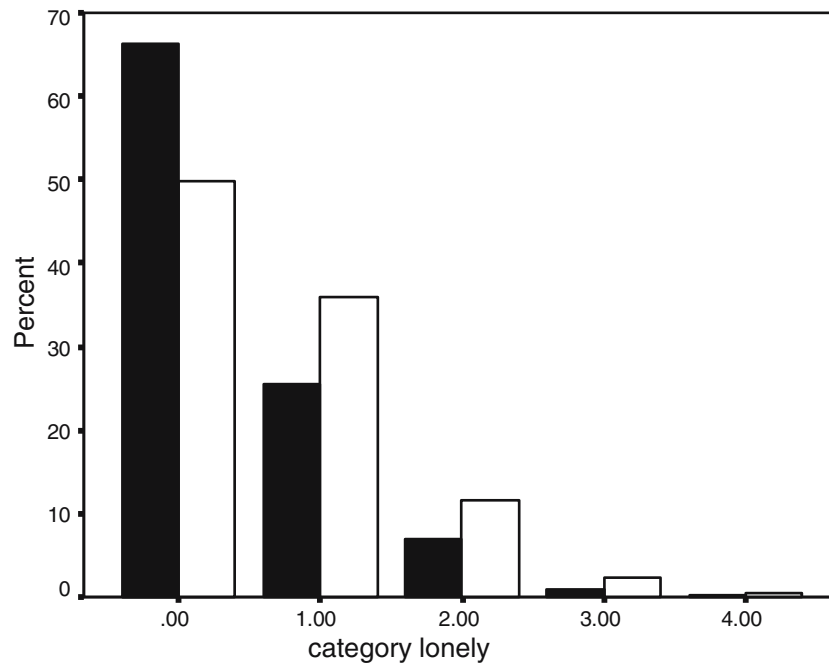
To determine whether the factor structure was stable across the period of the study, a second confirmatory factor analysis was carried out based on polychoric correlations among the six items in the 2000 wave of data collection ( $n=4442$ ). The two-factor structure again displayed reasonably good fit,  $RMSEA = 0.085$  (90% C.I. = 0.077–0.094), with a factor correlation of 0.77. In all analyses, items 12 and 33 loaded highly and comparably on the first factor (0.7–0.8). Based on item content for the factors, the two items in the first factor were summed to serve as the indicator of loneliness in the genetic analyses.

To validate the loneliness measure, a separate sample of 29 young adults completed these two items and a new short scale for measuring loneliness in large surveys which was developed and validated recently in two population based studies (Hughes *et al.*, 2004). Results indicated that the sum of the two items from the YASR was highly correlated with the loneliness score from the Hughes *et al.*, (2004) measure ( $r = +0.78$ ,  $p < 0.0001$ ).

The sum of the two items was obtained at every occasion for all participants. Because the items could be rated on a 3-point scale (0, 1, 2) the sum had 5 categories (0, 1, 2, 3, 4). Next, loneliness scores were averaged over occasions and recoded into the nearest (0 through 4) category. Subjects had to have at least scores on 2 items to be included in the study. Figure 1 shows the distribution of the scores. Because of the low endorsement of highest category, this category was pooled with the previous one. The resulting loneliness variable thus had 4 categories.

## Statistical Analyses

To investigate the inheritance of loneliness, the trait was modelled to have an underlying continuous distribution with multiple thresholds. This underlying distribution has been termed the liability or vulnerability (Falconer, 1989). The continuous variation in liability may be both genetic and environmental in origin. For loneliness the underlying liability distribution had 3 thresholds. The variance of the liability distribution was standardized. Prelis 2.53 (Joreskog and Sorbom, 1996) was used to obtain polychoric correlations between loneliness scores at different



**Fig. 1.** Distribution of loneliness scores in male (black bars;  $N = 3280$ ) and female twins (white bars;  $N = 5107$ ). The Y axis gives the percentage of males and females in each loneliness category.

time points for males and females and to estimate the polyserial correlation between age and loneliness within each occasion and between year of birth and loneliness.

The overall goodness-of-fit of the genetic model was tested against a saturated model, which specified 3 thresholds in males and in females and 5 correlations between twins for MZ males and females, DZ males and females and DZ twin pairs of opposite sex. Zygosity and sex differences in thresholds (i.e. prevalences) were evaluated by constraining thresholds to be equal in MZ and DZ twins and in males and females.

Genetic models specified individual differences in liability to loneliness to be a function of genotype and environment. The genetic factor, denoted "A", encompassed additive genetic effects, which represent the additive effects of alleles at a possibly large number of loci. Two environmental factors were considered: "C", common environmental influences shared by family members and "E", environmental influences that are not shared by family members and that include measurement error (Martin, *et al.*, 1997; Neale and Cardon, 1992; Plomin *et al.*, 2001).

The significance of additive genetic and common environmental influences was tested by comparing the fit of an AE or CE model to that of the ACE

model. Goodness-of-fit of submodels was assessed by likelihood ratio  $\chi^2$  tests. The raw data maximum likelihood estimation procedure from the structural equation modeling program Mx (Neale *et al.*, 2003) was used to analyze all available data, i.e. from complete and incomplete twin pairs.

## RESULTS

Table I lists the number of participants in each year in which loneliness data were collected and gives, separately for males and females, the polychoric correlations of loneliness scores over time. As may be seen, these analyses revealed that the test-retest reliability of loneliness was statistically significant for more than a decade for males and females. Within occasions there was neither a relation between age and loneliness, nor between birth year and loneliness (correlations between 0.09 and  $-0.04$ ). Next, all loneliness scores for a subject were averaged over occasions. Figure 1 shows the distribution of these scores for males ( $N = 3280$ ) and females ( $N = 5107$ ). Males score more often in the "0" category than females, indicating that they feel less lonely. Females score higher than males in all other categories. Because the scores were skewed, we obtained correlations between twins for the underlying liability to

**Table I.** Longitudinal (Polyserial) Correlations for Loneliness in Males (Above Diagonal) and Females (Below Diagonal). Number of Twins is Given in Brackets. Numbers on the Diagonal Give the Number of Male and Female Twin Participants Per Occasion

	1991	1995	1997	2000	2002/3
1991	1490/1807	0.36 (829)	0.39 (505)	0.42 (439)	0.27 (429)
1995	0.41 (1068)	1483/1882	0.50 (760)	0.40 (669)	0.33 (601)
1997	0.41 (752)	0.53 (1072)	1241/1971	0.62 (750)	0.50 (651)
2000	0.40 (799)	0.48 (1123)	0.59 (1333)	1493/3047	0.65 (923)
2002/3	0.30 (831)	0.43 (1099)	0.45 (1249)	0.66 (2062)	1413/2991

loneliness, using a threshold model that divided the liability distribution into 4 categories (Derks *et al.*, 2004). Constraining thresholds to be same in MZ and DZ twins (within sexes) showed that there were no differences between zygosity groups in loneliness, as indicated by a non-significant increase in  $\chi^2$  ( $\chi^2$  with 12 degrees of freedom (df) = 15.04,  $p=0.23$ ). However, constraining thresholds to be same in males and females was not allowed, confirming the lower thresholds for and higher prevalence of loneliness in females ( $\chi^2$  with 3 df = 202.25,  $p=0.00$ ). Estimates for the thresholds were 0.415, 1.373 and 2.230 in males and -0.006, 1.066 and 1.916 in females. The polyserial correlation between the loneliness and birth year was absent in men ( $r=-0.03$ ) and women ( $r=-0.01$ ).

Table II gives the twin correlations (polychoric) for MZM, DZM, MZF, DZF and DOS pairs. In both sexes the correlations are higher for MZ than for DZ twins and there are almost no differences in correlations between the sexes. The correlation in twins of opposite sex is remarkably similar to the DZ same-sex correlations. A series of likelihood-ratio tests showed that MZF and MZM correlations could be constrained to be equal, and that all DZ correlations were the same ( $\chi^2$  with 1 df for  $r(\text{MZM}) = r(\text{MZF})$  was 1.89; for  $r(\text{DZM}) = r(\text{DZF}) = r(\text{DOS})$  it was

0.38 with 2 df). The correlations among MZ and DZ twin pairs were significantly different ( $\chi^2$  with 4 df was 40.64). The estimate for the MZ correlation was 0.48 and for the DZ correlation it was 0.24, suggesting substantial additive genetic influences for variation in loneliness.

Next, we explored possible differences between younger and older subjects in twin correlations for loneliness (lower part of Table II). We divided the sample into 2 cohorts based on year of birth: twins born before 1974 ( $N = 4195$ , average age when completing the surveys was 32.7 years,  $SD = 12.6$ ) and twins born in or after 1974 ( $N = 4192$ , average age was 20.1 years,  $SD = 3.1$ ). A test of differences in correlations between birth cohorts, showed these differences not to be significant ( $\chi^2$  for constraining the MZ and DZ correlations in both cohorts to be equal was 3.3,  $df = 2$ ).

Results of genetic model fitting to the data of the entire sample are given in Table III. Model fitting confirmed that sex differences in genetic architecture were absent. The influence of a common environment was not significant. However, as the last two rows of Table III show, models that excluded a genetic component (CE and E) did not describe the data nearly as well as the AE model. Thus, the familial

**Table II.** Twin Correlations (polychoric) for Loneliness: For The Entire Sample and for 2 Separate Birth Cohorts (Twins Born before and in/after 1974)

	MZM	DZM	MZF	DZF	DOS	Total
<i>N</i> of twins from complete pairs	1210	866	2348	1322	1848	7594
<i>N</i> of twins from incomplete pairs	117	99	194	138	245	793
Twin Correlation	0.42	0.23	0.50	0.25	0.22	0.48 (MZ) 0.24 (DZ)
	MZM	DZM	MZF	DZF	DOS	Total
Born < 1974						
Twin Correlation	0.38	0.20	0.46	0.23	0.22	0.44 (MZ) 0.22 (DZ)
Born ≥ 1974						
Twin Correlation	0.45	0.24	0.55	0.28	0.22	0.52 (MZ) 0.24 (DZ)

Table III. Model Fitting for Loneliness

	-2Log-Likelihood	<i>N</i> parameters	$\Delta\text{Chi}^2$	$\Delta$ df	Tested against
1 Saturated	16197.08	11			
2 ACE (sex differences)	16197.09	10	0.01	1	1
3 ACE, no sex differences	16198.21	8	1.12	2	2
4 AE, no sex differences	16198.21	7	0	1	3
5 CE, no sex differences	16240.74	7	42.53	1	3
6 E, no sex differences	16509.12	6	310.91	2	3

*Note:* The saturated model specified 3 thresholds in males and 3 thresholds in females and 5 correlations between twins (for MZM, DZM, MZF, DZF, and DOS). All subsequent models also specified 3 thresholds for each sex and decomposed the variance of the underlying liability of loneliness into Additive genetic (A), Common (C) and unique Environmental (E) components.

clustering for loneliness cannot be explained by environmental influences that are common to twins, but stems from shared genes. The estimate of heritability was 48% (95% confidence interval 0.44–0.53), identical to the estimate of the MZ correlation.

## DISCUSSION

Several findings emerged in our study of loneliness in 8387 adult twins from the Netherlands Twin Register. First, significant genetic contributions to individual differences in feelings of loneliness in adults were found. The estimate of heritability was 48% (CI 0.44–0.53). Second, environmental influences were unique to each individual and no common environmental contributions to adult loneliness were discernible. Third, we examined whether environmental influences may be more apparent in adults than children. Heritability may decrease across the lifespan, if the frequency, duration, and range of exposure to environmental influences accrue. Alternatively, heritability may become larger, as with increasing age the individual may have more opportunity to structure his or her life according to his or her genotype and less according to the demands from the environment. The results did not support this reasoning, as the genetic contributions to adult loneliness were similar to those found in children by McGuire and Clifford (2000). Dividing our own sample into a younger and an older cohort also showed no evidence of a change in heritability with increasing age. Fourth, neither qualitative nor quantitative sex differences in the heritability of loneliness were found, indicating that the same genes influence loneliness in both sexes and that heritability estimates are the same in males and females.

An interesting implication of this research is that feelings of loneliness may reflect an innate emotional response to stimulus conditions over which an indi-

vidual may have little or no control. Hunter-gatherers thousands of years ago who struggled to survive in conditions of undernourishment may have been tempted to not share their food with their brood. Individuals who felt no loneliness in the absence of or rejection by family or comrades may have been more likely to survive, but their current offspring would have been less likely to survive. Individuals inclined to share food with their family may have lowered their own chances of survival, but increased those of their offspring, thereby propagating their genes. Of course, a hunter-gatherer who survives a famine may then live to propagate another day, suggesting as is so often found in evolutionary biology that no single strategy is necessarily best. The consequence of such an evolutionary scenario would be heritable individual differences in loneliness in adults.

The constellation of states and dispositions that covary with feelings of loneliness—anxiety, hostility, negativity, and social avoidance—may have evolved hand-in-glove with these feelings. Complementary genetic multivariate analyses are needed to illuminate whether it is loneliness or a related trait (e.g., temperament, negative affect, appraisal style) that is heritable and how environmental influences may foster or suppress the expression of these genetic influences. We looked at the polyserial correlation of loneliness with three major personality dimensions, i.e. extraversion, sensation seeking and neuroticism, in males and females. Extraversion was only modestly correlated with loneliness ( $r = -0.27$  in both sexes) and correlations with sensation seeking were around zero, making it unlikely that the current results are due to the heritability of these personality traits. Correlations of loneliness with neuroticism were 0.55 in males and 0.61 in females. Additional analyses must establish whether phenotypic causation (e.g. high neuroticism causes loneliness) or other bivariate models are appropriate to explain this association.

Both the correlational analyses and the model fitting results provide little support for the existence of genotype by age, genotype by sex or genotype by age by sex interactions. Neither the MZ nor the DZ correlations changed to a significant extent when we obtained estimates separately in each sex and/or separately in age cohort. The sample (over 8000 twins) was sufficiently large to have detected such effects if they would have been present. Of course, the “older” cohort is still a relatively young group with an average age of 32.7 years in 2002/3. The genetics of loneliness in middle-aged or elderly subjects may still differ from the results obtained in this sample.

Sex and age can both be considered as “measured” moderator variables. We have shown that they do not interact with the expression of genes that influence variation in feelings of loneliness. How important are other forms of genotype  $\times$  common family environment ( $G \times C$ ) or genotype  $\times$  unique environment ( $G \times E$ ) for loneliness? To test for such interactions, it is necessary to directly measure genotypes or environments (Boomsma and Martin, 2002; Carey, 2003; Martin, 2000) or to obtain quantitative, multivariate measures of the phenotype (Molenaar *et al.*, 1987). We do not know which genetic variants may be involved in loneliness and neither is it easy or straightforward to measure the relevant environmental factors. The fact that the correlation for loneliness in MZ twins is less than one indicates there must be important environmental contributions to loneliness which are not shared between family members. Identifying such influences may turn out to be even harder than finding the genes responsible for variation in loneliness. If there would be  $G \times C$  interaction, it would be part of the genetic variance in the twin model that was employed in this paper (Purcell, 2003), i.e. it is the genotype of the individual that determines the response to the common family environment. In contrast,  $G \times E$  interaction would become part of the environmental variance. The relatively large contribution of unique environmental factors that was seen in this study may contain  $G \times E$ .

In sum, significant genetic contributions were found to adult loneliness. Individual differences in loneliness reflect the expression of multiple genes, which operate in a similar manner in males and females. Importantly, individual differences in loneliness were quantified by averaging over situations and years of observation. The genetic and environmental contributions to individual differences in loneliness

studied here may reflect a dispositional set-point around which an individual fluctuates over time, whereas social and environmental influences may contribute to individual variations in the level of loneliness in specific situations at a given point in time. Finally, given the absence of an effect for common environment, we should also emphasize that this does not mean that such influences (e.g., parental responses) are unimportant. Writing about traits more generally, Reiss *et al.*, (2000) and Loehlin *et al.*, (2003) have argued that genetic factors may trigger processes that lead to individual differences during development, but “parental responses to heritable differences in their children may mediate the expression of genetic influence on adolescent adjustment” (Loehlin *et al.*, 2003, p. 386).

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## REFERENCES

- Achenbach, T. M. (1990). *The Young Adult Self Report*. Burlington, VT: University of Vermont, Dept of Psychiatry.
- Baumeister, R. F., and Leary, M. R. (1995). The need to belong: Desire for interpersonal attachment as a fundamental human motivation. *Psychol. Bull.* **117**:497–529.
- Berscheid, E., and Reis, H. T. (1998). Attraction and close relationships. In D. T. Gilbert and S. T. Fiske (eds.), *The Handbook of Social Psychology*. Vol. 2. (4th edn, pp. 193–281) New York: McGraw Hill.
- Boomsma, D. I., Koopmans, J. R., Doornen, L. J. P., van, and Orlebeke, J. F. (1994). Genetic and social influences on starting to smoke: a study of Dutch adolescent twins and their parents. *Addiction* **89**:219–226.
- Boomsma, D. I., Geus, E. J. C. de, Baal, G. C. M. van, and Koopmans, J. R. (1999). Religious upbringing reduces the influence of genetic factors on disinhibition: Evidence for interaction between genotype and environment. *Twin Res.* **2**:115–125.
- Boomsma, D. I., Beem, A. L., Berg, M. van den, Dolan, C. V., Koopmans, J. R., Vink, J. M., Geus, E. J. C. de, and Slagboom, P. E. (2000). Netherlands twin family study of anxious depression (NETSAD). *Twin Res.* **3**:323–334.
- Boomsma, D. I., Busjahn, A., and Peltonen, L. (2002). The classical twin study and beyond. *Nat. Genet. Rev.* **3**:872–882.
- Boomsma D. I., and Martin N. G. (2002). Gene-environment interactions, In H. D’haenen, J. A. den Boer and P. Wilner (eds), *Biological psychiatry*, (pp. 181–187), John Wiley & Sons Ltd.
- Boomsma, D. I., Vink, J. M., Beijsterveldt, T. C. van, Geus, E. J. van, Beem, A. L., Mulder, E. J., Derks, E. M., Riese, H.,

- Willemsen, G. A., Bartels, M., Berg, M., van den Kupper, N. H., Polderman, T. J., Posthuma, D., Rietveld, M. J., Stubbe, J. H., Knol, L. I., Stroet, T., and Baal, G. C. van (2002). Netherlands Twin Register: a focus on longitudinal research. *Twin Res.* 5:401–406.
- Bowlby, J. (1988). *A secure base: Parent-child attachment and healthy human development*. New York: Basic Books.
- Cacioppo, J. T., Berntson, G. G., Sheridan, J. F., and McClintock, M. K. (2000). Multi-level integrative analyses of human behavior: Social neuroscience and the complementing nature of social and biological approaches. *Psychol. Bull.* 126:829–843.
- Carey, G. (2003). *Human Genetics for the Social Sciences*. Thousand Oaks (CA): SAGE Publications.
- Derks, E. M., Dolan, C. V., and Boomsma, D. I. (2004). Effects of censoring on parameter estimates and power in genetic modeling. *Twin Res.* 7:659–669.
- Duck, S., Pond, K., and Leatham, G. (1994). Loneliness and the evaluation of relational events. *J. Soc. Pers. Relat.* 11:253–276.
- Ernst, J. M., and Cacioppo, J. T. (1999). Lonely hearts: Psychological perspectives on loneliness. *Appl. Prev. Psychol.* 8:1–22.
- Falconer, D. S. (1989). *Introduction to Quantitative Genetics*. London: Longman.
- Harlow, H. F., and Harlow, C. M. (1987). *From Learning to Love: The Selected Papers of H. F. Harlow*. New York: Praeger Publishers.
- Hawkey, L. C., Browne, M. W., and Cacioppo, J. T. (in press). How can I connect with thee?: Let me count the ways. *Psychological Science*
- House, J. S., Landis, K. R., and Umberson, D. (1988). Social relationships and health. *Science* 241:540–545.
- Hughes, M. E., Waite, L. J., Hawkey, L. C., and Cacioppo, J. T. (2004). A short scale for measuring loneliness in large surveys: Results from two population-based studies. *Res Aging* 26:655–672.
- Joreskog, K. G., and Sorbom, D. (1996). *PRELIS User's Manual, Version 2*. Chicago: Scientific Software, Inc..
- Koopmans, J. R., Slutske, W. S., Heath, A. C., Neale, M. C., and Boomsma, D. I. (1999). The genetics of smoking initiation and quantity smoked in Dutch adolescent and young adult twins. *Behav. Genet.* 29:383–393.
- Loehlin, J. C., Neiderhiser, J. M., and Reiss, D. (2003). The behavior genetics of personality and the NEAD study. *J. Res. Pers.* 37:373–387.
- Martin, N. G. (2000). Gene-environment interaction and twin studies. In T. Spector, H. Snieder and A. MacGregor (eds.), *Advances in twin and sib-pair analysis*. London: Greenwich Medical Media Ltd, pp. 143–150.
- Martin, N., Boomsma, D. I., and Machin, G. (1997). A twin-pronged attack on complex traits. *Nat. Genet.* 17:387–391.
- McGuire, S., and Clifford, J. (2000). Genetic and environmental contributions to loneliness in children. *Psychol. Sci.* 11:487–491.
- Molenaar, P. C. M., and Boomsma, D. I. (1987). Application of nonlinear factor analysis to genotype-environment interaction. *Behav. Genet.* 17:71–80.
- Neale M. C., Boker S. M., Xie G. and Maes H. H. (2003). *Mx: Statistical Modeling*. VCU Box 900126, Richmond VA 23298: Department of Psychiatry. 6th edition
- Neale, M. C., and Cardon, L. R. (1992). *Methodology for Genetic Studies of Twins and Families (NATO ASI Series D: Behavioural and Social Sciences-Vol. 67)*. Dordrecht: Kluwer Academic Publishers B.V..
- Peplau, L. A., and Perlman, D. (1982). Perspective on loneliness. In L. A. Peplau and D. Perlman (eds.), *Loneliness: A source-book of current theory, research and therapy*. New York: Wiley, pp. 1–20.
- Pinquart, M., and Sorensen, S. (2003). Risk factors for loneliness in adulthood and old age—a meta-analysis. In S. P. Shohov (ed.), *Advances in psychology research Vol. 19*. Hauppauge, NY, US: Nova Science Publishers, Inc., pp. 111–143.
- Plomin, R., DeFries, J. C., McClearn, G. E., and McGuffin, P. (2001). *Behavior Genetics, 4th edition*. New York: Worth Publishers and W.H. Freeman and Company.
- Purcell, S. (2003). Variance components models for gene-environment interaction in twin analysis. *Twin Res.* 5:554–571.
- Reiss, D., Neiderhiser, J. M., Hetherington, E. M., and Plomin, R. (2000). *The Relationship Code: Deciphering Genetic and Social Influences on Adolescent Development*. Cambridge, MA: Harvard University Press.
- Rook, K. S. (1988). Towards a more differentiated view of loneliness. In S. Duck (ed.), *Handbook of personal relationships: Theory, research and interventions..* Chichester: Wiley, pp. 571–590.
- Russell, D., Peplau, L. A., and Cutrona, C. E. (1980). The revised UCLA loneliness scale: Concurrent and discriminant validity evidence. *J. Pers. Soc. Psychol.* 39:472–480.
- Shaver, P. R., and Brennan, K. A. (1991). Measures of depression and loneliness. In J. P. Robinson, P. R. Shaver and L. S. Wrightsman (eds.), *Measures of personality and social psychological attitudes*. (Vol. 1, pp. 195–290). San Diego: Academic Press.
- Silk, J. B., Alberts, S. C., and Altmann, J. (2003). Social bonds of female baboons enhance infant survival. *Science* 302:1231–1234.
- Taylor, S. E. (2002). *The Tending Instinct: How Nurturing is Essential to Who We Are and How We Live*. New York: Time Books.
- Vink, J. M., Willemsen, G., Stubbe, J. H., Middeldorp, C. M., Ligthart, R. S., Baas, K. D., Dirkzwager, H. J., Geus, E. J. de, and Boomsma, D. I. (2004). Estimating non-response bias in family studies: application to mental health and lifestyle. *Eur. J. Epidemiol.* 19:623–30.
- Weis, R. S. (1973). *Loneliness: The Experience of Emotional and Social Isolation*. Cambridge MA: MIT Press.

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