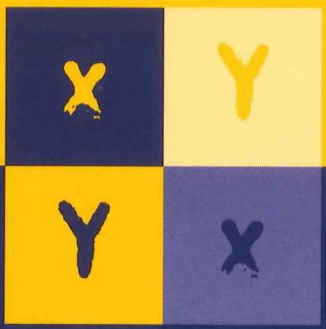
The genetics of health-related behaviors

A STUDY OF ADOLESCENT TWINS
AND THEIR PARENTS



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VRIJE UNIVERSITEIT

The genetics of health-related behaviors

A study of adolescent twins and their parents

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Introduction

Cardiovascular disease is the main cause of death in Western society. The risk for coronary heart disease (CHD) is influenced by our lifestyle. Alcohol use, smoking and physical inactivity are lifestyle factors that have a distinct relation with CHD risk. The status of smoking as a risk factor for CHD is well established and unequivocal. Another important risk factor is physical inactivity. Physical inactivity is as strong a risk factor for CHD as the three commonly accepted "traditional" risk factors: high blood pressure, high serum cholesterol and cigarette smoking (e.g. Caspersen, 1987). The risk of CHD is about twice as large in inactive persons as compared to highly active individuals (Berlin and Colditz, 1990; Powell et al., 1987). For alcohol use, the risk of CHD is less unequivocal. A daily small amount of alcohol seems to have a protective effect, possibly by increasing the level of high-density lipoproteins, interfering with thrombosis, and, in post-menopausal women, by increasing estrogen levels (for a review see Shalala, 1993). However, chronic abuse of alcohol is associated with hypertension, weakened heart muscle and arrhythmias (Shalala, 1993). Although heavy drinking and heavy smoking tend to go together, there is still a twofold increased risk of early death from both CHD and cancer for alcohol abuse that is independent of the effects of smoking and other risk factors (Vaillant et al., 1991).

A change in lifestyle can potentially have an enormous gain in health of the population. Though the CHD risk associated with smoking and physical inactivity is about equal in magnitude to the classical risk factors, the percentage of people at risk because of smoking and physical inactivity is much higher than for hypertension and cholesterol (Caspersen, 1987). For effective prevention and intervention programmes, it is therefore important to gain insight into the factors determining individual differences in health-related behavior. The determinants of health-related behavior during adolescence deserve special attention, because during that period the level of physical activity declines and many adolescents start to experiment with alcohol and cigarettes. Furthermore, health habits that establish during adolescence tend to track into adulthood.

Several studies have shown that health-related behavior of parents is associated with health-related behavior in their adolescent children. For example, Lewko and Greendorfer (1988) concluded in a review that parents influence sports involvement in their children. For alcohol use, there is evidence to suggest that parental alcohol use and parental attitudes toward alcohol use are to some extent associated with adolescent drinking behavior (Ary et al., 1993; Dielman, Butchart, and Shope, 1993; Duncan, Duncan, and Hops, 1994; Weinberg et al., 1994). The experimentation with and the onset of smoking in adolescents was found, among other factors, to be associated with smoking of the parents (Chassin and Presson, 1984; Green et al.,

1991; Murphy and Price, 1988). These studies however, were not designed to disentangle the effects of genetic inheritance and environmental influences. Parents and children can resemble each other because they share genes. Under random mating, parents and children have 50% of their genes in common. Genetic inheritance refers to the fact that parents transmit their genetic predisposition for a trait to their children. Besides the shared genes, parents and children share environmental influences. An informative design for the separation of genetic and environmental influences is the study of twins and their families. By comparing monozygotic (MZ) twins, who are genetically identical, with dizygotic (DZ) twins who have on average 50% of their genes in common, the relative contributions of genetic and shared environmental factors to individual differences can be estimated. By including the parents of the twins in the design, a distinction is possible between environmental influences that they share with their parents, so called cultural transmission, and environmental effects among the offspring that are not shared with their parents (Boomsma and Molenaar, 1987; Eaves et al., 1978; Fulker, 1982; Fulker, 1988; Heath and Eaves, 1985).

As CHD itself, alcohol use, smoking and physical (in)activity exhibit significant familial aggregation. This thesis examines the familial nature of alcohol use, smoking and sports participation in a large population-based sample of Dutch adolescent twins and their parents. The question will be addressed to what extent individual differences in alcohol use, smoking and sports participation are attributable to (1) genetic effects, (2) environmental factors that are shared by family members who grow up in the same home, and (3) environmental influences that are unique for each member of a family and that makes them different from each other. It is known that certain personality characteristics, such as extraversion, neuroticism, impulsivity and sensation seeking are associated with smoking and alcohol use (e.g. Gilbert, 1995; Zuckerman, 1994), and that impulsive and sensation seeking characteristics are associated with the risk of developing alcoholism (Cloninger, Sigvaardsson, and Bohman, 1988; McGue, 1995). In this thesis the contribution of genetic and environmental factors to individual differences in sensation seeking will be described, and the extent to which sensation seeking mediates the genetic and/or environmental influences on initiation of alcohol and tobacco use in adolescents. This study will thus provide critical knowledge about the determinants of health-related behavior in adolescents.

In this introduction a brief overview of the genetic and environmental determinants of alcohol use, smoking and sports participation is given. Next, the parent-twin design will be explained in more detail, and the Dutch twin-family study on health-related behavior will be introduced.

Alcohol Use

Early initiation of drinking and high density drinking in mid-adolescence are risk factors for later alcohol abuse (e.g. Ghodsian and Power, 1987; White, 1987). Thus, it is important to investigate the factors that determine initiation of drinking and the level of alcohol consumption in adolescence.

Several large-scale twin studies have investigated the determinants of alcohol-related behaviors (for a review, see Heath, 1995). Results from these studies leave no doubt that familial aggregation of social drinking - frequency, quantity, and density of consumption - among adults is largely attributable to shared genes. Evidence is also found for shared environmental factors, although the results are less consistent than for genetic effects, and vary with age and across cultures (Heath, 1995). Patterns of social drinking are stable over time, and this stability of drinking behavior is largely due to the continuity of genetic influences (Carmelli, Heath, and Robinette, 1993; Kaprio et al., 1992).

Not much is known about how genetic and environmental factors operate to determine initiation of drinking, progression to regular drinking and the development of problem drinking (Heath, 1995). Age at which initial drinking occurs is found to be influenced by shared environmental factors in Australian males, whereas for Australian females, age of onset is due to genetic factors and, to a lesser extent, to shared environmental factors (Heath and Martin, 1988). It has also been found that abstinence of alcohol use was determined by factors that were largely independent of the factors that determined frequency and quantity of alcohol consumption. Abstinence was strongly influenced by shared environment but not by genetic factors, while frequency and quantity were mainly determined by genetic factors (Heath et al., 1991b). Because most studies assessed adult drinking behavior, very little is known about the importance of genetic and social factors on drinking behavior in adolescents and young adults. Moreover, not much is known about the ratio of these factors in countries with a relatively liberal attitude toward drinking, such as The Netherlands.

Smoking

Adolescent smoking is irregular and develops gradually to a more steady smoking pattern in adults. The majority of adolescents experimenting with smoking do not progress to regular smoking. However, early smoking initiation predicts longer duration of smoking and heavier daily consumption and decreases the likelihood of

smoking cessation (Breslau and Peterson, 1996). For preventive purposes it is important to gain insight into the factors determining smoking initiation.

Although smoking shows familial aggregation, not much is known about the factors that determine the early interest in and further development of smoking behavior. Hughes (1986) reviewed available adoption, twin and family studies and concluded that the influence of heredity on smoking is only small to moderate. Recently, Heath and Madden (1995) reviewed the twin studies conducted from the 1960s onward and reanalyzed data from the Scandinavian twin panels by estimating twin-pair correlations for liability to smoking from the published probandwise concordance rates. Heath and Madden (1995) found important cross-cultural differences in the contribution of genetic and shared environmental factors on current smoking status but conclude that twin data consistently show an important genetic influence on risk of being a current smoker.

Few studies distinguish between acquisition, maintenance or quantity of smoking, although genetic and environmental influences on these processes may be quite different. Eaves and Eysenck (1980b) in a study of English twins found that taking up of cigarette smoking is determined by social factors, but its continuation by genetic influences. Heath et al. (1993) found different genetic and environmental influences on smoking initiation for Australian twins and two samples of American twins. In American twins, genetic factors were more important in smoking initiation than social factors. In Australian twins the genetic contribution to risk of becoming a smoker was larger in females than in males, while the effect of shared environmental factors was larger in males than in females. No birth cohort differences were seen, despite marked changes over time in the proportions of males who reported ever having smoked. Smoking persistence in Australian twins showed a genetic component which was independent of the genetic effects on smoking initiation (Heath and Martin, 1993). All the studies on smoking behavior derives from samples of adult and elderly twins.

Sports Participation

Information on genetic, psychological, and social influences on physical activity patterns is scarce, and many studies depend on volunteer samples of students and rehabilitating cardiac patients, rather than general population samples (Chubb, 1988). An exception to this is the Campbell survey on 23000 Canadians (Stephens and Craig, 1990). One of the most striking findings from this study is that physical activity at age 15 is an important predictor for activity levels later on in life.

Most research, including research with twins, has been directed at sport performance or correlates of performance (e.g. Malina and Bouchard, 1986). For example, aerobic power (Fagard, Bielen, and Amery, 1991), endurance performance (Bouchard et al., 1986) and motor development and performance (Maes et al., 1996b; Malina and Bouchard, 1986) are all under genetic control. Evidence for the presence of familial resemblance in leisure-time energy expenditure, level of habitual physical activity and sports participation was found in the Canada Fitness Survey (Perusse, Leblanc, and Bouchard, 1988). Familial correlations for spouses and siblings were higher than for parents and offspring. According to Perusse et al. (1988) this suggests that these familial resemblances may result primarily from environmental factors common to members of the same generation. A second study by Perusse et al. (1989) assessed environmental and genetic effects on overall level of habitual physical activity (including all types and intensities of activities) and on exercise/sports participation (requiring at least five times the resting oxygen consumption). Level of habitual physical activity was influenced by genetic factors (29%), while for exercise participation familial resemblance was explained by cultural transmission (12%). However, environmental factors shared in one generation and not shared with the other generation accounted for most of the variance of both of these physical activity indicators.

The Parent-twin Design

The relative contribution of genetic and environmental factors to individual differences in a phenotype can be estimated by fitting genetic models to observed familial correlations (Neale and Cardon, 1992). A widely used design to study the genetics of complex behavioral traits is the twin design, in which the resemblance between identical, monozygotic (MZ) twins is compared to the resemblance between fraternal or dizygotic (DZ) twins. MZ twins are genetically identical, whereas dizygotic (DZ) twins, like other siblings, have on average 50% of their genes in common. If genes influence a particular behavior, then the genetic similarity of MZ twins should make them more similar for that behavior than DZ twins.

The resemblances between twins can also be due to environmental influences that they have in common (e.g. parents, siblings, school). One of the assumptions of the classical twin method is that MZ and DZ twins are equally correlated for their exposure to environmental influences that are of etiologic importance to the trait under study. This so called equal environment assumption (EEA) has often been criticized. If the EEA is not correct and MZ twins would experience more similar

environmental influences than DZ twins, this would lead to elevated heritability estimates. However, empirical evidence suggests that the EEA is correct for many behavioral traits and psychiatric disorders (Hettema, Neale, and Kendler, 1995; Kendler, 1993; Kendler et al., 1993a; Plomin, DeFries, and McClearn, 1990).

In general, shared environmental factors indicate to what extent family members resemble each other due to common environmental influences. These common or shared environmental influences may be created by influences from the parents, siblings or peers. If parents of the twins are included in the design it becomes possible to assess the effects of parental influences on offspring (cultural transmission) and the effects of residual shared environment among the offspring that cannot be attributed to parental influences. Cultural transmission refers to the effect of the parental phenotype (e.g. alcohol use) on the shared environment of the children.

By including the parents, it is also possible to assess the presence of assortative mating, that is a correlation between spouses for the trait under the study. If spouses select each other based on a observed trait or phenotype, the genetic factors that influence the phenotype of the spouses will be correlated. Consequently, the genetic resemblance between siblings and DZ twins will be increased. In the classical twin design, this increased similarity of DZ twins relative to MZ twins due to the genetic effects of assortative mating, will be interpreted as shared environment (Fulker, 1982; Fulker, 1988). In the twin-family model that we use, these effects of phenotypic assortative mating are explicitly taken into account.

The Dutch Twin-Family Study of Health-related Behavior

The Dutch twin-family study of health-related behavior is a large scale longitudinal questionnaire study in Dutch adolescent twins and their families. Table 1.1 gives an overview of the variables that were assessed at three waves of data collection in 1991, 1993 and 1995. The results that are reported in this thesis represent part of the data that were collected. In future publications more results of this twin-family study will be described.

This thesis is mainly based on the questionnaires from 1700 families that were collected in the first wave of data collection. Families of adolescent twins were recruited in 1990 by asking all city councils in the Netherlands for addresses of twins aged 13-22 years. There were 252 city councils that supplied about 4000 addresses. Questionnaires on health and lifestyle were sent in 1991 to 2375 families who indicated that they were willing to participate. Completed questionnaires were obtained from 1700 twin pairs of which there were around 1300 complete families

Table 1.1 *Overview of data that were collected in the Dutch twin-family study on health-related behavior in 1991, 1993 and 1995. Questionnaires were collected in twins and their parents. At the third occassion siblings of the twins were included.*

	1991	1993	1995
Alcohol and Smoking			
ever used	✗	✗	✗
last 12 months	-	✗	✗
last 4 weeks	-	✗	✗
frequency	-	✗	✗
quantity	✗	✗	✗
alcohol problems (CAGE)	-	✗	✗
age of onset	✗	✗	✗
Peers			
substance use	-	✗	✗
number of friends	-	✗	✗
sex of friends	-	✗	✗
going out to disco	-	✗	✗
Observer ratings			
alcohol use, smoking and physical activity of parents	✗	✗	✗
twin	✗	✗	✗
siblings	-	✗	✗
best friend	-	✗	✗
Sports participation			
sports participation	✗	✗	✗
intensity level of sport	✗	✗	✗
level of physical activity	-	✗	✗
Health and personal disease history	✗	✗	✗
Socio-economic status	✗	✗	✗
Education	✗	✗	✗
Religion	✗	✗	✗
Personality			
Zuckermans Sensation Seeking Scale	✗	✗	-
Jenkins Activity Survey (Type A behavior)	✗	-	-
Neuroticism (ABV)	✗	✗	-
Extraversion (ABV)	✗	✗	-
Somatic complaints (ABV)	✗	✗	-
Test attitude (lie-scale, ABV)	✗	✗	-
Beck Depression Inventory	-	✗	-
Young Adult Self Report (CBCL)	✗	-	✗
Spielberger Trait Anxiety	✗	✗	-
Spielberger Trait Anger	✗	✗	-
Cognitive Failure Questionnaire	✗	-	-

personality measures were not available for the siblings of the twins; ABV = Amsterdamse Biografische Vragenlijst (Amsterdam Biographical Survey).

(father, mother and twins). Mean age of the twins at the first measurement occasion was 17.7 years (±2.3, range = 12-24 years), age of their mothers was 45.7 years (±5.2) and of their fathers 47.8 years (±5.6). Between 1991 and 1993, additional addresses were obtained of 1987 families. The new addresses included several of the larger cities in the Netherlands. The second questionnaire was sent in 1993 to the new addresses, to the families that participated in 1991 and to the families who did not respond in 1991 to our first request. Completed questionnaires were obtained from 1974 families; 959 families participated for the second time; 877 families came from the new addresses; 138 families were contacted before in 1991 but had not responded at the time. For the third wave, questionnaires were sent in 1995 to the 2712 families that participated in the first and/or second wave. This third wave included two questionnaires per family for the siblings of the twins. For the fourth wave we are planning to assess personality and health-related behaviors in the siblings of the twins and in the twins themselves. In addition to the data that were collected by questionnaire, a subsample of 213 twin pairs aged 16 years also participated in a longitudinal study on the electrophysiological indices of brain activity (Van Beijsterveldt, 1996) and in a study of nerve conduction velocity (Rijsdijk, 1997).

Representativeness of the Sample

In voluntary based twin-studies it is commonly seen that MZ female twin pairs are over represented. In our study all five zygosity groups are well represented; there were only slightly more female twin pairs (40%) than male twin pairs (32%). The proportion of opposite-sex twins in our sample (28%) was almost equal to the proportion of opposite-sex twins in the total population of twins born between 1970 and 1980 in The Netherlands (29.5%) (Tas, 1990). The twins in our sample are born between 1966 and 1980. Table 1.2 gives the percentage of twin pairs in each cohort.

The sample of participating families came from all regions of the Netherlands, including both rural and urban areas. The sample was representative of the general population with regard to the educational level of the parents (Koopmans et al., 1995). Furthermore, the number of adolescent twins who reported to have smoked, have used alcohol and to participate in sports was comparable to other national large scale surveys (De Zwart et al., 1993; Plomp, Kuipers, and van Oers, 1991; Sangster and Abrahamse, 1995).

Table 1.2 *Representation of the total sample of 2712 twin pairs in different birth cohorts.*

born between	%
1966 - 1969	5
1970 - 1973	37
1974 - 1976	30
1977 - 1980	28

Outline of the Thesis

This is one of the first large scale twin studies that assess the genetic and environmental determinants of health-related behavior during the critical developmental period from adolescence to young adulthood. In the first chapter the contribution of genetic and environmental factors to individual differences in smoking and sports participation is examined. Data from twins and their parents were used to distinguish between genetic influences, environmental factors shared by twins and the effects of cultural transmission. In chapter 2 the nature of the familial resemblances in alcohol use is examined. Because the prevalence of alcohol use was different for different age groups, the sample was divided into three cohorts: 12 to 14 year old twins, 15 and 16 year old twins, and twins of 17 years and older. The genetic analyses were carried out for the 403 families of 15 and 16 year old twins and for the 805 families of twins aged 17 years and older.

Sensation seeking is associated with adolescent alcohol and tobacco use (Zuckerman, 1994). Chapter 3 describes the genetic analyses of sensation seeking in adolescents. Sex differences in the genetic architecture of sensation seeking were analyzed by testing whether the magnitude of the genetic influences differed between males and females or whether different genes were expressed in males and females. With a multivariate genetic model it was determined to what extent the covariation between the subscales was explained by genetic and/or environmental covariation. Chapter 4 explores to what extent sensation seeking characteristics mediate the genetic and/or the environmental influences on initiation of alcohol and tobacco use in adolescents.

Not much is known about the determinants of various aspects of substance use in adolescents. In chapter 5 the inheritance of initiation of alcohol and tobacco use in adolescents and the inheritance of level of consumption is examined. Finally, the

association between alcohol use and smoking is studied in chapter 6. With a bivariate genetic model the comorbidity between alcohol use and smoking can be attributed to genetic and/or environmental factors that predispose to both alcohol use and smoking. For theses analyses the data on initiation of alcohol use and smoking from the first questionnaire were extended with data from 1015 twin pairs that participated for the first time at the second measurement occasion in 1993. This enabled the division of the sample of twins into three different cohorts: 12 to 14 year old twins, 15 and 16 year old twins, and young adult twins aged 17 years and older. The thesis concludes with a summary and a discussion of the results.

2

The Genetics of Smoking and Sports Participation

Judith R. Koopmans, Lorenz J.P. van Doornen, and Dorret I. Boomsma

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Smoking and sports participation

JUDITH R. KOOPMANS, LORENZ J. P. VAN DOORNEN and DORRET I. BOOMSMA

It has long been recognized that both smoking and sports participation tend to cluster in families. In this chapter, we first describe the current status of smoking and sports participation as cardiovascular risk factors. After an outline of the principles of the quantitative genetic approaches to the analysis of individual differences in behaviour, we will review the literature on genetic and environmental determinants of smoking and sports participation. In the second half of this chapter, results from the Dutch Twin/Family Study of Health-Related Behavior are presented.

SMOKING AND PHYSICAL INACTIVITY AS CHD RISK FACTORS

Cardiovascular disease, the main cause of death in our western society, is to a considerable extent a product of our lifestyle. The parallel decline in mortality of coronary heart disease (CHD) and of the levels of its risk factors since the mid-1960s seems to support this statement. It is not clear, however, to what extent the decline in mortality can be attributed to a favourable change in risk factors[1,2]. Moreover, the decline in incidence of CHD is much smaller than the decline in mortality. This suggests that the decline in mortality is due to improved survival of new cases rather than to a substantial decline in incidence. The exact balance between the contributions to the decline in CHD mortality of reduced incidence, improved case/fatality rate as the result of improved medical care, and the effects of primary and secondary prevention on risk factors will remain a matter of dispute in the near future.

Setting aside the result of this dispute, it is agreed that behavioural factors, like diet, smoking and physical activity, do affect CHD risk. The status of smoking as a risk factor for CHD is well established and unequivocal. Smokers have at least twice the risk of CHD of non-smokers. The effect depends upon current dose and cumulative consumption. The risk is similar for males and females. On the other hand, the effects of smoking seem to fade away relatively fast after cessation. The largest risk decrement, of about

50%, is in the first year with a gradual return to the level of non-smokers in 5–10 years[3]. In younger people, the decline in risk after cessation seems to occur even more rapidly[4].

There is general agreement now that a sedentary lifestyle is associated with increased CHD incidence. The results of about 50 epidemiological studies were reviewed by Powell et al.[5] and quantified by meta-analysis later on by Berlin and Colditz[6]. Both reviews observed a median risk ratio of about 2 across all studies, which means that CHD occurred about twice as often in inactive persons compared with the highly active. The better-quality studies were more likely to report a favourable association. Two thirds of the studies allowed the assessment of a dose–response relationship. The chance of developing CHD appeared to increase linearly with decreasing physical activity level. Some studies allowed an adjustment of the relationship between physical activity and CHD risk for the confounding effect of traditional risk factors [e.g. Reference 7]. These adjustments had only moderate effects on the risk ratios of physical activity, supporting its role as an independent CHD risk factor. Strictly speaking, this association does not necessarily represent a causal one, as selection factors may form an alternative explanation. Nevertheless, based on the well-accepted criteria for causality in epidemiological research (consistency and strength of the association, dose–response relationship and biological plausibility), we tend to conclude with Powell et al.[5] that, 'the accumulated data do point to a causal relationship between inactivity and CHD risk'.

A good reason to focus our attention on the factors that influence these behavioural risk factors is that the potential gain in health on the population level is enormous. Though the CHD risk associated with smoking and inactivity is about equal in magnitude to the classical risk factors, hypertension and elevated cholesterol levels, the 'population-attributable risk' is much larger. The percentage of people at risk because of smoking and inactivity is much higher than for hypertension and cholesterol. For instance, only about 10% of the population have systolic blood pressure levels above 150 mmHg (roughly doubling their risk as compared with persons with pressures lower than 130 mmHg) whereas the Campbell's Survey of 22 000 Canadians indicated that only 11% of the population older than 10 years of age performed physical activity with an intensity and frequency high enough to maintain or improve their physical fitness[8]. This leaves 89% of the population 'at risk' because of their inactivity.

Because the habits of smoking and physical activity are established early in life and tend to track into adulthood, the determinants of these habits in younger age groups deserve special attention. Adolescence is a transitional period with respect to physical activity level: it typically declines. In the Campbell's Survey, the only exception to the positive time trend was observed in a younger age group. Young men and women (age 20–24) decreased their activity by 10% between 1981 and 1988. Adolescent smoking is irregular and develops gradually to a more steady smoking pattern in adults. The majority of adolescents experimenting with smoking do not progress to regular smoking. For preventive purposes, it is important to gain insight into the factors determining the large variation in smoking across lifetime.

BEHAVIOUR GENETIC APPROACHES

The genetics of complex behavioural traits can be studied with twin, family, or adoption designs. Evidence for the influence of genetic factors on smoking behaviour and sports participation comes mainly from the first two types of studies, i.e. with twin and nuclear families.

Traditionally, heritability estimates (abbreviated to h^2) based on twin data have been obtained by doubling the difference between MZ and DZ twin correlations: $h^2 = 2(r_{MZ} - r_{DZ})$, where h^2 represents the part of the total or phenotypic variance that is accounted for by genetic factors and where r_{MZ} and r_{DZ} are the correlations between MZ and DZ twins, respectively[9]. When $r_{MZ} < 2r_{DZ}$, this additional resemblance indicates the importance of a common environment shared by twin siblings. This common environment may be created by influences from family or peers. The contribution of common or shared environment (abbreviated to c^2) to phenotypic variance may be estimated by the formula $c^2 = 2r_{DZ} - r_{MZ}$. However, this intuitively simple method of comparing twin correlations does not test any explicit model for individual differences. It only works with twins and does not generalize to more complex data sets, and it does not consider non-genetic transmission from parents to children[10]. If parents of twins are included in the design, it becomes possible to assess the presence of assortative mating, that is a correlation between spouses for the trait under study, the effects of parental influences (cultural inheritance) on offspring, and the effect of residual shared environment among the offspring that cannot be attributed to parental influences[11–13]. In nuclear family designs, correlations between phenotypic data of siblings and/or parents and offspring provide an estimate of the degree of familial clustering for a certain characteristic. However, these data do not permit a distinction between shared genes and shared family environment. Separation of genetic from environmental influences is possible if, in addition to the phenotype, family members are also measured on environmental variables that affect the phenotype[14]. However, if this so-called environmental index is itself influenced by genetic factors, heritability will tend to be underestimated while common environmental influences will be overestimated[15].

For many traits, heritability estimates obtained from twin data are often higher than estimates obtained from other family groupings. This may reflect the possible bias in heritabilities obtained from family data if an environmental index is used, the presence of genetic non-additivity, the presence of a special (MZ) twin environment, age-dependent trends in the magnitude of the genetic effects, or a correlation between genetic effects across time that is less than unity.

In adoption studies, the resemblance between foster parents and offspring and/or between siblings who are not biologically related yields estimates of the importance of common environmental influences shared by family members. The resemblance between biological parents and their adopted offspring gives an estimate of genetic influences, but, for smoking and sports participation, no studies of biological parents and their adopted children are currently available.

GENETIC AND ENVIRONMENTAL DETERMINANTS OF SMOKING BEHAVIOUR

Most studies on the genetic aspects of smoking have focused on adult and elderly twins. Hughes[16] reviewed adoption, family and twin studies on smoking. The family studies showed that adolescent smoking was associated with parental and sibling smoking. One study of nuclear families and adoptees[17] indicated that these resemblances were influenced by genetic factors. In this study, the correlation for number of cigarettes smoked per day of parents and offspring was significant whereas the correlations of adoptees with their adoptive parents were zero. The twin studies showed consistently that the concordance rates for smoking were higher in MZ twins than in DZ twins. Reported heritability estimates ranged from 0.28 to 0.84 (mean 0.53). Hughes concluded that genetic factors have a small influence on both the acquisition and the maintenance of smoking. In a study of 5044 adult male twins from the Finnish Twin Registry[18], also reviewed by Hughes, factor scores for cigarette smoking were used for analyses. The factors for smoking consisted of years smoking, cigarettes smoked per day, current smoker and ever smoker. A problem with this factor analytical method is that different aspects of smoking behaviour, which may show different patterns of inheritance, are summarized into one score. The heritability of this factor was estimated for five age groups. With increasing age, concordance rates declined for both MZ and DZ twins. The heritability remained fairly stable (from 0.55 in twins aged 18–29 years to 0.42 in the age group 50–59 years), except for those older than 60 years in which h^2 was 0.12. Overall, the estimate of heritability was 0.45 for cigarette smoking.

Other studies employing very large samples of twins have suggested substantial genetic influences on several aspects of smoking behaviour. In a study of 4380 adult male twin pairs (American World War II veterans), Carmelli et al.[19] reported a heritability (h^2) of 53% for quantity smoked. After adjustment for alcohol and coffee use, occupation and socioeconomic status, by means of regression analysis, the estimate of the heritability was reduced to 35%. Alcohol use and number of cigarettes ever smoked per day were significantly correlated ($r = 0.22$). A multivariate genetic path model approach would have been more informative to estimate the separate and the shared genetic and environmental effects that underlie this correlation. A follow-up 16 years later of this same population showed that never smoking, current smoking and quitting were moderately influenced by genetic factors[20]. Within the group of current smokers, concordance rates were higher in MZ twins than in DZ twins for both light and heavy smoking, suggesting genetic effects on the dependence of smoking.

Indications that independent genetic factors influence different aspects of smoking come from several other studies. Heath et al.[21] showed, in a study of adult Australian twins, that factors which determine smoking onset were not identical to factors that influence the age at which smoking starts. Shared environmental and genetic influences were both important in determining whether or not smoking would occur, while, for age of onset of smoking, only genetic factors contributed to the variance. In a cohort aged 31 years

and older, the genetic effect on smoking persistence was independent of the genetic effect on smoking initiation[22]. For smoking persistence, 53% of the variance was explained by genetic factors. In a study of the Virginia Twin Registry, Meyer et al.[23] found that starting to smoke and quantity smoked were inherited independently. As in the Australian sample, additive genetic and shared environmental factors both contributed to the variance in starting to smoke ($h^2 = 48\%$ and $c^2 = 33\%$). For quantity smoked, only genetic influences were significant ($h^2 = 69\%$). In 3 cross-sectional samples of adult twins, Heath et al.[24] investigated self-reported data on smoking initiation. With different birth cohorts, they tested whether the decline in the percentages of smokers had led to a change in the relative contributions of genes and environment to the risk of becoming a smoker. There was no evidence for cohort differences in the genetic and environmental effects, despite the marked decline over time in the proportion of males who ever smoked. There were sex differences and cross-cultural differences in the estimates of the genetic and environmental contributions to the risk of becoming a smoker. Among American males, 60% of the variance was explained by genetic factors and 23% by shared environment. For females, these estimates were 51% and 28%, respectively. Among Australian twins, the genetic contribution was larger in females ($h^2 = 67\%$) than in males ($h^2 = 33\%$). Shared environmental effects explained 15% in females and 39% in males. These estimates came from models in which the correlation between shared environmental effects in opposite sex twins was 0.33 in the Americans and 0.49 in Australians.

Gurling et al.[25] reviewed the behavioural genetic approaches used in the studies on substance use. They pointed to the need to investigate both environmental and genetic influences and to account for cultural transmission and assortative mating within the genetic models of substance use. Only a few studies take assortment for smoking behaviour into account. Assortment may result in either more genetic or environmental resemblances between relatives or both. Therefore, heritability estimates in twin and family studies for smoking behaviour that do not take assortative mating into account, may be biased. In a study of changes which take place in smoking behaviour of married couples over time, Price et al.[26] fitted different probability models. They showed that spouses with identical smoking habits at the time they first began dating each other, tended to be more stable in their smoking behaviour than spouses who had initially dissimilar smoking habits. A study from the Colorado Adoption Project examined spouse similarity for biological, adoptive and non-adoptive parents[27]. Assortative mating coefficients were calculated for 55 pairs of biological parents, 116 adoptive and 76 non-adoptive parents. The results indicated moderate to large assortment for current smoking (0.69 in biological parents, 0.32 in adoptive parents and 0.39 in non-adoptive parents). The biological parents were considerably younger than either the adoptive or the non-adoptive parents. The assortative mating coefficients were significantly different among the three types of parents, but Ho gives no explanation for these differences. For ever-smoked assortative mating coefficients were smaller (0.23, 0.28 and 0.21, respectively). Pérusse et al.[28] assessed, as a part of the Canada Fitness Survey, the degree of familial resemblance for smoking. They observed a spouse

correlation of 0.61 for smoking status. Parent–offspring and sibling correlations were 0.40 and 0.57, respectively. The spouse and sibling correlations were higher than the parent–offspring correlations. This suggests that familial resemblance for smoking may result primarily from environmental factors common to members of the same generation.

Several studies have focused on the environmental factors that predict the experimentation with and the subsequent onset of smoking in adolescents. Chassin and Presson[29] found among 3015 adolescents that the initial experience with smoking was dependent on the presence of parents and older siblings who smoked and on deviance-prone personality characteristics. Two other studies showed that peer group influence is the most important factor that predicts the experimentation with cigarettes[30,31]. Mittelmark et al.[31] also found evidence for the influence of smoking siblings on experimentation with smoking. Evidence that prior experimentation is associated with the subsequent onset of smoking comes from two studies[32,33]. On the other hand, Pederson and Lefcoe[30] followed 2245 subjects for 8 years from young adolescence to late adolescence/early adulthood and found that early experimentation was not a strong predictor of increased involvement with smoking in adolescence.

Several studies found that the risk of taking up regular smoking is associated with smoking siblings, peer influences, spending time with opposite-sex friends and having a boy/girl friend[29,33,34]. The influence of peer smoking increased over the adolescence years and girls were more vulnerable to external influences than boys[29]. An association between smoking of parents and adolescent smoking was also found[33,35]. Another study showed an influence of maternal smoking for girls only[34]. In the study by McNeill et al.[32], family smoking was not a significant predictor for the subsequent onset of smoking in adolescence. Bauman, Foshee, Linzer and Koch[36] found that ever smoking of parents was more strongly correlated with adolescent smoking than was current parental smoking. Ever smoking of parents was as strongly related as peer smoking with adolescent smoking. Other factors that increase the risk of taking up regular smoking are attitudes and beliefs about smoking and behavioural intentions to smoke[29,30,32,33], being dismissive of the hazards of smoking[31,34], lower social class[35], low self-esteem[33] and having been drunk[32].

These studies did not take the possible genetic influences into account. For example, studies which show a relationship between parental smoking and children's smoking assume that parental smoking is a component of the environmental influences in children. However, parents and offspring not only share, to some extent, their environment but also share on average 50% of their genes. Within the genetic models, it is possible to account for the genetic relatedness between parents and offspring and to separate environmental factors that are shared between parents and children from environmental factors that are shared in siblings only. In this way, the contribution of parental smoking to the environmental influences of their children can be estimated.

DETERMINANTS OF PHYSICAL ACTIVITY

There is not much research on the determinants of adolescent participation in physical activities. Lewko and Greendorfer[37] reviewed the family influences and sex differences in children's socialization into sports. They stated that the family rather than the school and peers are most influential on children's sports socialization, that parents are more influential than siblings and that the father is most relevant in the sports socialization process, regardless of the sex of the child. In an update of this review[38], these statements were adjusted. The peer group, rather than the family, was now considered the most influential social system. Whether parents or siblings were more influential remains unanswered, but some evidence was provided to support the father's role as the most influential for socialization into sports. In a study of the correlates of sports participation among adolescent girls, Snyder and Spreitzer[39] found that socialization into sports begins in childhood with encouragement by parents and continues into adolescence with encouragement from significant other individuals (peers, teachers and coaches).

Gregson and Colley[40] examined the association between parental sports involvement and sports participation in adolescent males and females. The results indicated a more important role of parents in sports socialization for females than for males. For females, there were significant correlations between sports participation and father's participation ($r = 0.22$), mother's participation ($r = 0.20$) and mother's achievement ($r = 0.21$). Maternal and paternal sports participation were also correlated. No significant correlations were found between parental sports involvement and sports participation in males. The difference in the socialization of males and females into sports is also supported by the finding that the school is more influential for males than for females[37,38]. Familial aggregation in physical activity was observed in 30 children, aged 5–9 years, and their parents[41]. Children of active and less active parents exhibited physical activity patterns similar to their parents.

The above-cited studies showed evidence for parental influences in sports participation and physical activity of their children. However, the question of whether these familial influences are mediated by cultural inheritance or by genetic relatedness was not addressed.

The degree of familial resemblance for activity level was assessed in 16 477 subjects, aged 10 years and older, from the Canada Fitness Survey[28]. Pairs of spouses, siblings and parent–offspring were formed to compute familial correlations in energy expenditure, time on activity and activity level. Evidence for familial resemblance was observed for all these variables. Familial correlations were higher within generations (spouses and siblings) than across generations (parent–offspring). The correlations within generations were similar for spouses and for siblings. This suggests that familial resemblance may result primarily from environmental factors common to members of the same generation. A second study by Perusse et al.[42], in a large family cohort (1610 subjects from 375 families), assessed environmental and genetic effects on overall level of habitual physical activity (including all types and intensities of activities) and on exercise/sports participation (activites requiring at least five times the resting oxygen consumption).

Different kinds of familial correlations were computed, including foster parent with adopted child and twin correlations. With a path analytical model, transmission from one generation to the other was separated into genetic and cultural components of inheritance. Level of habitual physical activity was significantly influenced by genetic factors (29%). For exercise participation, transmission was accounted for by cultural factors (12%). However, non-transmissible environmental factors (i.e. factors shared in one generation not shared with the other generation) accounted for most of the variance of both of these physical activity indicators. In this study, habitual activity levels were corrected for age, sex, body mass index, socioeconomic status and physical fitness as assessed by PWC 150. Fitness levels have a rather strong genetic component[43] so correcting for this variable may lead to underestimation of the influence of genetic factors on physical activity. This might explain why 'participation in sports', a potentially preferred choice for genetically fit persons, shows no genetic contribution.

Evidence that genetic factors influence physical activity comes from a study on adult male twins in the Finnish Twin Registry. Kaprio et al.[18] factor analysed physical activity variables (amount, intensity, duration and number of years of physical activity) assessed by questionnaires. The factor score obtained for physical activity was used to compute correlations in MZ and DZ twins, resulting in a heritability estimate of 0.62. A genetic contribution to activity levels was also observed in two studies on twins under 10 years of age[44,45]. In a study by Fagard et al.[46] of 48 male twins aged 18–31 years, an index of sports activity, including present and previous involvement in sports, showed identical intrapair differences in monozygotic and dizygotic twin pairs, whereas most indices of maximal aerobic power showed a strong contribution of genetic factors.

THE DUTCH TWIN/FAMILY STUDY OF HEALTH-RELATED BEHAVIOR

The Dutch Twin/Family Study of Health-Related Behavior is a large-scale study on the genetic and environmental determinants of alcohol consumption, smoking and physical activity. Data are collected by mailed questionnaire. Almost 1600 adolescent twins and their parents participated in the first wave of data collection. Over the next four years, we will measure this population another twice and add siblings of the twins to the design. The first results for smoking and sports participation are presented here.

Subjects

All city councils in the Netherlands (699) were asked by letter for addresses of twins aged 13–22 years. A positive response was received from 252 city councils, representing all parts of the Netherlands, which supplied 3859 addresses; 177 addresses were available from other sources. Of these, 2375 families of twins indicated their willingness to participate in the twin project.

These families received mailed questionnaires on health and lifestyle. A total of 1610 families (68%) returned questionnaires. Data from 17 families were not used because the twins were either too young or too old or because one or both twins had not completed the questionnaire. This leaves a total of 1593 families. Of these, 1339 families included both parents and twins.

The questionnaires consisted of items on zygosity, health, alcohol and tobacco use, sports participation and personality. Age of the twins was between 13 and 22 years, mean age was 18 years (SD = 2.3). Mean age of the fathers and mothers was 48 years (SD = 5.7) and 46 years (SD = 5.2), respectively. Zygosity of the twins was determined by questionnaire, consisting of items about physical similarity (similarity of face, eye colour, hair colour, skin colour) and frequency of confusion of the twins by family and strangers. In a group of 131 same-sex adolescent twin pairs who participated in a study on cardiovascular risk factors[47], agreement between zygosity based on this questionnaire and zygosity based on bloodgroup polymorphisms and DNA fingerprinting was 95%. The twins were divided into five groups by sex and zygosity; MZ males, MZ females, DZ males, DZ females and DZ opposite sex twins. Both twins and parents were asked, 'Do you participate in sports?' and, 'Did you ever smoke?' In addition we also asked the parents whether they were currently smoking. The questions could be answered with 'yes' or 'no', resulting in dichotomous variables.

Statistical analyses

To perform quantitative genetic analyses with dichotomous data, it is assumed that the underlying distribution of the variable is continuous and normal[9]. The variance of this distribution is caused by multiple genetic and environmental factors. A threshold divides the distribution into two categories, for example 'never smoked' and 'ever smoked'. Due to the sum of different genetic and environmental influences, an individual can exceed the threshold and express the trait, e.g. starts to smoke. The correlation between two dichotomous variables (e.g. smoking in twin 1 with smoking in twin 2) is called the tetrachoric correlation. PRELIS, a preprocessor for LISREL, was used to estimate the tetrachoric correlation by maximum likelihood, under the assumption that the two variables have a bivariate normal distribution[48].

By comparing the MZ and DZ correlations, the relative contributions of genetic and environmental influences to individual differences were estimated, using the method of path analysis[49]. A path diagram of the twin model is given in Figure 15.1. In the full model, the total phenotypic variance is explained by an additive genetic factor, a unique (individual-specific) environmental factor, and a shared environmental factor. If a variable is related to age, as was the case with smoking and sports participation, then differences between twin pairs in age will contribute to estimated shared environment variance. Therefore age was included in the model as a separate factor, explaining part of the total variance. The expected correlations between the phenotypes of the twins can be derived by tracing all connecting

routes in the path diagram. With LISREL7, a linear structural equation modelling package, the path coefficients of this path analytical model were estimated and the expected correlations were fitted to the observed correlations, using the weighted least squares (WLS) approach[50]. WLS requires, as a weight matrix, an asymptotic covariance matrix of the sample correlations, which was estimated by PRELIS. Different genetic models were fitted by constraining the genetic factor or the shared environmental factor to zero. The goodness of fit of the models was assessed by likelihood-ratio χ^2 tests. The acceptabilty of a model, not only depends on how well it fits the data, the model also needs to be consistent; it needs to be simple and the parameters of the model need to be significant[49].

Within the twin model, two kinds of sex differences in the genetic architecture of a trait can be tested[51]:

1. The same genes or environmental factors contribute to trait variation in males and females, but the magnitude of their effects is different,
2. Genes or shared environmental influences expressed in one sex are not expressed in the other sex.

By comparing the heritability based on data from male MZ and DZ twins with heritability estimated from data of female MZ and DZ twins, the first hypothesis was examined. By including opposite-sex DZ twins in the design, a group traditionally excluded from most twin studies, it was possible to test the second hypothesis and to estimate the genetic or the environmental correlation between these effects shared by male twins and these effects shared by female twins. With twin data only, it is not possible to test simultaneously for imperfect correlations in both gene effects and shared environmental effects, since there are no opposite-sex MZ twins[52].

Including the parents of twins in the design makes it possible to account for sources of variation that are confounded in twins[53]. The correlation between spouses was modelled as based on phenotypic assortment. Cultural transmission was modelled as the influence of the parental phenotype on the shared environment of the children. In this way, the variance of the shared environmental factor in twins was partitioned in cultural transmission and environmental effects that are shared by twins only. The genetic relatedness between parents and offspring was modelled as a path (with value 0.5) from the genotype of the parent to the genotype of the child. The effects of cultural transmission and phenotypic assortment induce a correlation between the genetic and environmental factors. It is assumed that these effects are going on for some generations and have reached a state of equilibrium[11,12]. Estimation of the parameters in this model involves a set of non-linear constraints[13]. Because of these constraints, it is not (yet) possible to use the LISREL computer program for these analyses. We used Mx, a structural equation modelling package specifically designed for modelling genetically informative data[54].

Smoking behaviour

There were 1582 twin pairs with complete data for smoking, and 1324 families in which both parents and children completed the questions. Table

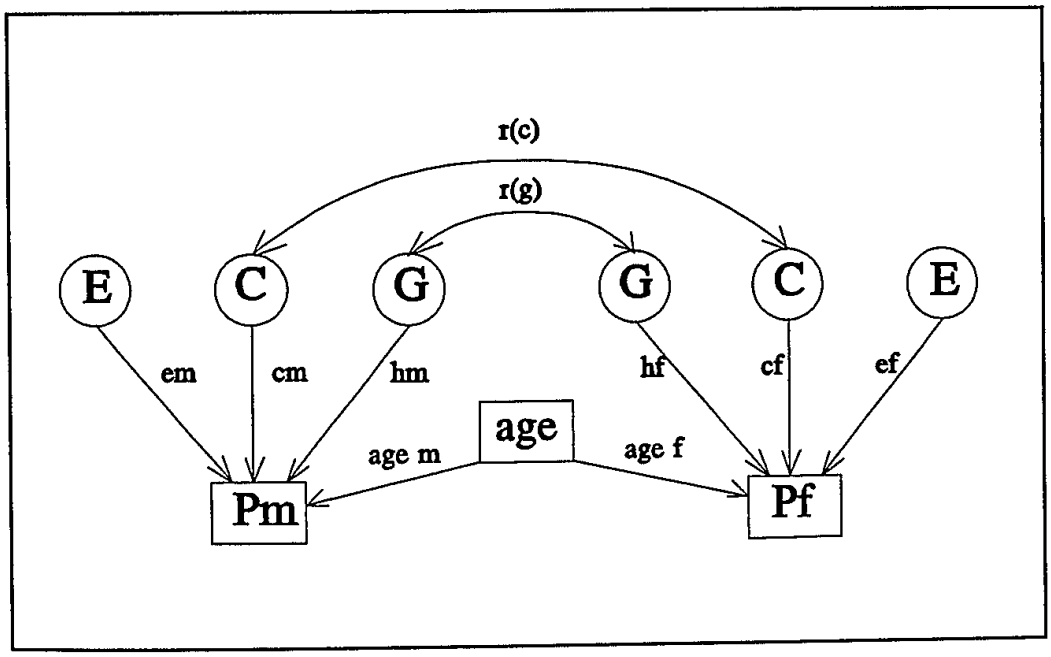

Figure 15.1 Path diagram for DZ opposite-sex twins. Squares represent observed variables and circles represent latent variables. Pm = phenotype male; Pf = phenotype female. E stands for the environmental factors that are not shared between twins, C stands for shared environmental influences, G for additive genetic influences; e, c, h and age represent the path coefficients of these respective factors; m and f stand for male and female. The proportion of variance due to genetic and environmental influences is equal to the squared path coefficients. The correlation between the genetic factors is represented by r(g); r(g) = 1 for MZ twins and r(g) = 0.5(1 + γ) (γ = correlation between the genotypes of the parents) for DZ twins. The correlation between the shared environmental factors is represented by r(c). Sex differences can be expressed by different path coefficients for males and females or by an imperfect correlation between either the shared environmental factors or the genetic factors

15.1 gives the number of twins in each sex by zygosity group, and the prevalence, concordance and tetrachoric correlation for smoking. There were no sex differences in smoking status, 26% of male twins and 23% of female twins had ever smoked ($\chi^2 = 2.66$, df = 1, $p = 0.10$). In the parental generation, there were significant sex differences for ever smoked (fathers 84%, mothers 66%, $\chi^2 = 106.7$, df = 1, $p < 0.01$) and for smoking at present (fathers 38%, mothers 29%, $\chi^2 = 20.8$, df = 1, $p < 0.01$).

The polyserial correlation between smoking and age of the twins was 0.33 in both sexes. Heterogeneity tests of the twin correlations showed that MZ male and female tetrachoric correlations were not significantly different (the constrained estimate was 0.91), and that DZ same-sex correlations also did not differ (constrained estimated = 0.75), but that the DZ opposite-sex correlation was lower than the DZ same-sex correlation (χ^2 for difference = 6.16 with 1 df). Model fitting with the twin data showed that the best fitting model included both genetic and shared environmental influences and, in addition, allowed the correlation between the shared environments of boys and girls to take its own value. Under this model, 9% of the total variance was accounted for by individual specific factors, 11% by age, 30% by additive genetic factors, and 50% by environmental influences shared by siblings growing up in the same family. The estimated correlation between

Table 15.1 Percentage, concordances and tetrachoric correlations for smoking behaviour in twins

	n *(pairs)*	*% Smoking*	*Concordance (%)*			*Tetrachoric correlation*	
			Both	*One*	*Neither*	r	*SE*
MZM	245	23	17.1	12.6	70.2	0.87	0.042
DZM	236	26	16.1	19.5	64.4	0.73	0.067
MZF	329	22	17.6	9.5	72.9	0.92	0.026
DZF	301	23	14.0	16.2	69.8	0.77	0.056
DOS	454	29 male 26 female	14.1	26.0	59.5	0.54	0.064

MZM = monozygotic male twins; DZM = dizygotic male twins; MZF = monozygotic female twins; DZF = dizygotic female twins; DOS = dizygotic opposite-sex twins; r = tetrachoric correlation; SE = standard error of the correlation

Table 15.2 Spouse correlations and parent–offspring correlations for ever smoking in children with currently smoking and ever smoking in parents

		Currently smoking		*Ever smoked*	
	n	r	*SE*	r	*SE*
Father–mother	1324	0.43	0.040	0.18	0.052
Father–son	1222	0.19	0.048	0.24	0.060
Mother–son	1222	0.14	0.050	0.05	0.051
Father–daughter	1426	0.17	0.046	0.21	0.055
Mother–daughter	1426	0.23	0.046	0.20	0.047

r = tetrachoric correlation; SE = standard error of the correlation

boys and girls for these shared environmental influences was 0.55 (SE = 0.13).

Table 15.2 presents the correlations between spouses for smoking at present and at any time, and the correlations between these variables in parents and smoking status of their sons and daughters. The association between spouses for 'ever smoked' was significant, but rather low (0.18), and quite high (0.43) for 'smoking now'. Correlations between parents and offspring were also low (between 0.05 and 0.24) and did not depend on either the sex of the parent or the offspring. Correlations between 'smoking now' in the parents and smoking in children were not systematically higher than correlations between 'ever smoking' in parents and smoking in children. Genetic model fitting to smoking data of twins and parents gave estimates for cultural transmission parameters from parents to offspring that did not differ significantly from zero (Table 15.3). Resemblance between parents and offspring could be accounted for completely by their genetic relatedness, both when considering smoking behaviour in children with 'smoking now' in their parents and smoking in children with 'ever smoked' in their parents. However, the first model showed a better fit to the data than the second one, probably due to the low correlation between mothers and sons for 'ever smoking'. From both analyses, we obtain similar heritability estimates, resembling the estimate obtained from the analysis of the twin data. From the analysis with 'smoking now' in the parents, the estimates for h^2 and c^2 were 30% and 62%, and from the analysis with 'ever smoking' in parents, these estimates were 32% and 61%, respectively.

Table 15.3 Model fitting results of the phenotypic assortment/cultural transmission model for ever smoked in twins with currently smoking and ever smoking in parents

	Currently smoking		*Ever smoked*	
	Full model	*Cult. trans.* = 0	*Full model*	*Cult. trans.* = 0
h	0.70	0.54	0.64	0.57
c	0.74	0.79	0.75	0.78
e	0.26	0.28	0.26	0.27
Spouse correlation	0.45	0.45	0.21	0.20
Cultural transmission	−0.12	—	−0.06	—
G × C correlation	−0.11	—	−0.04	—
r(Cm, Cf)	0.56	0.55	0.66	0.64
χ^2	23.50	25.87	45.02	45.67
df	25	26	25	26
p	0.55	0.53	0.01	0.02

h represents the influence of the genotype on the phenotype, c the influence of shared environment, and e the influence of unique environment. The square of the path coefficients gives the proportion of variance due to each component; total variance = $h^2 + c^2 + e^2 + 2hsc = 1$, where s = genotype–environment covariance (G × C). The spouse correlation is an estimate of the correlation between the phenotypes of husband and wife. The cultural transmission parameter represents the influence of the parental phenotype on the shared environment of the children. This transmission induces a correlation (G × C) between genotype and environment. r(Cm, Cf) represents the correlation between shared environmental influences of males and females

Sports participation

The complete data for sports participation were available from 1587 twin pairs and 1294 parents. In Table 15.4, the percentages for sports participation are shown. Boys reported more often participating in sports than did girls (74% vs 70%, $p = 0.006$). In the parents, there were no significant sex differences, 50% of the fathers and 53% of the mothers reporting sports participation.

The tetrachoric correlations in Table 15.4 showed that resemblances in sports participation were higher in MZ twins than in DZ twins, suggesting that genetic factors contribute to individual differences in sports participation. The correlations did not differ for MZ males and MZ females (constrained estimate = 0.87) or for DZ males and DZ females (constrained estimate = 0.68). The correlation in the opposite-sex twins was significantly lower than the correlations in the same-sex DZ twins ($p \sim 0.000$). This suggests different factors influencing the behaviour of males and females. There was a small ($r = -0.16$) biserial correlation between age of the twins and sport participation, indicating that participation in sports declined with age.

Different genetic models were fitted to these observed twin correlations. A model in which the resemblances in twins were explained by both genetic and shared environmental factors gave the best fit ($p = 0.531$). The contributions of the genetic and environmental factors did not differ for males and females. The low correlation in the opposite-sex group was explained by the absence of correlation for shared environmental influences in this group. In this model, 48% of the total variance was explained by

Table 15.4 Percentages, concordances and tetrachoric correlations for sports participation in twins

	n *(pairs)*	*% sport*	*Concordance (%)*			*Tetrachoric correlations*	
			Both	*One*	*Neither*	r	*SE*
MZM	249	76	69.9	11.6	18.5	0.89	0.036
DZM	241	76	64.7	22.8	12.4	0.60	0.086
MZF	329	67	59.0	16.1	24.9	0.85	0.037
DZF	303	70	59.7	21.1	19.1	0.72	0.058
DOS	456	70 male 72 female	54.4	32.7	12.9	0.35	0.074

MZM = monozygotic male twins; DZM = dizygotic male twins; MZF = monozygotic female twins; DZF = dizygotic female twins; DOS = dizygotic opposite-sex twins; r = tetrachoric correlation; SE = standard error of the correlation

Table 15.5 Spouse and parent–offspring correlations for sports participation

		Tetrachoric correlation	
	n	r	*SE*
Father–mother	1294	0.49	0.035
Father–son	1190	0.37	0.049
Mother–son	1190	0.32	0.047
Father–daughter	1398	0.29	0.051
Mother–daughter	1398	0.30	0.048

SE = standard error of the correlation

genetic factors, 38% was explained by shared environmental factors and 12% was explained by unique environmental factors. Only 2% of the total variance was explained by age of the twins.

Table 15.5 lists the spouse and parent–offspring correlations for sports participation. A high spouse correlation ($r = 0.49$) was observed. The correlations between parents and offspring did not depend on the sex of the parent or the sex of the children. Overall, the estimation of the parent–offspring correlation was 0.32 (SE = 0.03). A model which accounts for assortment in the parental generation and cultural transmission from the parents to their offspring, was fitted to the data of 1294 families. The results are given in Table 15.6. In the full model phenotypic assortment, cultural transmission and the correlation between the shared environment of boys and girls were estimated. As in the twin model, the correlation in the opposite-sex twins between the shared environment in boys and girls did not differ significantly from zero. The estimation of the cultural transmission was also not significant, indicating that the correlation between parents and offspring was due to their genetic relatedness. For the best-fitting model, the estimation of the heritability was 45%; shared environment explained 44% of the total variance. These estimations were comparable to the estimations from the twin model.

Table 15.6 Model fitting results of the phenotypic assortment/cultural transmission model for sports participation

	Full model	r*(Cm, Cf) = 0*	*Cult. trans. = 0*
h	0.69	0.71	0.67
c	0.66	0.65	0.67
e	0.33	0.32	0.33
Spouse correlation	0.49	0.49	0.49
Cultural transmission	−0.02	−0.04	—
G × C correlation	−0.02	−0.04	—
r(Cm, Cf)	0.13	—	—
χ^2	26.93	27.36	27.50
df	25	26	27
p	0.360	0.391	0.437

For explanation, see Table 15.3

DISCUSSION

For both smoking and sports participation, we found evidence for genetic influences in adolescents. Although the genetic effects in our study were substantial, shared and unique environmental influences together were more important. For smoking, the shared environmental influences contributed more to the total variance than the genetic factors, whereas, for sports participation, their contribution was about equal. For other cardiovascular risk factors, a smaller influence of shared environmental factors is usually found. Most studies of lipid and lipoprotein levels, for example, show no or only a very small influence of common environmental factors shared by family members[55].

The most important sources for sibling resemblance in smoking and sports participation were environmental factors shared between siblings but not between parents and offspring. Parent–child correlations were even lower than spouse correlations for currently smoking and sports participation. Pérusse et al.[28] observed the same patterns of familial resemblances for smoking and activity levels. This pattern of higher resemblance within generations (spouses and siblings) than across generations (parent–offspring) suggests that familial resemblance results from environmental influence common to members of the same generation. Biometric analyses of our data confirm this indication. The results strongly suggest that parental smoking behaviour does not directly influence smoking behaviour of their children. This is in agreement with other studies of adolescent smoking behaviour[32,34]in which parental smoking was only a weak predictor of the taking up of smoking in their children. The parent–offspring correlations for sports participation, too, were not explained by cultural inheritance, in line with other studies. Lewko and Greendorfer[38] found that for sports participation peers and school wield more influence than parents. Pérusse et al.[42] showed that non-transmissible environmental factors were most important for physical activity. Intensive family-based health promotion programmes with healthy families did not increase children's or parents' physical activity[56]. The absence of cultural transmission for smoking and sports participation might also have been the result of the model that we used to analyse parent–

offspring resemblances. This model assumes that the genetic correlation between parents and offspring is 0.5. When genes are expressed at different ages, a lower correlation between parents and offspring is found. Unfortunately, this age-dependent expression of genes can only be tested in a longitudinal design.

In opposite-sex twins, an imperfect correlation between environmental effects shared by males and environmental effects shared by females was found. This sex difference is in agreement with results from other studies. Swan et al.[34] found, for example, that sports participation decreased the risk of taking up smoking in girls, but not in boys, whereas organized social activities increased risk in girls but not in boys. Lewko and Greendorfer[37] noted that sports activities are valued more highly in boys than in girls. In line with several other studies, our results showed that males are more physically active than females[56,57]. Another explanation for the lower correlation in the opposite-sex twins might be that genetic factors are not correlated for males and females. However, as far as we know, there is no biological relevance to assume different genes in males and females for smoking and sports participation.

Several studies have shown that smoking and physical activity are related. Kaprio et al.[18] showed in adult males a small negative correlation ($r = -0.16$) between physical activity and smoking. In a longitudinal study on 6000 adolescents, girls were less likely to take up smoking if they were involved in sports or games[34]. For boys, sporting activities did not seem to affect their risk of uptake. Marti and Vartianen[58] showed that the clustering of behavioural CHD risk factors starts early in adolescence. They found, for boys and girls aged 15, an inverse relationship between physical activity and daily smoking, an association independent of the socioeconomic family background. Results from our study also showed that participation in sports somewhat reduced the risk of taking up smoking for both males and females. In a crosstabulation of sports participation and smoking, 21% who participated in sports, compared with 33% of those who did not, had ever smoked. Thus, smoking and physical activity tend to be weakly correlated.

How do genetic factors influence complex behaviours, such as smoking and sports participation? The possible mechanisms involved in the regulation of tobacco use are: the sensitivity of an individual to the pharmacological and toxicological effects of nicotine, the ability to develop tolerance to the effects and the severity of the withdrawal symptoms[59]. In a review of animal studies[59], Collins found evidence that sensitivity and tolerance development are under genetic control. Inbred strains of mice showed differences in a dose required to elicit a standard effect. There were also differences in the direction of the effect. In some strains, nicotine elicited a stimulation effect, whereas in others a depression/relaxation effect was shown. These differences in sensitivity to nicotine were partially due to differences in the number of the receptors that bind nicotine. Strain differences were also evident for tolerance development. Strains most sensitive to an acute dose of nicotine also developed tolerance more readily. Translating these results to humans, people with a certain genetic make-up might be unique in experiencing a stimulating or relaxing effect of nicotine, and become regular smokers. For

sports participation, there is evidence that genes influence correlated aspects. For example, aerobic power[46], endurance performance[60] and motor development and performance[61], are all under genetic control. Genetically fit persons might be selectively attracted to participate in sports.

In our study of adolescent twins and their parents, we found, for smoking, a much larger influence of shared environment and a lower influence of genetic factors than commonly observed in studies of adult twins. For sports participation, evidence was found for both genetic and shared environmental influences. Parents did not contribute to the environmental effects in twins. The results have important implications for prevention. Successful prevention should concentrate on environmental factors outside the family. For example, physical education programmes at school may be more successful than family-based intervention programmes. Besides, prevention needs to be targeted at boys and girls separately, at least partly.

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3

Familial Resemblances in Alcohol Use: Genetic or Cultural Transmission?

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Familial Resemblances in Alcohol Use: Genetic or Cultural Transmission?*

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ABSTRACT. *Objective:* Resemblances between parents and children for alcohol use can be due both to cultural transmission and genetic inheritance. We examined the genetic and environmental determinants of the familial resemblances in alcohol use. *Method:* With a parent-twin design a distinction was made between the contribution of genetic effects, the environmental influences shared by siblings and the effects of cultural transmission from parents to offspring. By questionnaire, data on whether subjects had ever used alcohol were obtained from 403 Dutch families with a twin aged 15-16 years old and from 805 families with a twin aged 17 years and older. *Results:* For 15-16 year olds, the resemblance between parents and offspring could be explained either by genetic inheritance or cultural transmission. Shared environment explained between 58% and 88% of the individual differences in adolescent alcohol use. For twins aged 17 years and older, 43% of the individual differences in alcohol use could be attributed to genetic factors and 37% to shared environment. There was no evidence for cultural transmission in this age group. *Conclusions:* For adolescents aged 17 years and older, parental alcohol use did not create an environment that stimulated alcohol use in children. The resemblance for alcohol use between parents and their children aged 17 years and older could be explained by their genetic relatedness. For 15-16 year old adolescents, shared environmental influences were more important than for older adolescents. Only 10% of this shared environmental variance might be influenced by parental alcohol use due to cultural transmission. (*J. Stud. Alcohol* **57:** 19-28, 1996)

THE FAMILIAL aggregation of alcoholism is well established. In a review, Merikangas (1990) showed that first-degree relatives of alcoholics have, on average, a seven-fold increase in the risk of developing alcoholism as compared to controls. Several reviews of family, twin and adoption studies have shown that the familial nature of alcoholism is in part due to genetic factors (Anthenelli and Schuckit, 1990; Devor and Cloninger, 1989; Merikangas, 1990), although the degree of heritability of alcoholism and the extent to which genetic factors play a role in women remain controversial (Heath and Martin, 1994; Kendler et al., 1992). To date, there is not much insight into the mechanisms that are involved in the transmission of alcoholism. Besides the genetic transmission of biochemical traits (Schuckit, 1994) another possible explanation is that familial aggregation of alcoholism is due to cultural transmission, that is the influences of parents' behavior on behavior in their offspring. Of considerable interest is the modeling of parental drinking behavior during adolescence, a transitional period in which adolescents start to use alcohol. There is evidence to suggest that parental alcohol use and parental attitudes toward alcohol use influence adolescents drinking behavior, at least to some extent (Ary et al., 1993; Dielman et al., 1993; Duncan et al., 1994; Weinberg et al., 1994). However, these familial influences may be due both to cultural inheritance and to the genetic relatedness between parents and children.

The separation of genetic effects, environmental influences shared by siblings and cultural transmission from parents to offspring is possible by using a parent-twin design (Boomsma and Molenaar, 1987; Eaves et al., 1978; Fulker, 1982, 1988; Heath et al., 1985). By comparing monozygotic (MZ) twins with dizygotic (DZ) twins, the relative contributions of genetic and shared environmental factors to individual differences can be estimated (Neale and Cardon, 1992). By including the parents of the twins, a distinction is possible between the effects of parental influences (cultural transmission) and the shared environmental effects among the offspring that are not shared with the parents (e.g., peers), while accounting for the genetic relatedness between parents and children.

Several large-scale twin studies have investigated the determinants of alcohol-related behaviors. In these studies self-reported measures of quantity, frequency and density were assessed with questionnaires. Kaprio et al. (1991) reviewed the cross-sectional and longitudinal studies of alcohol use and abuse in the Finnish Twin Cohort, a population-based sample of same-sex adult twin pairs. Results showed modest but significant genetic influences on quantity, density and frequency of alcohol use in men and women, with h^2 (the proportion of the total variance due to genetic factors) ranging from 29% to 45%. Evidence was found for shared environmental influences: twins in more frequent contact showed greater similarity for alcohol use. Carmelli et al. (1993) showed, in a 16-year follow-up of World War II veteran

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twins, significant genetic effects for alcohol consumption at baseline (up to 40%) and follow-up (up to 48%) and somewhat lower shared environmental influences (0-32% at baseline, 1-20% at follow-up). Longitudinal stability of drinking behaviors in this cohort was largely due to the continuity of genetic influences.

A study of 572 families of adult twins and their parents in the U.K. found evidence that the amount of alcohol consumption in 1 week was influenced both by genetic factors (37%) and shared environment (42%) (Clifford et al., 1984). The parent-offspring correlations for alcohol consumption were around 0.20. Clifford et al. did not assess the contribution of cultural transmission or genetic inheritance to this parent-offspring resemblance. The shared environmental influences on twins consisted of two parts; one part was manifest when twins lived together, whereas the other part persisted when twins lived apart. The contribution of genetic and shared environmental effects did not differ between men and women. In another study, sex differences in the relative contribution of genetic and environmental factors to variation in alcohol consumption were found in 3,810 pairs of adult Australian twins (Jardine and Martin, 1984). Variation of alcohol consumption in women was explained by genetic factors (56%) without evidence for shared environmental influences. In men, 36% of the total variance was explained by genetic factors and 20% was due to shared environmental effects. The effects of genetic and shared environmental factors were dependent on age. For women, results were similar in younger (30 years and younger) and older (over 30) twins. However, for younger male twins 60% of the individual differences in weekly alcohol consumption were explained by genetic factors and not by shared environment, whereas for older male twins no genetic effects were found and 50% of the total variance was explained by shared environment. Heath et al. (1991a,b) analyzed the same sample of adult Australian twins and showed that abstinence of alcohol use was determined by factors that were largely independent of the factors that determined frequency and quantity of alcohol consumption. Abstinence was strongly influenced by shared environment but not by genetic factors, while frequency and quantity were mainly determined by genetic factors. Consistent with these findings, results from a study of alcohol use in a U.S. volunteer sample of 3,049 female and 1,070 male twins aged 50 to 96, suggested that determinants of whether one drinks differed from those underlying amount of consumption (Prescott et al., 1994). Both genetic (40%) and shared environmental (42%) factors contributed to lifetime abstinence in both men and women, while among drinkers resemblances for alcohol consumption were only explained by genetic influences (43%). The twin studies cited so far all described adult drinking behavior. To our knowledge, there are only two twin studies in which adolescent drinking behavior was assessed. In a study of 1,400 adolescent Australian twin pairs, aged 11 to 18 years, drinking in the previous month was assessed with the question, "Have you had an alcoholic drink in the last four weeks?" (Hopper et al., 1992). Twin associations were represented by log odds ratios. Higher odds ratios in MZ male twins compared to DZ male twins indicated that genetic factors play a role in determining alcohol use in male adolescents. In female twins, MZ and DZ odds ratios were equal, suggesting only shared environmental influences. Retrospective information about abstinence from teenage alcohol use and age of onset of drinking was obtained from 1,589 Australian twin pairs aged 20-30 years (Heath and Martin, 1988). Abstinence from teenage alcohol use was determined by both genetic and shared environmental factors, to differing degrees in males and females. The shared environmental factors that influenced initiation of alcohol use were uncorrelated in males and females. Individual differences in age of onset of teenage drinking in males were not explained by genetic factors but by shared environmental influences (51%). Age of onset of drinking in females was determined by moderate genetic influences (44%) and to a lesser extent by shared environmental factors (14%).

To summarize, twin studies of adult drinking behavior show that genetic factors, and to a lesser extent shared environmental influences, contribute to individual differences in alcohol consumption. For adolescent drinking behavior shared environmental effects seem to be more important. No studies have explicitly addressed the question of cultural transmission for alcohol use. Kendler et al. (1994) used the extended twin-family design to examine the transmission of the vulnerability to alcoholism in 1,030 pairs of adult female twins and their parents. They concluded that alcoholism in parents was genetically transmitted to their children and that there was no evidence for cultural transmission.

In this article we examine to what extent genetic and shared environmental factors contribute to adolescent alcohol use, whether parents and children resemble each other for alcohol use and whether this resemblance is best explained by cultural transmission or by genetic inheritance. Under random mating parents and children have 50% of their genes in common. Genetic inheritance refers to the fact that parents transmit their genetic predisposition for alcohol use to their children. Besides the shared genes, parents and children may share environmental influences. In general, shared environmental factors indicate to what extent family members resemble each other due to the environmental influences that they have in common. In the parent-offspring model that we used the shared environment of the children can be partitioned into environmental influences that the children share with each other but not with their parents and cultural transmission. Cultural transmission refers to the effect of parental behavior (e.g., parental alcohol use) on the shared environment of the children. Several studies have shown that alcohol use in spouses is correlated (Clifford et al., 1984; Gleiberman et al., 1992; Hall et al., 1983; Price and Vandenberg, 1980; Tambs and Vaglum, 1990). This correlation between spouses can be due to assortative mating or to environmental influences shared by spouses. Price and Van-

denberg (1980) found some evidence that spouse similarity for alcohol consumption increased with the length of marriage, but they also showed that there was a significant association for amount of drinking when spouses began dating. This suggests that there is initial assortment for alcohol use. We modeled the correlation between alcohol use in spouses as phenotypic assortative mating. Under this model spouses select each other based on a observed trait or phenotype (e.g., Fulker, 1982). Consequently, the genetic and environmental factors that influence the paternal phenotype become correlated with the latent factors that influence the maternal phenotype. The correlation between the genetic factors of the spouses increases the genetic resemblance between relatives. The increased similarity of DZ twins relative to MZ twins, due to these genetic effects of assortative mating, will inflate the estimates of shared environment in the classical twin model (Fulker, 1982, 1988). In the twin-family model that we use, these effects of phenotypic assortative mating are explicitly taken into account.

We collected questionnaires on health-related behaviors from 1,700 pairs of adolescent twins and their parents. We have previously examined smoking initiation and sports participation in this sample and found that environmental factors that influenced smoking and sports participation were shared between twins but not between parents and children. The resemblance between parents and offspring for smoking and sports participation could entirely be explained by their genetic relatedness and not by cultural transmission (Boomsma et al., 1994; Koopmans et al., 1994).

Method

Subjects and measures

This study is part of the Dutch twin family study on health-related behavior (Boomsma et al., 1994; Koopmans et al., 1994). Questionnaires on health and lifestyle were mailed in 1991 to adolescent twins and their parents. Twin families were recruited by asking all city councils (720) in the Netherlands for addresses of twins aged 12-22 years. A positive response was received from 252 city councils which supplied 3,859 addresses; 177 addresses were available from other sources. After contacting these families by letter, 2,375 twin families indicated that they were willing to participate and 1,700 families returned the questionnaires.

Age of the twins was between 12 and 24 years, less than 4% of the sample were younger than 14 years and 7% were older than 21, the mean ($\pm$SD) age was 17.7 $\pm$ 2.26 years. The average age of the fathers and mothers was 48 $\pm$ 5.6 years and 46 $\pm$ 5.2 years. Zygosity of the twins was determined by questionnaire items about physical similarity and frequency of confusion of the twins by family and strangers (Goldsmith, 1991; Magnus et al., 1983). The classification of zygosity was based on a discriminant analysis, relating the questionnaire items to zygosity based on bloodgroup polymorphisms and DNA fingerprinting in a group of 131 same-sex adolescent twin pairs who participated in a study of cardiovascular risk factors (Boomsma et al., 1993). In that sample zygosity was correctly classified by questionnaire in 95% of the cases. We were able to control the validity of the zygosity questionnaire in a subsample of 88 same-sex twins, aged 16 years, who participated both in our study and in a longitudinal study of brain function (van Beijsterveldt et al., 1994). For these same-sex twins, the agreement between zygosity based on the questionnaire and zygosity based on blood/DNA polymorphisms was 88%. Of the 11 pairs who were misclassified by questionnaire, nine pairs were MZ twins mistakenly assigned as DZ twins.

The questionnaire contained questions about alcohol and tobacco use, sport activities, health, social economical status, religion and a number of personality factors. We asked both parents and twins whether they used or had used alcohol. The question could be answered with "no, seldom or never," "yes, but not any more" and "yes." Less than 2% of the sample of twins and less than 4% of the parents answered "yes, but not any more." Therefore, the last two answers were collapsed into one category, leaving a dichotomous variable for alcohol use. Those who answered "no, seldom or never" but indicated that the quantity of alcohol they consumed in a week was one or more glasses were considered alcohol users. Thus, the variable under study divides the sample into never used alcohol versus ever used alcohol. Of the 1,700 families who returned questionnaires, 1,396 families provided complete data for alcohol use from both father and mother and the twins. The families were divided in five groups by sex and zygosity of the twins; monozygotic males (MZM) and females (MZF), dizygotic males (DZM) and females (DZF) and dizygotic opposite sex twins (DOS).

Statistical analysis

The way we defined alcohol use, a person can be either a drinker or a nondrinker. Quantifying the genetic and environmental factors that contribute to such a dichotomous variable is possible by assuming that the variable has an underlying continuous distribution (Falconer, 1989). This underlying continuous variable has been termed the liability. The liability is due to multiple genetic and environmental influences, giving a normal distribution in liability. A threshold divides the distribution into two classes, affected or not-affected. The correlation in liability, between two family members for example, is called the tetrachoric correlation. We used PRELIS2 (Jöreskog and Sörbom, 1993) to estimate the tetrachoric correlations between twins, spouses and parents and offspring. For each pair of family members (e.g., twin1-twin2; father-mother; father-twin1) a two-by-two contingency table is obtained from which the maximum likelihood estimate of the tetrachoric correlation is computed by PRELIS2, under the assumption that the two variables (e.g.,

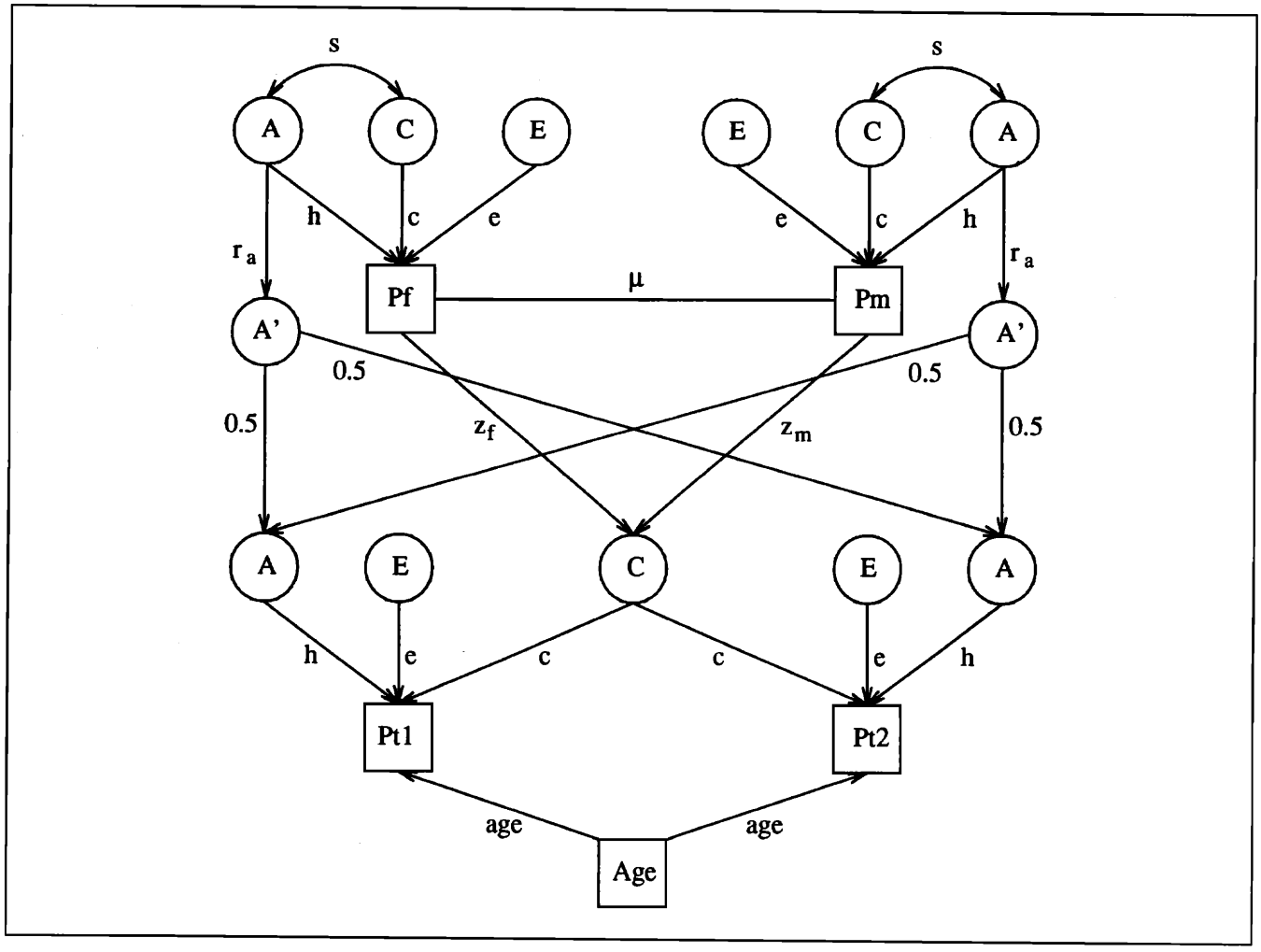

FIGURE 1. Path diagram of the full twin-family model. Circles represent the latent variables and squares the observed variables. Pf and Pm are the observed phenotypes of father and mother, Pt1 and Pt2 the phenotypes of twin1 and twin2. Part of the total variance in twins is explained by the effects of age of the twins. A represents the additive genetic influences, C the shared or common environmental effects and E the unique environmental influences that are specific for each individual. The influence of A, C and E on the phenotype is given by path coefficients h, c and e, respectively. The path coefficients equal the standardized regression coefficients. The model allows for the possibility that genetic factors in the parental generation are different from the genetic factors in the twin generation. r_a estimates the correlation between the parents' genotype and the parents' latent genotype (A') that is transmitted to their children, $r_a = 1$ in the full model. Cultural transmission is represented by z_f and z_m, for father and mother, respectively. The genotype-environment correlation s is induced by cultural transmission and assumed to be at equilibrium. Phenotypic assortative mating is represented by a copath μ (Cloninger, 1980). This path induces correlations among the spouses' latent variables without affecting their within-person covariance structure before assortment. The correlation between the genetic factors in the parents can be expressed as $\gamma = (h+sc)^2 \mu$. The total variance of the twins is computed as $h^2+c^2+age+e^2+2hcs=1$.

drinking in twin1 and drinking in twin2) have a bivariate normal distribution.

A structural equation model was fitted to the twin, spouse and parent-offspring correlations simultaneously to obtain estimates of the genetic and environmental factors that contribute to the familial resemblance of alcohol use. In the full model, the total phenotypic variance in twins is partitioned into an additive genetic part, an individual-specific or unique environmental part, and a shared environmental part (Figure 1). The genetic factors are correlated one in MZ twins, as they are genetically identical. Under random mating, the genetic correlation in DZ twins is a half, as they share on average 50% of their genes. Under phenotypic assortative mating, the genetic correlation in DZ twins is inflated by the correlation between the genotypes of the parents (Falconer, 1989). The genetic correlation in DZ twins thus becomes $0.5(1 + \gamma)$, where γ is the correlation between the genetic factors of the parents (see Figure 1).

By definition, the correlation between the shared environmental factors is unity in MZ and same-sex DZ twins. In opposite-sex twins the correlation between the shared environmental factors in males and females can be less than unity, indicating the extent to which males and females experience different environmental influences. The shared environment of twins is partitioned into a part due to cultural transmission (i.e., the influence of parental drinking behavior on children's environment) and into a part due to environmental influences that are shared by twins only, such as

peers and school. The cultural transmission parameter from the paternal phenotype to the environment in children is allowed to be different from the maternal influences. The genetic inheritance was modeled as a path (with value 0.5) from the parents' genotype to their children's genotype. If there is assortative mating, the genetic resemblance between parents and children is inflated by the correlation between the genotypes of the parents. The model allows for the possibility that genetic factors in the parental generations are different from genetic factors in the twin generation. This genetic correlation between generations is estimated as a path from the parents' genotype to the parents' latent genotype that is transmitted to their offspring. This path is one in the full model. The genetic correlation between generations can only be estimated in a model without cultural transmission, because these two parameters are confounded. The correlation between the spouses was modeled as assortment based on the phenotypes. Phenotypic assortative mating induces correlations between the latent factors that determine the paternal phenotype and the latent factors that determine the maternal phenotype. Due to the effects of cultural transmission the genetic and shared environmental factors within a person become correlated and inflate the phenotypic variance. The assumption of the model is that the effects of assortative mating and cultural transmission have been going on for some generations and have reached a state of equilibrium (Eaves et al., 1978; Fulker, 1982, 1988).

Age of the twins was included in the model as a separate factor, explaining part of the total variance. The effects of age contributes to differences between twin pairs and not to differences within pairs, since twins are always of the same age. If we did not correct for the effects of age, the estimated share environmental influences would be inflated (Neale and Martin, 1989).

For each twin family group, a 5×5 matrix of observed correlations was computed with PRELIS2, giving the correlations for alcohol use between each pair of family members (father, mother, first-born twin, second-born twin) and the correlations between alcohol use and age of the twins. For opposite-sex twins a correlation between male and female twins was computed. Age was recoded to an ordinal variable, resulting in a polychoric correlation between age and alcohol use, because PRELIS still has some problems in estimating the asymptotic weight matrix of the polyserial correlation (a correlation between a continuous and an ordinal variable).

We used Mx, a structural equation modeling package specifically designed for modeling genetically informative data (Neale, 1993), to fit the twin family model to the observed correlation matrices. Parameters were estimated using weighted least squares (WLS). The asymptotic covariance matrix of the observed correlations, which is required as a weight matrix for WLS estimations, was computed with PRELIS2. Different models of familial resemblance were fitted. Under a model where familial resemblance is explained by additive genetic factors, MZ twins, who are genetically identical, are expected to be twice as similar as DZ twins and parents and offspring, who have on average half of their genes in common. Under a shared environmental model, MZ and DZ correlations are predicted to be the same, and parent-offspring correlations depend on the size of the cultural transmission parameters. Under a model where both genetic and shared environmental influences contribute to familial resemblance, DZ correlations are expected to be more than half the MZ correlations. The goodness-of-fit of the models was assessed by likelihood-ratio χ^2 tests and by Akaike's Information Criterion (AIC) (Akäike, 1987). AIC is computed as the χ^2 minus two times the degrees of freedom. This is a measure of the parsimony of the model. The model with the lowest (i.e., largest negative) value of AIC is the most parsimonious and best-fitting model.

TABLE 1. Frequency of alcohol use in males and females for different age groups

	Males		Females	
Age (years)	*n*	%	*n*	%
13<	59	3	68	0
14	145	11	175	6
15	194	26	230	22
16	258	46	270	31
17	231	71	251	48
18	175	73	253	46
19	204	75	264	53
20	165	83	207	52
21>	119	74	131	48
Overall	1,550	55	1,849	37

Results

The number of adolescents who use alcohol is shown in Table 1. Most adolescents start to drink alcohol after the age of 15. At 17 years of age, 71% of the boys and 48% of the girls have used alcohol. The figures in Table 1 show that alcohol use is more common in boys than in girls. This sex difference is also seen in their parents: 88% of the fathers and 65% of the mothers have used alcohol. Because of the prevalence differences in alcohol use between the age cohorts the sample was divided into three age groups: 12 to 14 year old twins, 15 and 16 year old twins, and twins of 17 years and older. For the three different age groups, Table 2 gives the percentages of alcohol users for each zygosity group. In each age group, we tested if alcohol use was independent of zygosity. The alcohol use patterns did not differ significantly between MZ males, DZ males and males from opposite sex twins for the 12 to 14 year old twins ($\chi^2 = 3.42$, 2 df, $p = .18$), for 15-16 year olds ($\chi^2 = 3.41$, 2 df, $p = .18$) and for twins aged 17 years and older ($\chi^2 = 3.95$, 2 df, $p = .14$). For females, alcohol use was also independent of zygosity (12-14: $\chi^2 = 3.26$, 2 df, $p = .20$; 15-16: $\chi^2 = 0.62$, 2 df, $p = .73$; 17 and older: $\chi^2 = 1.80$, 2 df, $p = .41$).

TABLE 2. Concordances and tetrachoric correlations for alcohol use in each zygosity group for different age groups

			Drinking status			Correlation	
	n^a	%Yes	%Both	%One	%Neither	r	SE
12-14 years old[b]							
MZM	40	6	25	75	90		
DZM	32	14	6	16	78		
MZF	46	8	7	2	91		
DZF	49	3	–	6	94		
DOS	51	6m 2f	–	8	92		
15-16 years old							
MZM	68	36	27	19	54	0.80	0.09
DZM	64	34	27	14	59	0.89	0.07
MZF	74	26	22	9	69	0.94	0.05
DZF	73	30	21	19	60	0.78	0.10
DOS	124	44m 30 f	22	31	48	0.58	0.11
17 years and older							
MZM	122	71	61	20	19	0.74	0.09
DZM	129	78	67	22	11	0.60	0.12
MZF	172	47	37	21	42	0.79	0.06
DZF	153	51	35	31	33	0.55	0.10
DOS	229	78m 52f	45	40	15	0.35	0.11

[a] n is the number of complete twin pairs in 12-14 year olds, and n is the number of complete families in the other two age groups.
[b] Due to the small number of subjects in this age group and the empty cells in the DZF and DOS group tetrachoric correlations were not computed.
Note: MZM = monozygotic male twins; DZM = dizygotic male twins; MZF = monozygotic female twins; DZF = dizygotic female twins; DOS = dizygotic opposite-sex twins; m = male; f = female; r = tetrachoric correlations; SE = standard error.

Twin resemblances were expressed as concordances and as tetrachoric correlations (Table 2). Twins in the youngest age group (12-14 years) were highly concordant for not drinking alcohol. For this cohort (n = 218) the tetrachoric correlations could not be computed because of the small numbers of subjects, the low rate of alcohol use and the empty cells in the concordance tables for the DZF and DOS twins. Therefore, genetic analyses were carried out only for the 403 families of 15-16 year old twins and for the 805 families of twins aged 17 years and older. The tetrachoric correlations showed that twins highly resembled each other for drinking behavior. In the group aged 15-16 years, the DZM correlations were as high as the MZM correlations. For females, the DZ correlations seem to be lower than the MZ correlations. In the oldest cohort, the DZ twins were less alike than the MZ twins. The pattern of correlations in the two age groups suggests that shared environment is an important factor in the familial resemblance of alcohol use. With increasing age, the difference between MZ and DZ twins increased, suggesting that genetic factors become more important. In both age groups, the opposite-sex twins were less alike for alcohol use than were the same-sex dizygotic twins. This indicates that drinking in males and females is, to some extent, influenced by different factors.

TABLE 3. Spouse and parent-offspring correlations for alcohol use for two different age groups in the offspring

	15-16 years old			17 years and older		
	n	r	SE	n	r	SE
Spouses	403	0.41	0.06	805	0.55	0.04
Father-son	388	0.12	0.07	731	0.34	0.06
Mother-son	388	0.33	0.06	731	0.31	0.05
Father-daughter	418	0.33	0.08	879	0.37	0.05
Mother-daughter	418	0.22	0.07	879	0.25	0.04

Note: r = tetrachoric correlation; SE = standard error.

TABLE 4. Model fitting results–parent-offspring model for 15-16 year old offspring

Model	χ^2	df	p	AIC
1. ACE, cult.trans. fa ≠ mo	40.80	43	0.57	−45.20
2. ACE, age = 0	57.66	44	0.08	−30.34
3. ACE, cult.trans. fa = mo	40.82	44	0.61	−47.18
4. ACE, cult.trans = 0	41.50	45	0.62	−48.50
5. ACE, cult.trans. = 0,r(G) free	41.54	44	0.58	−46.46
6. CE, cult.trans. fa ≠ mo	43.39	44	0.50	−44.61
7. CE, cult.trans. fa = mo	43.40	45	0.54	−46.60
8. CE, cult.trans. = 0	67.18	46	0.02	−24.82

Note: A = additive genetic factor; C = shared environmental factor; E = unique environment; fa = father; mo = mother; r(G) = the genetic correlation between generations.

Table 3 shows the spouse and parent-offspring correlations in these two age groups. The spouse correlations suggests that the parents of the younger twins resemble each other less than parents of the older twins. However, this difference was not significant, equating the spouse correlations across the 2 age groups by 5 zygosity groups gave χ^2 = 13.33, 9 df, p = 0.15. The overall (± SE) spouse correlation was estimated at 0.51 ± 0.03. The parent-offspring correlations were much lower than would be expected from the twin and spouse correlations. The parent-offspring correlations were not dependent on the sex of the parents nor on the sex of the offspring, both for the 15-16 year old offspring ($\Delta\chi^2$ = 3.57, 3 df, p = 0.31) and for the offspring aged 17 years and older ($\Delta\chi^2$ = 2.63, 3 df, p = 0.45). For the 15-16 year olds the overall parent-offspring correlation was estimated at 0.25 ± 0.04; for the oldest cohort the estimated overall parent-offspring correlation was 0.31 ± 0.03.

With a structural equation model we tested whether the parent-offspring correlations could be explained by cultural transmission or by genetic inheritance or by both. First, the parent-offspring models were fitted separately for twins aged 15-16 years and for the twins aged 17 years and older. The goodness-of-fit parameters for the different models that were considered for the 15-16 year olds are given in Table 4. Under all models, the correlation between the shared environmental factors in boys and girls was estimated as a free parameter; constraining this correlation to one worsened the fit of the model significantly ($\Delta\chi^2$ = 8.00, 1 df, $p < .01$). The first model in Table 4 is the full model with an additive genetic factor (A), a shared environmental factor (C), a unique environmental factor (E) and age of the twins. Under this model, different cultural transmission parameters were esti-

mated for fathers and mothers. The second model shows that the effects of the age of the twins on alcohol use were significant and could not be constrained to zero ($\Delta\chi^2 = 16.86$, 1 df, $p < .001$). The correlation (± SE) between alcohol use and age was 0.26 ± 0.05. Therefore, the factor loading on age of the twins was estimated as a free parameter in the subsequent models. In the third model the cultural transmission parameters were constrained to be equal for fathers and mothers. Model 4 showed that the cultural transmission parameter was not significant. Cultural transmission could be set to zero without a significant increase in the chi-square. Model 5 estimated the correlation between the genetic factors in the parents and genetic factors transmitted to their children. The estimated genetic correlation was equal to one, indicating that the genetic factors influencing alcohol use did not differ between generations. The additive genetic factor could be constrained to zero (Model 6) without worsening the fit of the model, compared to the first model ($\Delta\chi^2 = 2.59$, 1 df, $p = .11$). Under this model, in which only shared environment explained familial resemblance in alcohol use, cultural transmission was significant (Model 8) and equal for fathers and mothers (Model 7).

The model fitting results for the group aged 15-16 years showed that both Model 4 and Model 7 gave a good description of the data. It is not possible to make a distinction between the two models based on likelihood-ratio χ^2 tests. The AIC indicated that Model 4 is a slightly better fitting model. Under Model 4, the resemblances between parents and their 15-16 year old offspring were explained by their genetic relatedness and not by cultural transmission. For this model, additive genetic factors explained 34% of the total variance in alcohol use, 58% was accounted for by shared environmental factors and 7% by age of the twins (Table 6). Under Model 7, familial resemblances in alcohol use were explained by shared environmental influences (88%) and age of the twins (7%) (Table 6). Cultural transmission explained 10% of the shared environmental variance in twins. This means that 79% of the total variance was explained by shared environmental influences in the children that were not shared with their parents, and 9% was explained by cultural transmission. The correlation between shared environmental factors in boys and shared environmental factors in girls was estimated at 0.49 under Model 4 and at 0.44 under Model 7.

The model fitting results for the families of twins aged 17 years and older are given in Table 5. For this age group the additive genetic influences on alcohol use were significant. Constraining the additive genetic component to zero (Model 3) gave a significant reduction of the goodness-of-fit, compared to the first model ($\Delta\chi^2 = 10.92$, 1 df, $p < .001$). The best fitting model for the twins aged 17 years and older was Model 5. Under this model there was no cultural transmission for alcohol use (i.e., the shared environment of twins was not influenced by parental alcohol use). Additive genetic factors accounted for 43% of the individual differences in alcohol use, 37% was accounted for by shared environmental influences and 1% by age of the twins (Table 6). Although the proportion of the total variance that was explained by age of the twins was only 1%, this was significant (Model 2). The correlation (± SE) between alcohol use and age was 0.06 ± 0.03. Under Model 6, the genetic correlation between the generations was estimated at 0.64. However, the fit of this model was not significantly better than Model 5 with a genetic correlation of one. As in the 15-16 year old twins, boys and girls of 17 years and older experienced to some extent different shared environmental influences. The correlation between the shared environmental factors in boys and girls of opposite-sex twins was 0.41.

TABLE 5. Model fitting results–parent-offspring model for offspring aged 17 years and older

Model	χ^2	df	p	AIC
1. ACE, cult.trans. fa ≠ mo	70.67	43	0.005	−15.33
2. ACE, age=0	75.13	44	0.002	−12.87
3. CE, cult.trans. fa ≠ mo	81.60	44	0.000	−6.40
4. ACE, cult.trans. fa=mo	73.10	44	0.004	−14.90
5. ACE, cult.trans.=0	75.01	45	0.003	−14.99
6. ACE, cult.trans.=0,r(G) free	73.10	44	0.004	−14.90

Note: A=additive genetic factor; C=shared environmental factor; E=unique environment; fa=father; mo=mother; r(G)=the genetic correlation between generations.

Next, it was tested whether the same model could explain familial resemblances in alcohol use for both the 15-16 year old twins and the twins of 17 years and older. First, a full parent-offspring model was specified with different parameter estimates for the two age groups, giving $\chi^2 = 111.48$, 86 df, $p = .03$. Then, the parameter estimates were constrained to be equal across the two age groups, giving a significant reduction in the goodness-of-fit ($\Delta\chi^2 = 29.71$, 7 df, $p < .001$). Fitting a model in which the effects of age were allowed to be different for the two age groups still gave a worse fit than the first model ($\Delta\chi^2 = 24.93$, 6 df, $p < .001$). Thus, the magnitude of the genetic and environmental influences on alcohol use in 15-16 year olds was significantly different from the magnitude of the latent factors influencing alcohol use in the older cohort. For 15-16 year old twins the resemblance between parents and offspring could be explained by either genetic inheritance or cultural transmission. For twins aged 17 years and older there was no evidence for cultural transmission.

Discussion

This is the first genetic study in which the transmission of parental alcohol use to their adolescent offspring is examined. The question whether the familial resemblance of alcohol use could be accounted for by cultural transmission was studied in parents and twins aged 15-16 years old and in parents and twins aged 17 years and older. For the adolescents aged 17 years and older we found no evidence for cultural transmission (i.e., parents' alcohol use did not directly influ-

TABLE 6. Standardized parameter estimates for the best fitting twin-family models of alcohol use

Model	h^2	c^2	age	e^2	μ	z_f	z_m	s	r(C)
15-16 year									
Model 4	0.34	0.58	0.07	0.01	0.41	–	–	–	0.49
Model 7	–	0.88	0.07	0.05	0.37	0.19	0.19	–	0.44
17 years and older									
Model 5	0.43	0.37	0.01	0.19	0.57	–	–	–	0.41

Note: h^2 represents the proportion of the total variance that is due to genetic factors; c^2 is the proportion due to shared environment and cultural transmission; age is the proportion of the total variance that can be explained by age of the twins; e^2 is the effect of unique environment. The total variance is computed as $h^2 + c^2 + age + e^2 + 2hcs = 1$, where s = genotype-environment covariance induced by cultural transmission. z_f and z_m represent the cultural transmission parameters for father and mother, respectively. The residual shared environmental variance in twins that is not influenced by cultural transmission is computed as $1 - 2z^2(1 + \mu)$. μ is the assortative mating parameter; r(C) is the correlation between the shared environmental factors in boys and girls.

ence alcohol use in the children). For this age group the resemblance in alcohol use between parents and offspring was explained by their genetic relatedness. The results for the 15-16 year old twins are less conclusive. It was not possible to make a distinction between a model in which the familial resemblances of alcohol use were explained by cultural transmission and a model in which familial resemblances were explained by genetic inheritance. Both models fitted the data equally well. Under a model with cultural transmission, there was no evidence for genetic influences on alcohol use. Resemblances in drinking behavior were explained by shared environmental influences. Due to cultural transmission, part of the shared environment in twins was influenced by parental alcohol use. However, this influence of cultural transmission was rather small. Parental alcohol use contributed only 10% to the shared environmental variance in twins. The residual 90% of the shared environmental variance may consist of the influences of peers, siblings and parental influences that we could not account for in the model, such as parental attitudes towards alcohol use.

Under a model with genetic transmission, the resemblances between parents and offspring for alcohol use were explained by the resemblances in their genetic make-up. Besides the genetic influences in this model, alcohol use in 15-16 year old adolescents was determined by shared environmental influences. These shared environmental factors were not influenced by parental drinking. For older adolescents we found a substantial genetic influence on alcohol use. It is possible that the genetic factors expressed at age 17 and older are correlated with genetic factors expressed at age 15-16. If we can find evidence for such a genetic correlation, a model in which the familial resemblance of alcohol use in 15-16 year olds is explained by genetic transmission will be more likely. This can be resolved by including siblings of the twins to the design. That gives the possibility to compute the correlation in alcohol use between siblings aged 15-16 and siblings aged 17 years and older. Under a model with genetic and shared environmental influences on both 15-16 year old siblings and siblings aged 17 years and older, the expected correlation between the siblings will be higher than under a model with cultural transmission and no genetic effects for 15-16 year old siblings.

Kendler et al. (1994) used the same twin-family design in a study of alcoholism in adult female twins and showed that there was no cultural transmission for alcoholism in women. Tambs and Vaglum (1990) studied alcohol consumption in parents and children aged 18 years and older. The nuclear family design cannot make a distinction between shared genes and shared environment. However, based on the pattern of correlations and estimates of genetic transmission from previous twin studies, Tambs and Vaglum (1990) concluded that there was no evidence for cultural transmission. We have previously examined smoking and sports participation and found that there was no evidence for cultural transmission for these health-related behaviors (Boomsma et al, 1994; Koopmans et al., 1994). The resemblances between parents and offspring for smoking and sports participation were explained by genetic inheritance.

The parent-offspring correlations that we found are consistent with other studies of adolescent alcohol use that found a moderate association between parental drinking and children's alcohol use (Ary et al., 1993; Dielman et al., 1993; Duncan et al., 1994; Hopper et al., 1992; Weinberg et al., 1994). For adolescents aged 17 years and older, we have shown that this association is not due to the shared family environment but due to shared genes. For 15-16 year old adolescents, there is some evidence to suggest that initiation of alcohol use is partly due to the modeling of parental alcohol use. However, the parent-offspring correlations that we found for alcohol use were lower than the spouse and DZ twin correlations. This same pattern of lower correlations between generations than within generations was also found for smoking and sports participation (Boomsma et al., 1994; Koopmans et al., 1994; Pérusse et al., 1988). It suggests that for alcohol use, and for other health-related behaviors, horizontal cultural transmission within generations is more important than vertical cultural transmission between generations.

In all models for parent-offspring resemblances in the families of 15-16 year old twins, shared environmental influences were the most important contributor to the individual differences in adolescent alcohol use. Peers constitute a major part of these shared environmental influences. Several studies have shown that peer use and peer pressure are strongly related to adolescent alcohol use (Ary et al., 1993; Dielman et al., 1993; Duncan et al., 1994; Hopper et al., 1992). Our results showed that shared environmental influences were important for both 15-16 year old twins and twins aged 17 years and older. However, the magnitude of these influences differed between the two age groups. The shared environmental influences on alcohol use become less important as adolescents grow older, whereas the contribution of genetic factors to the individual differences in alcohol use increases. We

found that opposite-sex twins were less alike for alcohol use than were same-sex dizygotic twins. This lower opposite-sex correlation was explained by the reduced correlation between the shared environmental factors in boys and girls of opposite-sex twins. This means that boys and girls experience different types of shared environmental influences, at least to some extent. These sex-specific environmental influences were also found for abstinence from teenage alcohol use (Health and Martin, 1988), smoking (Boomsma et al., 1994) and sports participation (Koopmans et al., 1994). Another explanation for the lower opposite-sex correlation, compared to the same-sex DZ twin correlations, can be a reduced genetic correlation, suggesting that different genes are expressed in males and females. However, sex-specific genetic factors would have resulted in sex-differences in the parent-offspring correlations. We did not observe such sex-differences; parent-offspring correlations were independent from sex of the parent and sex of the children.

With our measure of alcohol use, we assessed whether or not people use alcohol. This may be a broad definition; we did not make a distinction between light and heavy drinkers. However, understanding the factors that influence alcohol use gives us more insight into the development of alcohol-related problems. Only those who initiate alcohol use can develop alcohol problems in the future. Therefore, it is important to investigate the factors that determine why some people drink alcohol and others do not.

Adolescent alcohol use is widely accepted in the Netherlands. The legal age to buy alcohol in a liquor store is 16 years. Even with the availability of alcohol for adolescents there was still a considerable proportion of the sample that stated that they did not use alcohol. For example, in the oldest cohort of twins aged 17 years and older, around 25% of the males and 50% of the females did not use alcohol. This gave us the possibility to assess the factors that contribute to the individual differences in alcohol use. It will be interesting to see if the determinants of adolescent alcohol use are different in countries with a more restricted policy regarding alcohol use.

Our sample is representative of the general population with regard to alcohol use. The number of adolescents who used alcohol in our study was comparable with the percentage of high-school students that spend money on alcohol consumption in a large scale survey of around 11,000 high-school students in the Netherlands (de Zwart et al., 1993), but somewhat lower than the percentage of adolescents aged 10 to 20 that consumed alcohol in the previous month in a national youth health care survey ($N = 8{,}019$) (Plomp et al., 1991).

A problem in our study was that, in a small subsample of same-sex twins, 12% of the twins were misclassified for zygosity by questionnaire. The most common error was that MZ twins were mistakenly classified as DZ twins, which could have resulted in elevated same-sex DZ twin correlations. This would result in overestimated shared environmental influences and underestimated genetic influences. However, we have previously studied sensation seeking in the same sample of 1,700 adolescent twins, using the same classification for zygosity, and found no evidence for elevated DZ twin correlations. As for other aspects of personality, we found for sensation seeking that the DZ correlations were about half the MZ correlations (Koopmans et al., 1995).

In conclusion, the shared environment was the most important determinant of alcohol use in 15-16 year old adolescents. If there is cultural transmission of parents' alcohol use, this explains only 10% of the shared environmental variance in their offspring. This small influence of parental drinking is reduced to zero in adolescents aged 17 years and older. As adolescents grow older, the influence of genetic factors becomes more important and the influence of shared environment decreases.

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4

A Multivariate Genetic Analysis of Sensation Seeking

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A Multivariate Genetic Analysis of Sensation Seeking

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The genetic architecture of sensation seeking was analyzed in 1591 adolescent twin pairs. Individual differences in sensation seeking were best explained by a simple additive genetic model. Between 48 and 63% of the total variance in sensation seeking subscales was attributable to genetic factors. There were no sex differences in the magnitude of the genetic and environmental effects. The different dimensions of sensation seeking were moderately correlated. The strongest correlations were between the subscales Thrill and Adventure Seeking and Experience Seeking ($r = 0.4$) and between Boredom Susceptibility and Disinhibition ($r = 0.4$ in males, $r = 0.5$ in females). A triangular decomposition showed that the correlations between the sensation seeking subscales were induced mainly by correlated genetic factors and, to a smaller extent, by correlated unique environmental factors. The genetic and environmental correlation structures differed between males and females. For females, higher genetic correlations for Experience Seeking with Boredom Susceptibility and Disinhibition and higher correlations among the unique environmental factors were found. There was no evidence that sex-specific genes influenced sensation seeking behavior in males and females.

KEY WORDS: Sensation seeking; adolescent twins; multivariate genetic analysis.

INTRODUCTION

Sensation seeking can be described as the need for new experiences, a nonconforming lifestyle, and the desire to engage in riskful activities. The Sensation Seeking Scale was developed by Zuckerman (1971) within the framework of studies on sensory deprivation, to assess individual differences in optimal levels of stimulation or arousal. Zuckerman (1971) postulated that "the need for change, variety and intensity of stimulation would manifest itself in many aspects of behavior, including sensory, social and thrill-seeking types of activity." The questionnaire measures four dimensions of sensation seeking, identified with factor analysis: Thrill and Adventure Seeking (TAS), Experience Seeking (ES), Boredom Susceptibility (BS), and Disinhibition (DIS) (Zuckerman, 1971; Zuckerman *et al.*, 1978). Zuckerman *et al.* (1978) described Thrill and Adventure Seeking as "the desire to engage in sports or other activities involving speed or danger." Experience Seeking is a measure of "the seeking of new experiences through the mind and senses, and through an unconventional, non-conforming life-style." Boredom Susceptibility assesses "the dislike of repetition of experience, routine work, predictable dull or boring people, and restlessness when things are boring." Disinhibition measures "the desire to find release through social disinhibition, drinking, going to parties and having a variety of sexual partners." A number of studies have shown that sensation seeking was related to psychophysiological and biochemical measures such as the orienting reflex, augmenting–reducing of the averaged evoked potential, and levels of

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monoamine oxidase and gonadal hormones (reviewed by Zuckerman, 1984; Zuckerman *et al.*, 1980). On the behavioral level there is a relation between high sensation seeking and a greater variety of heterosexual activities with more partners, multidrug use, and the tendency to experiment with different drugs, alcohol use, cigarette smoking, volunteering for experiments and unusual activities, physically dangerous activities, gambling, vocational interests, and social attitudes (Zuckerman, 1979; Zuckerman *et al.*, 1980). Scores on sensation seeking are sex and age dependent. The sex differences are most pronounced for TAS and DIS; males score higher on these scales than females (Zuckerman *et al.*, 1978). From the age of 16 through the early 20s there are no important changes, but after the age of 20 a decline in scores is evident (Zuckerman, 1979). Recent reviews of twin, family, and adoption studies showed that for personality traits, such as extraversion and neuroticism, almost 50% of the total variance can be explained by genetic factors (Loehlin, 1992; Eaves *et al.*, 1989). For sensation seeking itself, Fulker *et al.* (1980) estimated a heritability of 58% for the general scale of the Sensation Seeking Scale Form IV. As for most aspects of personality (Plomin and Daniels, 1987) there was no evidence for shared environmental influences on sensation seeking. This study was based on 422 pairs of adult twins from the Maudsley Twin Register (mean age, 31 years). There were more female twins (286 pairs) than males (85 pairs) and opposite-sex twins (51). A number of studies have described different analyses of the sensation seeking data of these twins (Zuckerman *et al.*, 1978; Eysenck and Zuckerman, 1978; Martin *et al.*, 1979; Eysenck, 1983; Resnick *et al.*, 1993). Eysenck (1983) reported for each dimension of sensation seeking the proportion of the total variance due to genetic effects. The heritability estimates were lowest for BS (0.41 for males, 0.34 for females) and highest for ES (0.58 for males, 0.57 for females). To our knowledge, there is only one other twin study of Zuckerman's Sensation Seeking Scale. This study by Buchsbaum (published by Zuckerman, 1974) was based on a small sample of 34 MZ and 30 DZ same-sex twins (half males, half females) of high-school age. The results showed a genetic influence on sensation seeking. For the general scale the heritability (Holzinger's h^2) was 0.28; for the subscales the h^2 ranged from -0.02 for ES to 0.40 for TAS.

In this paper we describe the genetic analyses of sensation seeking in 1700 pairs of adolescent twins. Sex differences in the genetic architecture of sensation seeking were analyzed by testing whether the magnitude of the genetic influences differed between males and females or whether different genes were expressed in males and females.

A multivariate model was used to determine to what extent the covariation between the subscales can be explained by correlated genetic and/or environmental factors (Martin and Eaves, 1977; Boomsma and Molenaar, 1986). The different subscales of sensation seeking are moderately correlated (Zuckerman *et al.*, 1978). They were not expected to be independent because Zuckerman (1971) hypothesized a second-order sensation seeking tendency underlying the four factors. The multivariate model is a more powerful method to calculate the proportions of the total variance due to genetic and environmental factors than separate univariate analyses for each variable, because it also takes the covariations between the variables into account. With a triangular decomposition (Neale and Cardon, 1992) we explored the genetic and environmental correlation structure between the different dimensions of sensation seeking. Zuckerman's hypothesis of a second-order factor model for the four subscales was tested with a common factor model.

METHODS

Subjects

This study is based on completed questionnaires on health and lifestyle, mailed in 1991 to adolescent twins and their parents (Boomsma *et al.*, 1994; Koopmans *et al.*, 1994). Twin families were recruited by asking all city councils (720) in The Netherlands for addresses of twins aged 12–22 years. A positive response was received from 252 city councils, which supplied 3859 addresses; 177 addresses were available from other sources. After contacting these families by letter, 2375 twin families indicated that they were willing to participate and 1700 families returned the questionnaires. The sample of participating families came from all regions of the Netherlands, including both rural and urban areas and two of the four biggest cities.

The questionnaire consisted of items on zygosity, health, alcohol and tobacco use, sports par-

ticipation, and personality. Of the 1700 twin pairs who returned questionnaires, 1591 provided responses from both twins to the personality scales. The incomplete pairs did not differ significantly from the complete pairs with respect to the means and variances of the sensation seeking scales. The age of the twins was between 12 and 24 years, less than 4% of the sample was younger than 14 years and 7% was older than 21 years, and the mean age was 17.7 years (SD = 2.26). The sample was representative of the general population with regard to educational level of the parents: 13.9% of the fathers and 15.3% of the mothers had a basic education at the elementary school, 61.8% of the fathers and 72.5% of the mothers had a high school education, and 24.3% of the fathers and 12.1% of the mothers had attained a college or university level. In the same age group of the general population, these figures are 16.9, 60.6, and 22.5% for men, respectively, and 21.5, 64.4, and 13.9% for women (Netherlands Central Bureau of Statistics, 1994).

Zygosity of the twins was determined by questionnaire items about physical similarity and frequency of confusion of the twins by family and strangers (Goldsmith, 1991; Magnus *et al.*, 1983). The classification of zygosity was based on a discriminant analysis, relating the questionnaire items to zygosity based on blood-group polymorphisms and DNA fingerprinting in a group of 131 same-sex adolescent twin pairs who participated in a study of cardiovascular risk factors (Boomsma *et al.*, 1993). In that sample zygosity was correctly classified by questionnaire in 95% of the cases. We looked at the validity of the zygosity questionnaire in a subsample of 86 same-sex twins, aged 16 years, who participated both in our study and in a longitudinal study of brain function (van Beijsterveldt *et al.*, 1994, submitted). For these twins, agreement between zygosity based on the questionnaire and zygosity based on blood-group polymorphisms was 88%. Of the 10 pairs who were misclassified by questionnaire, 9 pairs were MZ twins mistakenly assigned as DZ twins. The total sample consisted of 275 monozygotic male twins, 258 dizygotic male twins, 360 monozygotic female twins, 322 dizygotic female twins, and 485 opposite-sex twins. All five zygosity groups were well represented in our sample; there were only slightly more female twins (40.1%) than male twins (31.4%). The proportion of opposite-sex twins in our sample (28.5%) was almost equal to the proportion of opposite-sex twins in the total population of twins born between 1970 and 1980 in The Netherlands (29.5%) (Tas, 1990).

Table I. Summary Statistics for the Sensation Seeking Scales in Males (N=1475) and Females (N=1799)[a]

	No. of items	Min–max	Male		Female	
			Mean	SD	Mean	SD
TAS	12	12–60	41.49	9.07	36.96	9.73
			(39.93)	(8.84)	(37.75)	(9.59)
ES	14	14–64	34.86	7.10	34.27	7.45
			(45.51)	(8.89)	(45.09)	(8.18)
BS	13	13–64	38.59	6.74	37.93	7.45
			(40.82)	(7.73)	(41.33)	(7.51)
DIS	12	12–58	35.35	7.28	30.64	6.69
			(37.09)	(8.10)	(34.07)	(7.40)

[a] Means and SD of the norm sample (Feij *et al.*, 1982) in parentheses (174 males, 147 females). TAS, Thrill and Adventure Seeking; ES, Experience Seeking; BS, Boredom Susceptibility; DIS, Disinhibition.

Measures

Sensation Seeking was surveyed with the Dutch version of Zuckerman's Sensation Seeking Scale, form IV (Feij and van Zuilen, 1984). The Dutch scale consists of 67 Likert-type items, covering Thrill and Adventure Seeking (TAS), Experience Seeking (ES), Boredom Susceptibility (BS), and Disinhibition (DIS). There is no overlap between the items of the subscales. The four scales in the Dutch version of the Sensation Seeking Scale have reasonably high internal consistencies (between 0.72 and 0.81) (Feij *et al.*, 1982). Table I presents the summary statistics for each sensation seeking scale. Each item has to be answered on a scale from 1 to 5, giving, for example, for TAS (12 items) a minimal score of 12 and a maximal score of 60. Compared with a Dutch sample on which the construction of the scale was based (Feij *et al.*, 1982) the means for TAS were about the same, whereas for ES, BS, and DIS the means in our sample were lower. This might be explained by the different samples that were surveyed; the norm sample consisted of 331 (174 males and 147 females) first-year undergraduate psychology students with a mean age of 21.5 years (SD = 4.6 years), while our sample is younger and based on the general population. For each scale a model was

fitted to the means, variances, and covariances of the five zygosity groups. Within the most saturated genetic model (a model with additive genetic, shared environmental, and unique environmental factors with sex differences), the heterogeneity of means was tested (Neale and Cardon, 1992). In the first model 10 means (for first- and second-born twins in the five zygosity groups) were estimated, giving a perfect fit to the data with regard to the mean structure. The second model tested whether the means for the first- and second-born twins can be equated for same-sex twins. In the next step the mean of the male opposite-sex twins was equated to the mean of the same-sex DZ male twins, and the same was done for females. Next, it was tested whether the means differ between MZ and DZ twins, for males and females separately. Finally, the means for males and females were equated. For TAS, BS, and DIS there were no significant differences between first- and second-born twins and between MZ and DZ twins. This was also true for the means of ES in the same-sex twins. For ES the means in opposite-sex twins were significantly different from the means in same-sex DZ twins ($\Delta^2_\chi = 8.46$, df = 2, $p < .05$). Male opposite-sex twins had a higher mean (35.30) than the male same-sex DZ twins (34.34), while means for female opposite sex-twins (34.00) were reduced compared to female same-sex DZ twins (34.98). For same-sex twins there were no significant sex differences for ES. Differences between males and females were significant for TAS ($\Delta^2_\chi = 154.38$, df = 9, $p < .001$) and for DIS ($\Delta^2_\chi = 262.11$, df = 9, $p < .001$).

Genetic Analysis

The variances and covariances of the four sensation seeking scales were calculated for each zygosity group with PRELIS 1.2 (Jöreskog and Sörbom, 1986), resulting in 8 × 8 twin pair covariances matrices (four scales for the first twin and for the second twin). Same-sex twins were assigned as first or second twin based on the birth order. Opposite-sex pairs were reordered so that the male twin was the first twin and the female twin the second twin. To test whether the correlations between the sensation seeking scales were induced by correlated genetic and environmental factors, a triangular or Cholesky decomposition was carried out on the covariance matrices (Neale and Cardon, 1992). A Cholesky factorization decomposes the genetic and environmental covariance matrices into triangular matrices of factor loadings. The number of factors equals the number of variables. Figure 1 shows the triangular decomposition of the genetic and environmental factors for the four sensation seeking variables. The first factor contributes to all four variables, the second factor influences the subsequent three variables, and so on. The genetic or environmental covariance matrix is calculated by the product of the triangular matrix and its transpose. Mx (Neale, 1993) was used to fit the Cholesky decomposition with additive genetic, shared environmental, and unique environmental factors to the data. Goodness of fit was assessed by likelihood-ratio chi-square tests. To test Zuckerman's hypothesis of a second-order sensation seeking factor, we fitted a genetic common factor model. In this model one common genetic factor was specified that influences the four sensation seeking scales and one common unique environmental factor. In addition, unique genetic and unique environmental variances were allowed for each scale.

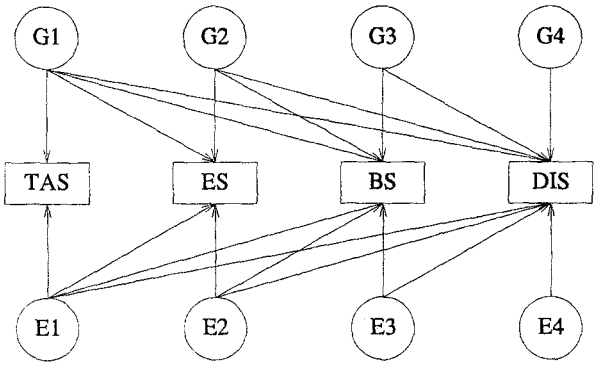

Fig. 1. Triangular decomposition of the genetic and environmental factors for the four sensation seeking scales: Thrill and Adventure Seeking (TAS), Experience Seeking (ES), Boredom Susceptibility (BS), and Disinhibition (DIS).

Different sex-limitation models were tested. In the scalar model the female variances were constrained to be equal to a scalar multiple of the male variance components (Neale and Cardon, 1992). In this model the total variances may differ between males and females but the proportions of the total variance due to genetic and environmental effects are the same. The general sex-limitation model tested whether the magnitude of the genetic and environmental effects differs between males and females and whether different genes or environmental factors operate in males and females. The latter

was modeled as an imperfect correlation between the genetic factors in opposite-sex twins. In this model the first genetic factor in males was correlated with the first genetic factor in females, the second genetic factor in males with the second genetic factor in females, and so on. This is a reduced model of the full model in which each genetic factor in males is allowed to correlate with all the four genetic factors in females.

The correlation between age and the sensation seeking scales ranged from −0.14 to −0.12 in females and from −0.09 to 0.01 in males. Although the correlations in females were significantly different from zero ($\chi^2 = 43.47$, df = 4, $p < .001$), they were weak and therefore were not included in the analyses.

RESULTS

The twin correlations for each zygosity group are presented in Table II. Overall the MZ correlations were about twice the DZ correlations, suggesting that genetic factors influence individual differences in sensation seeking. Table III shows the phenotypic correlations between the four sensation seeking scales. The correlations were moderate, ranging from 0.16 to 0.46. Thrill and Adventure Seeking correlated highest with Experience Seeking ($r = 0.40$), and Disinhibition correlated highest with Boredom Susceptibility ($r = 0.41$ in males, $r = 0.46$ in females). Although the pattern of correlations looked the same for males and females, the correlations could not be constrained to be equal across the sexes ($\Delta\chi^2 = 22.31$, df = 6, $p < .05$).

Table IV presents the goodness-of-fit indices of the different multivariate models that were fitted to the data. A Cholesky decomposition model with additive genetic, shared environmental, and unique environmental factors that were constrained to be equal in males and females gave a poor fit (model 1). A sex-limitation model in which the correlational structure was constrained to be equal in males and females but the variances for the males were allowed to differ from the female variances gave a significantly better fit (model 2) but was still worse than model 3, which allowed for sex-specific parameter estimates ($\Delta\chi^2 = 45.31$, df = 30, $p < .05$). Model 3 is the full Cholesky decomposition with sex-specific estimates for the factor loadings, allowing the genetic correlations between males and females to be less than 0.5. Constraining the genetic correlations to be 0.5 (model 4) did not reduce the fit of the model significantly. Without a significant loss of fit, the shared environment component could be set to zero, for both males and females (model 5). A common factor model, with a common genetic factor, a common unique environmental factor, and unique genetic and environmental variances did not fit the data. In summary, a triangular decomposition with additive genetic and unique environmental factors gave the best de-

Table II. Twin Correlations for Each Zygosity Group[a]

	MZM (260)[b]	DZM (230)	MZF (348)	DZF (304)	DZMF (449)
TAS	0.62	0.42	0.63	0.31	0.25
ES	0.53	0.35	0.60	0.29	0.25
BS	0.45	0.33	0.55	0.34	0.24
DIS	0.59	0.42	0.58	0.45	0.30

[a] MZM, monozygotic males; DZM, dizygotic males; MZF, monozygotic females; DZF, dizygotic females; DZMF, dizygotic male-female twins.
[b] Number of complete pairs in parentheses.

Table III. Phenotypic Intercorrelations for the Sensation Seeking Scales: Correlations for Males (N=1475) in the Lower Triangle and for Females (N=1799) in the Upper Triangle[a]

	TAS	ES	BS	DIS
TAS	—	0.40	0.22	0.26
ES	0.40	—	0.34	0.34
BS	0.16	0.23	—	0.46
DIS	0.27	0.22	0.41	—

[a] TAS, Thrill and Adventure Seeking; ES, Experience Seeking; BS, Boredom Susceptibility; DIS, Disinhibition.

Table IV. Multivariate Model-Fitting Results[a]

Model	χ^2	df	p	AIC
1. No sex differences, *ACE*	184.33	150	0.03	−115.67
2. Scalar model, *ACE*	146.17	146	0.48	−145.83
3. Six-differences, r(g) free, *ACE*	100.83	116	0.84	−131.17
4. Six differences, r(g)=0.5, *ACE*	106.33	120	0.81	−133.67
5. No *C* in males & females	130.45	140	0.71	−149.55
6. Common factor model, *AE*	282.76	148	0.00	−13.24

[a] *A*, additive genetic factors; *C*, common environmental factors; *E*, unique environmental factors; r(g), genetic correlation between males and females of opposite-sex twins.

scription of the observed pattern of variances and covariances in MZ and DZ twins.

The standardized variance components for the best-fitting model are presented in Table V. For each scale the additive genetic and the unique environmental standardized variance components are summed over the four factors, giving the proportions of the total variance. For males additive genetic factors explained 62, 56, 48, and 62% of the total variance of TAS, ES, BS, and DIS, respectively. For females 63, 58, 54, and 60% of the total variance of these traits is attributable to additive genetic factors.

Table V also shows the genetic and unique environmental correlations between the dimensions of sensation seeking. The highest genetic correlations for males were between BS and DIS (r = 0.54) and between TAS and ES (r = 0.51). For females these correlations were 0.55 and 0.45, respectively. Additionally, in females ES correlated 0.47 with BS and 0.48 with DIS. Other genetic correlations were more modest. The unique environmental correlations were smaller than the genetic correlations, but they were still significant. Fitting a model with independent unique environmental factors, by estimating only the diagonal elements for these factors in males and females, gave a significant increase in the χ^2 of 165.31 for 12 df, compared with model 4.

DISCUSSION

Genes play a major role in the individual differences in sensation seeking. Between 48 and 63% of the total variance in sensation seeking scales was explained by genetic influences. This is comparable to the heritability estimate of 58% for the general scale of sensation seeking found by Fulker *et al.* (1980). The heritabilities for the subscales in the Fulker *et al.* study (reported by Eysenck, 1983) were somewhat lower than the ones we found, except for Experience Seeking. In our study the genetic variance was highest for Thrill and Adventure Seeking (62% for males, 63% for females) and Disinhibition (62% and 60%) and lowest for Boredom Susceptibility (48% for males, 54% for females). Eysenck reports the highest heritabilities for Experience Seeking (58 and 57%) and the lowest for Boredom Susceptibility (41 and 34%). For Thrill and Adventure Seeking and Disinhibition he found heritabilities between 51 and 41%.

The heritabilities for the sensation seeking subscales in twins aged 12 to 24 years are consistent with twin studies of other personality traits in adolescence. In the London Twin Study (262 pairs, aged 7–17 years) heritabilities for extraversion and neuroticism were 54 and 44%, respectively (Eaves *et al.*, 1989). A reanalysis of Loehlin and Nichols study (1976) of 850 pairs of high school juniors (18 years old) showed heritabilities of 61% for extraversion and 52% for neuroticism (Eaves *et al.*, 1989).

Although the pattern of twin correlations in Table II suggests that, especially in males, there might be some influence of shared environment, we did not observe a significant contribution of shared family environment on individual differences in sensation seeking in the model-fitting results. In the triangular decomposition of the data the shared environment matrix could be dropped in both sexes without a significant increase in chi-square. However, for personality traits, such as extraversion or neuroticism, the pattern of MZ and DZ correlations typically is somewhat different from what we observe. For sensation seeking we find high DZ correlations relative to the MZ correlations whereas for most other personality traits the DZ correlation usually is lower than half the MZ correlation (Loehlin, 1993).

Testing for sex differences in the genetic architecture of sensation seeking showed no evidence that different genes influence sensation seeking behavior in males and females. Allowing the correlation between the genetic factors in males and females to be less than one-half did not improve the goodness of fit compared to a model in which the genetic correlation was constrained to be 0.5. Although we fitted a reduced model in which four genetic correlations between males and females were estimated, this model fits the data very well.

The differences in the magnitude of the genetic effects in males and females were very small. Univariate genetic analyses for the subscales showed heritabilities to be the same in males and females (with a scalar model accounting for differences in total variance between the sexes in Thrill and Adventure Seeking, Boredom Susceptibility, and Disinhibition). The significant sex differences in the multivariate analysis were thus caused by differences in the pattern of genetic and environmental correlations. The higher phenotypic correlations in females are explained by higher

Table V. Standardized Variance Components, and Genetic and Environmental Correlations Between the Sensation Seeking Scales for Males and Females Under the Best-Fitting Model[a]

	Variance component		Genetic correlation				Unique environmental correlation			
	A	*E*	TAS	ES	BS	DIS	TAS	ES	BS	DIS
Males										
TAS	0.62	0.38	1.00				1.00			
ES	0.56	0.44	0.51	1.00			0.22	1.00		
BS	0.48	0.52	0.24	0.35	1.00		0.06	0.11	1.00	
DIS	0.62	0.38	0.37	0.32	0.54	1.00	0.12	0.08	0.26	1.00
Females										
TAS	0.63	0.37	1.00				1.00			
ES	0.58	0.42	0.45	1.00			0.32	1.00		
BS	0.54	0.46	0.29	0.47	1.00		0.12	0.16	1.00	
DIS	0.60	0.40	0.34	0.48	0.55	1.00	0.12	0.12	0.34	1.00

A, proportion of total variance attributable to additive genetic factors; *E*, proportion of total variance due to unique environmental factors; TAS, Thrill and Adventure Seeking; ES, Experience Seeking; BS, Boredom Susceptibility; DIS, Disinhibition.

correlations among unique environmental factors for females than for males and by higher genetic correlations for Experience Seeking with Boredom Susceptibility and Disinhibition in females.

Males scored higher on Thrill and Adventure Seeking and Disinhibition than females. These sex differences in means in our sample are in accordance with what is generally observed for sensation seeking (Zuckerman *et al.*, 1978; Zuckerman, 1979). Recently, Resnick *et al.* (1993) reanalyzed the sensation seeking data of the 422 twin pairs, including 51 opposite-sex pairs, studied by Fulker *et al.* (1980). They found a higher level of Disinhibition, Experience Seeking, and overall sensation seeking in female members of opposite-sex twins. It was hypothesized that this increase was due to influences of prenatal androgen exposure. We found no evidence for increased sensation seeking in female members of 449 opposite-sex pairs. Testing for heterogeneity of means across zygosity groups and across males and females did not show any significant differences between females of opposite-sex twins and female same-sex DZ twins. The differences we found for Experience Seeking were in the opposite direction; females of opposite-sex twins had lower means compared to female same-sex DZ twins. Our study is based on adolescents, while Resnick and co-workers' (1993) study was based on adults, but it seems unlikely that this difference could explain the discrepancy in results.

Sensation seeking is positively related to extraversion, phychoticism, and impulsivity, but not to neuroticism (Eysenck and Zuckerman, 1978; Zuckerman, 1979; Martin *et al.*, 1979; Haapsalo, 1990). For extraversion and neuroticism the influence of heredity is well established; genetic factors explain almost 50% of the total variance of these traits (Loehlin, 1992; Eaves *et al.*, 1989). Martin *et al.* (1979) tested the hypothesis that the covariation between impulsiveness and sensation seeking could be explained in terms of an extraversion factor. They did not find much evidence for this hypothesis and concluded that impulsiveness and sensation seeking are not simple reflections of extraversion. Phenotypically, Thrill and Adventure Seeking correlated highest with Experience Seeking, and Boredom Susceptibility correlated highest with Disinhibition. These phenotypic correlations were induced mainly by correlated genetic factors and, to a smaller extent, by correlated unique environmental factors. The genetic correlations were substantial, but not as large as one would expect when the traits are entirely under the control of the same genetic factors. We fitted a genetic common factor model and found no evidence for one genetic factor underlying the genetic constitution that influences the different dimensions of sensation seeking. Eysenck (1983) also did not find much evidence for one genetic factor underlying the sensation seeking subscales. These results do not support Zuckerman's hypothesis of a second-order

sensation seeking factor underlying the four subscales. Although all four dimensions of sensation seeking are positively correlated and were in fact originally developed by Zuckerman (1971) as part of one scale, our study shows that there is not one underlying genetic dimension of sensation seeking that can explain the covariation between the sensation seeking subscales.

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5

The Relation between Sensation Seeking, Alcohol Use and Smoking: A Multivariate Genetic Analysis

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The hypothesis that sensation seeking mediates the genetic influences on initiation of alcohol and tobacco use was tested in a population-based sample of 1632 Dutch adolescent twin pairs. Sensation seeking was found to be associated with initiation of alcohol use and smoking in adolescents. The sensation seeking scales that correlated highest with alcohol use and smoking were Boredom Susceptibility (r = 0.19 - 0.24) and Disinhibition (r = 0.28 - 0.46). Multivariate genetic analyses showed that the small to moderate genetic influences on initiation of alcohol and tobacco use could entirely be attributed to the genetic variance in sensation seeking. The association between Boredom Susceptibility and smoking was explained by highly correlated genetic factors. The association between Boredom Susceptibility and alcohol use could be attributed to genetic factors that were highly correlated and to modestly correlated shared environmental factors. The association between Disinhibition and alcohol and tobacco use was explained by correlated shared environmental factors, except for alcohol use in females for which common genetic factors also contributed to the association with Disinhibition. Thus, one of the pathways to the genetic inheritance of initiation of alcohol and tobacco use is through the inheritance of sensation seeking characteristics that predispose to substance use.

Numerous studies have shown that smoking is associated with personality characteristics, such as extraversion, neuroticism, and sensation seeking (reviewed by (Gilbert, 1995). Evidence from large-scale population-based twin studies suggests substantial genetic influences on individual differences in adult smoking behavior (Heath and Madden, 1995) and more moderate genetic influences on adolescent smoking behavior (Koopmans, van Doornen, and Boomsma, 1994). It has been hypothesized that part of the genetic influences on tobacco use are mediated by personality factors (Eaves and Eysenck, 1980b; Gilbert, 1995). It is well established that genetic factors explain between 40-50% of the personality differences and that there is no effect of shared environmental influences (Eaves, Eysenck, and Martin, 1989; Loehlin, 1992; Plomin and Daniels, 1987). Preliminary analyses of Australian females twins suggested a substantial genetic correlation between Novelty Seeking and risk of becoming a smoker (Madden et al., 1993). Moreover, smoking is associated with different aspects of psychopathology, such as depression and anxiety disorders (Gilbert, 1995; Patton et al., 1996). Results from a study of 1566 female twin pairs, suggested that correlated genetic factors predisposed to smoking and major depression (Kendler et al., 1993b).

Initiation of alcohol use and adolescent alcohol use are associated with unconventional and deviant behavior, depressive moods, impulsivity and hyperactivity (e.g. Bucholz, 1990). Furthermore, alcohol use in adolescents is related to sensation seeking and sensation seeking tendencies during early adolescence predicts later substance use (Zuckerman, 1994). It has also been found that personality characteristics, such as impulsivity, aggressiveness and neuroticism, are associated with the risk of developing alcoholism and with alcoholism (McGue, 1995; Tarter, 1988; Tarter and Edwards, 1988). There is a substantial genetic contribution to risk of alcoholism (reviewed by Heath, Slutske, and Madden, 1995) and it has been hypothesized that inherited personality differences might explain part of the genetic influence on risk of alcoholism (Cloninger, 1987; McGue, 1995; Tarter, 1988). Kendler et al. (1993) found that alcoholism in female twins was genetically correlated with major depression. Evidence from twin studies suggests that there is a genetic contribution to individual differences in adult drinking behavior (reviewed by Heath, 1995) and adolescent alcohol use (Koopmans and Boomsma, 1996a; Maes et al., 1996a). These last two findings raise the question to what extent personality contributes to the genetic influences on alcohol use.

In this chapter we explore the relation between sensation seeking and initiation of alcohol and tobacco use in Dutch adolescent twins from a behavioral genetic perspective. Sensation seeking is the tendency to seek new experiences, to have a nonconforming lifestyle and to engage in riskfull activities (Zuckerman, 1971). High

sensation seekers are more likely to experiment with different drugs, to drink alcohol and to smoke cigarettes (Zuckerman, 1994). Twin studies from adult and adolescent samples have shown that between 40-60% of the individual differences in sensation seeking are attributable to genetic influences (Eysenck, 1983; Fulker, Eysenck, and Zuckerman, 1980; Koopmans et al., 1995). Previously, we have shown that besides substantial shared environmental influences, there are small to moderate genetic influences on initiation of alcohol use and smoking in Dutch adolescent twins (Boomsma et al., 1994; Koopmans and Boomsma, 1996a). We will use a multivariate genetic model to address the question to what extent measures of sensation seeking may mediate the genetic and/or environmental influences on initiation of alcohol and tobacco use.

Table 5.1 *Sample characteristics of the Dutch Twin/Family Study on Health-Related Behavior.*

	total N	effective N	age	sd	min	max
MZM	275	265	17.6	2.3	13.3	24.0
DZM	258	245	17.7	2.3	12.1	22.9
MZF	360	349	17.7	2.1	13.5	22.5
DZF	322	309	17.8	2.4	13.2	24.6
DOS	485	464	17.8	2.2	12.6	24.2
total	1700	1632				

MZM = monozygotic male twins; DZM = dizygotic males; MZF = monozygotic females; DZF = dizygotic females; DOS = dizygotic opposite-sex twins.

Methods

Subjects

This study is based on completed questionnaires on health and lifestyle, mailed in 1991 to adolescent twins and their parents. The recruiting of the families of twins aged 12-25 years is described elsewhere (Boomsma et al., 1994; Koopmans et al., 1995; Koopmans, van Doornen, and Boomsma, 1994). The questionnaire consisted of items on zygosity, health, alcohol and tobacco use, sports participation and personality. Zygosity of the twins was determined by questionnaire items about

physical similarity and frequency of confusion of the twins by family and strangers (Goldsmith, 1991; Magnus, Berg, and Nance, 1983). In two different samples of adolescent twins zygosity was correctly classified by questionnaire in 88% and 95% of the cases, compared to bloodgroup polymorphisms and DNA fingerprinting (Koopmans et al., 1995). The sample was divided into five groups by sex and zygosity. Table 5.1 shows the sample characteristics of the five zygosity groups. The total sample consisted of 275 monozygotic male twins (MZM), 258 dizygotic male twins (DZM), 360 monozygotic female twins (MZF), 322 dizygotic female twins (DZF) and 485 dizygotic opposite-sex twins (DOS). Of the 1700 twin pairs who returned questionnaires, 1632 provided responses from both twins to the sensation seeking scales and the questions about alcohol and tobacco use. Age of the twins was between 12-24 years, the mean age was 17.7 years (± 2.26).

Measures

Sensation Seeking was surveyed with the Dutch version of Zuckerman's Sensation Seeking Scale, form IV (Feij and van Zuilen, 1984). The Dutch scale consists of 67 Likert-type items on a 5-point scale, covering Thrill and Adventure Seeking (12 items), Experience Seeking (14 items), Boredom Susceptibility (13 items) and Disinhibition (12 items). There is no overlap between the items of the subscales. In a subsample of the twins (n=961) the Sensation Seeking Scale was assessed twice with a time interval of 27 months (± 5 months). Stability-coefficients for the four scales were between 0.39 and 0.58 for the twins and between 0.61 and 0.81 for the parents (Feij et al., 1996). The questionnaire measures four dimensions of sensation seeking. Thrill and Adventure Seeking (TAS) measures the desire to engage in dangerous sports, or other activities. Experience Seeking (ES) is a measure of the need for new experiences, and an unconventional, non-conforming life-style. Boredom Susceptibility (BS) assesses the dislike of repetition of experience, routine work, and predictable, dull, or boring people. Disinhibition (DIS) assesses the desire to find release through social disinhibition, drinking, going to parties and having a variety of sexual partners.

To assess initiation of alcohol use, we asked twins whether they used or had used alcohol. The question could be answered with "No, seldom or never", "Yes, but not anymore" and "Yes". Those who answered "Yes, but not anymore (less than 2% of the sample) were classified as alcohol consumers. Smoking initiation was assessed with the questions "Have you ever smoked?" and "Are you a smoker?". The twins were classified as nonsmokers if they answered no to both questions. Current smokers (17.0%) and former smokers (7.7%) were classified as ever-smoked.

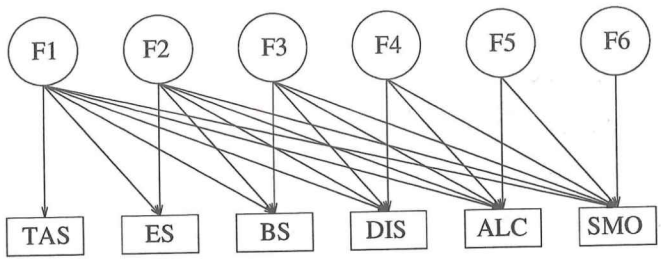

Figure 5.1 *Triangular factor decomposition for the sensation seeking scales, alcohol use and smoking.*

Genetic Analysis

The correlation between a continuous variable (e.g. Sensation Seeking) and a dichotomous variable (e.g. ever used alcohol) is called a polyserial correlation. Suchs correlations can be calculated with PRELIS (Jöreskog and Sörbom, 1993). Polyserial correlations can be analysed in structural equation models using Weighted Least Squares (WLS) (Neale and Cardon, 1992). To fit genetic models by method of WLS a weight matrix is needed. The weight matrix is an estimate of the variances and covariances of the correlations. However, PRELIS has problems with the computation of the weight matrix for polyserial correlations. Therefore, the four sensation seeking scales were reordered into ordinal variables with 10 categories based on the decile scores. For each zygosity group, the polychoric correlations between sensation seeking and initiation of alcohol and tobacco use were calculated with PRELIS 2.12a (Jöreskog and Sörbom, 1993). Same-sex twins were assigned as first or second twin based on the birth-order. Opposite-sex pairs were reordered so that the male twin was the first twin and the female twin the second twin.

With the classical twin design it is possible to decompose the phenotypic correlation between two variables into a genetic and environmental component (Neale and Cardon, 1992). To resolve the contribution of the genetic and environmental components to the correlation between the sensation seeking scales and initiation of alcohol and tobacco use, a triangular or Cholesky decomposition was carried out (Neale and Cardon, 1992). A Cholesky factorization decomposes the genetic and environmental covariance matrices into the product of triangular matrices of factorloadings and its transpose:

$$M = TT' \qquad (5.1)$$

where T is a triangular matrix of factorloadings with fixed zeros in all elements above the diagonal. The number of factors equals the number of variables. Figure 5.1 shows the triangular decomposition of the genetic and environmental factors for the six observed variables. The first factor contributes to all six variables, the second factor influences the subsequent five variables and so on. The genetic covariance between two variables is obtained by multiplying the factor loadings of the two paths from the genetic factor that connect the variables. The same can be done for the environmental covariance. The total phenotypic covariance matrix is obtained by summing the genetic and environmental covariance matrices:

$$P = GG' + CC' + EE' \qquad (5.2)$$

where G is the additive genetic triangular matrix, C is the shared environmental triangular matrix and E the unique environmental triangular matrix.

The first four variables of the Cholesky decomposition were the sensation seeking scales, followed by alcohol use and smoking. By ordening the variables in this way, part of the genetic and environmental variance in alcohol use and smoking is mediated by the sensation seeking scales and part of the genetic and environmental variance is specific for alcohol use and smoking. It can be tested whether the four sensation seeking scales mediate all the genetic and/or environmental variance by constraining the last two factors that are specific for alcohol use and smoking to zero.

Different models were fitted to the data with Mx (Neale, 1995) by method of Weighted Least Squares (WLS). Goodness-of-fit was assessed by likelihood ratio χ^2 tests. Under the full model, a Cholesky decomposition with additive genetic, shared environmental and unique environmental factors was fitted to the data. This model tested whether the magnitude of the genetic and environmental effects was different for males and females and whether different genes or environmental factors operate in males and females. The latter was modelled as an imperfect correlation between the shared environmental or the genetic factors in opposite-sex twins. The first factor in males was correlated with the first factor in females, the second factor in males with the second factor in females, and so on. The full model was reduced by constraining either the genetic or the shared environmental factors to zero. By reducing the genetic and shared environmental factor structure to four factors it was tested whether sensation seeking mediated the genetic and environmental influences on alcohol and tobacco use.

Table 5.2 *Sensation seeking scores (with standard deviations) for alcohol abstainers and drinkers and for nonsmokers and smokers.*

	males			
	abstainer (n = 676)	drinker (n = 836)	nonsmoker (n = 1127)	smoker (n = 385)
TAS	40.72 (9.4)	42.16 (8.7)	41.22 (9.0)	42.39 (9.2)
ES	34.73 (6.6)	34.98 (7.5)	34.63 (6.9)	35.55 (7.7)
BS	37.33 (6.5)	39.54 (6.7)	37.87 (6.4)	40.53 (7.1)
DIS	32.44 (6.4)	37.75 (7.1)	34.40 (6.9)	38.24 (7.6)
	females			
	abstainer (n = 1138)	drinker (n = 673)	nonsmoker (n = 1373)	smoker (n = 438)
TAS	36.26 (9.8)	38.27 (9.4)	36.84 (9.8)	37.54 (9.5)
ES	33.44 (7.1)	35.54 (7.6)	33.88 (7.2)	35.29 (7.9)
BS	36.90 (7.3)	39.70 (7.3)	37.33 (7.3)	39.83 (7.6)
DIS	28.99 (6.1)	33.50 (6.7)	29.91 (6.3)	33.05 (7.2)

Results

More males (55.3%) than females (37.2%) reported to have ever used alcohol ($p < 0.001$). This sex difference was not observed for smoking, 25.5% of the males and 24.2% of the females reported to have ever smoked ($p = 0.20$). A multivariate analysis of variance, with alcohol use (never, ever), smoking (never, ever) and sex as between subject factors, was used to investigate whether alcohol and tobacco users had higher means on the four sensation seeking scales than non-users. Table 5.2 shows for males and females, the means and standard deviations on the sensation seeking scales according to alcohol use (never, ever) and smoking (never, ever). A significant main effect for alcohol use ($p < 0.001$) was found. Those who reported to have used alcohol had significantly higher means on the sensation seeking scales, especially on Boredom Susceptibility and Disinhibition. Smokers were significantly higher on sensation seeking compared to non-smokers ($p < 0.001$), except for Thrill and Adventure Seeking ($p = 0.44$ for the univariate test). The main effect for sex was also significant ($p < 0.001$), males had higher means on sensation seeking than females. Multivariate analysis of variance showed that there were no significant

interactions between the effects of alcohol use, smoking and sex.

The correlations between the four sensation seeking scales and initiation of alcohol and tobacco use are given in Table 5.3. Only small to moderate correlations were found. The subscales that correlated best with alcohol use and smoking were Boredom Susceptibility ($r = 0.19$ - 0.24) and Disinhibition ($r = 0.28$ - 0.46), for both males and females. For females, a moderate correlation was also found between alcohol use and Experience Seeking ($r = 0.17$).

Table 5.3 *Phenotypic correlations between Sensation Seeking, Alcohol Use and Smoking. Lower triangular males (N=1484); upper triangular females (N=1780).*

	TAS	ES	BS	DIS	ALC	SMO
TAS	-	.41	.22	.25	.13	.05
ES	.40	-	.33	.33	.17	.10
BS	.16	.21	-	.46	.24	.19
DIS	.27	.20	.41	-	.41	.28
ALC	.09	.03	.21	.46	-	.53
SMO	.08	.07	.22	.31	.61	-

TAS = Thrill and Adventure Seeking; ES = Experience Seeking; BS = Boredom Susceptibility; DIS = Disinhibition; ALC = alcohol use; SMO = smoking.

Genetic Analysis

Table 5.4 shows the twin pair correlations for each sensation seeking scale and for alcohol use and smoking. As expected for a personality trait, the MZ twin pair correlations for TAS, ES and BS are about twice the DZ twin pair correlations, indicating additive genetic influences. For Disinhibition, the pattern of twin pair correlations suggest that there might be some additional shared environmental influences. For alcohol use and smoking the pattern of twin pair correlations suggest both additive genetic and shared environmental influences. A Cholesky decomposition with additive genetic, shared environmental and unique environmental factors was fitted to the observed correlation matrices. The model fitting results are given in Table 5.5. The fit of the full model was marginal. The magnitude of the genetic and environmental effects was significantly different for males and females (model 3 vs model 1: $\Delta\chi^2 = 152.23$, df = 63, $p < 0.01$). There was evidence that different shared environmental factors operate in males and females (model 2).

Table 5.4 *Twin correlations for sensation seeking, alcohol use and smoking.*

	MZM (n=265)	DZM (n=245)	MZF (n=349)	DZF (n=309)	DOS (n=464)
TAS	.65	.42	.65	.30	.26
ES	.51	.36	.59	.32	.25
BS	.48	.31	.52	.35	.24
DIS	.62	.46	.60	.44	.29
ALC	.84	.83	.87	.72	.56
SMO	.87	.69	.91	.74	.56

MZM = monozygotic male twins; DZM = dizygotic males; MZF = monozygotic females; DZF = dizygotic females; DOS = dizygotic opposite-sex twins.

The correlation between the shared environmental factors in opposite-sex twins could not be constrained to unity without a significant reduction in the goodness of fit ($\Delta\chi^2 = 15.72$, df = 6, $p = 0.02$). Both additive genetic and shared environmental factors were needed to explain the data. Constraining the shared environmental factors (model 4) or the genetic factors (model 5) to zero gave a significant deterioration in fit compared to model 1.

Table 5.5 *Model fitting results multivariate model (triangular decomposition).*

Model	χ^2	df	p	AIC
1. sex differences, r(c) free	256.13	210	0.016	-163.87
2. sex differences, r(c) = 1	271.85	216	0.006	-160.15
3. no sex differences	408.36	273	0.000	-137.64
4. no shared env. factors, r(g) free	538.28	252	0.000	34.28
5. no genetic factors, r(c) free	368.95	252	0.000	-135.05
6. no specific genetic factors for ALC and SMO	264.22	216	0.014	-167.79
7. no specific genetic and shared env. factors for ALC and SMO	271.72	222	0.013	-172.28

The genetic and the shared environmental factorization could be reduced to four factors without a significant deterioration in the goodness of fit (models 6 vs model 1: $\Delta\chi^2 = 8.09$, df = 6, $p = 0.23$; model 7 vs model 1: $\Delta\chi^2 = 15.59$, df = 12, $p = 0.21$). Thus, the four genetic and shared environmental factors that influenced the sensation seeking scales could entirely explain the genetic and shared environmental variances in alcohol use and smoking.

The proportion of the total variance that is explained by genetic and environmental factors for each variable is given in Table 5.6 for males and in Table 5.7 for females. There was a major influence of genetic factors on individual differences in Sensation Seeking (19-55%). There was an additional effect of shared environmental factors (9-38%), especially for Disinhibition (37% and 38%, for males and females) and for Boredom Susceptibility in females (31%). Alcohol use in males was mainly influenced by shared environment (86%). For females, both shared environmental factors (61%) and moderate genetic influences (27%) contributed to individual differences in alcohol use. Variance in smoking was explained by shared environment (52% and 69%) and by genetic factors (39% and 28%), for males and females.

The genetic and environmental covariance matrices were standardized, giving the genetic and environmental correlations between the sensation seeking scales and initiation of alcohol and tobacco use (Tables 5.6 and 5.7). The genetic and environmental correlations are a measure of the extent to which the same genes or environmental factors contribute to the observed phenotypic correlation. For males, there was a high genetic correlation between Boredom Susceptibility and alcohol use ($r = 0.85$) and smoking ($r = 0.86$), suggesting that the same genes influence alcohol and tobacco use and Boredom Susceptibility (Table 5.6). Moderate shared environmental correlations were found between Disinhibition and alcohol use ($r = 0.52$) and smoking ($r = 0.66$). There were only small unique environmental correlations between sensation seeking and alcohol use and smoking in males, except for Disinhibition and alcohol use ($r = 0.63$). For females, a high genetic correlation between alcohol use and Disinhibition ($r = 0.90$) and a high genetic correlation between smoking and Boredom Susceptibility ($r = 0.98$) was observed (Table 5.7). Moderate shared environmental correlations were observed between Disinhibition and alcohol use ($r = 0.44$) and between Disinhibition and smoking ($r = 0.46$). The unique environmental correlations between sensation seeking and alcohol and tobacco use in females ranged from 0.09 to 0.54.

Table 5.8 summarizes the contribution of the genetic and environmental components to the phenotypic correlations. Only the sensation seeking scales that correlated highest with initiation of alcohol and tobacco use are shown. Due to the

Table 5.6 *Genetic and environmental correlations and variances for males.*

	TAS	ES	BS	DIS	ALC	SMO
genetic correlations						
TAS	1.0					
ES	.34	1.0				
BS	.48	.59	1.0			
DIS	.59	.37	.36	1.0		
ALC	.84	.46	.85	.66	1.0	
SMO	.17	.15	.86	.12	.63	1.0
h^2	*0.49*	*0.31*	*0.22*	*0.26*	*0.04*	*0.39*
shared environmental correlations						
TAS	1.0					
ES	.99	1.0				
BS	.09	.17	1.0			
DIS	.29	.34	.71	1.0		
ALC	.02	.02	.20	.52	1.0	
SMO	.13	.13	.03	.66	.79	1.0
c^2	*0.20*	*0.21*	*0.20*	*0.37*	*0.86*	*0.52*
unique environmental correlations						
TAS	1.0					
ES	.22	1.0				
BS	.02	.07	1.0			
DIS	.03	.08	.28	1.0		
ALC	.08	.05	.32	.63	1.0	
SMO	.06	.10	.14	.30	.57	1.0
e^2	*0.31*	*0.48*	*0.58*	*0.37*	*0.10*	*0.09*

h^2 = proportion of total variance due to additive genetic factors; c^2 = the proportion of the total variance due to shared environmental factors; e^2 = unique environmental variance.

Table 5.7 *Genetic and environmental correlations and variances for females.*

	TAS	ES	BS	DIS	ALC	SMO
genetic correlations						
TAS	1.0					
ES	.43	1.0				
BS	.18	.42	1.0			
DIS	.27	.49	.21	1.0		
ALC	.21	.23	.43	.90	1.0	
SMO	.21	.25	.98	.13	.43	1.0
h^2	*0.55*	*0.50*	*0.19*	*0.20*	*0.27*	*0.28*
shared environmental correlations						
TAS	1.0					
ES	.99	1.0				
BS	.75	.74	1.0			
DIS	.78	.77	.86	1.0		
ALC	.23	.24	.29	.44	1.0	
SMO	.04	.04	.02	.46	.59	1.0
c^2	*0.09*	*0.10*	*0.31*	*0.38*	*0.61*	*0.69*
unique environmental correlations						
TAS	1.0					
ES	.32	1.0				
BS	.15	.16	1.0			
DIS	.11	.07	.35	1.0		
ALC	.23	.20	.16	.16	1.0	
SMO	.09	.13	.08	.54	.85	1.0
e^2	*0.36*	*0.40*	*0.50*	*0.42*	*0.12*	*0.03*

low genetic variance for alcohol use in males (4%) the genetic covariances between alcohol use and sensation seeking are low and cannot contribute much to the phenotypic correlations. The association between Boredom Susceptibility and alcohol use in males could be attributed to correlated genetic and correlated environmental factors. For initiation of alcohol use in females, both correlated genetic factors and correlated shared environmental factors contributed to the correlation with Boredom Susceptibility, Disinhibition and Experience Seeking. The association between smoking initiation and Boredom Susceptibility was entirely explained by correlated genetic factors, for both males and females. The correlation between smoking and Disinhibition could be attributed to correlated shared environmental factors.

Table 5.8 *Decomposition of phenotypic correlations into genetic and environmental components.*

		r_{obs}	r_{exp}	G	C	E
males						
alcohol use	BS	0.21	0.24	0.08	0.08	0.08
	DIS	0.46	0.48	0.07	0.29	0.12
smoking	BS	0.22	0.28	0.25	0.00	0.03
	DIS	0.31	0.38	0.04	0.29	0.05
	ALC	0.61	0.66	0.08	0.53	0.05
females						
alcohol use	BS	0.24	0.27	0.10	0.13	0.04
	DIS	0.41	0.46	0.21	0.21	0.04
	ES	0.17	0.19	0.08	0.06	0.05
smoking	BS	0.19	0.23	0.23	0.00	0.00
	DIS	0.28	0.33	0.03	0.24	0.06
	ALC	0.53	0.55	0.12	0.38	0.05

r_{obs} = observed phenotypic correlation; r_{exp} = expected phenotypic correlation; $G = h_1 r_g h_2$, $C = c_1 r_c c_2$, $E = e_1 r_e e_2$, where r_g, r_c, and r_e denote the correlation between the genetic, shared environmental and unique environmental factors, respectively and h_1, c_1, e_1, and h_2, c_2, e_2 represent the square roots of the genetic and environmental variances for the first and second variable, respectively.

Discussion

The association between sensation seeking and initiation of alcohol and tobacco use was explored with a multivariate genetic model in a sample of 1632 Dutch adolescent twin pairs. The correlation between the variables was partitioned into genetic and environmental factors with a Cholesky decomposition. We tested whether sensation seeking mediated the genetic and environmental influences on alcohol and tobacco use.

Sensation seeking was moderately associated with initiation of alcohol use and smoking in adolescent twins. Those who reported to have used alcohol had higher means on the sensation seeking scales than those who had never used alcohol. This difference was most pronounced for Boredom Susceptibility and Disinhibition in both males and females, and for Experience Seeking in females. Smokers had higher means on Boredom Susceptibility and Disinhibition than those who had never smoked. Zuckerman (1994) reviewed the studies that examined the association between sensation seeking and alcohol and tobacco use in adolescents and found that Disinhibition, Boredom Susceptibility and Experience Seeking are the strongest correlates of adolescent alcohol use and smoking. The association between Disinhibition and alcohol use might be due to the items of the scale that are related to alcohol use (e.g. I feel best after taking a couple of drinks). However, after deleting the three alcohol related items from the scale, we found that Disinhibition was still significantly associated with alcohol use and smoking (results not shown).

Support was found for the hypothesis that sensation seeking mediates the genetic influences on alcohol use and smoking. All the genetic variance in alcohol use and smoking was explained by the four genetic factors on which the sensation seeking scales loaded. However, the genetic variance explained only a relatively small proportion of the total variance in initiation of alcohol use and smoking. The genetic correlations suggest that there are common genetic factors that influence Boredom Suceptibility, alcohol use and smoking. The association between Boredom Susceptibility and smoking was entirely due to correlated genetic factors, for both males and females. Part of the association between Boredom Susceptibility and alcohol use could be attributed to genetic factors that were highly correlated, the remainder of the association was due to modestly correlated environmental factors. The results suggest that the genetic predisposition to Boredom Susceptibility increases the risk to initiation of alcohol use and smoking in males and females. There is also evidence to suggest that there is a common set of genes that influences Disinhibition and alcohol use, especially for females. Evidence from a study of female Australian twins suggests that there is a significant genetic correlation

between Novelty Seeking and smoking initiation and between Novelty Seeking and alcohol problems (Madden et al., 1993). However, Heath et al., (1995) concluded that most of the genetic variance in smoking behavior could not be accounted for by mediational effects of personality, attitudinal or sociodemographic variables.

Our results showed that the small to moderate genetic influences on alcohol and tobacco use could entirely be attributed to the genetic variance in sensation seeking. This suggests that one of the pathways to initiation of alcohol use and smoking in adolescents is through the inheritance of personality characteristics that predispose to substance use. One of the other pathways to the initiation of substance use is through shared environmental influences. For both males and females, the shared environmental factors that influenced Disinhibition, alcohol use and smoking were moderately correlated. These correlated shared environmental factors explained most of the associations between Disinhibition and alcohol use and smoking, except for alcohol use in females for which correlated genetic factors also contributed to the association with Disinhibition. The lower correlation between the shared environmental factors in opposite-sex twins suggests that some of these shared environmental influences are sex-specific. Evidence from an adoption study in 653 adopted families suggested that there are sibling environmental effects on adolescent alcohol involvement (McGue, Sharma, and Benson, 1996). McGue et al. found that nonbiological siblings were significantly correlated for involvement with alcohol ($r = 0.24$) and that same-sex, similar-age adoptive siblings were substantially more similar ($r = 0.45$) than opposite-sex, dissimilar-aged adoptive siblings ($r = 0.05$). The shared environmental influences that contribute to the correlations between the shared environmental factors on alcohol use, smoking and Disinhibition remain to be identified. Sibling and peer influences are likely candidates.

We found substantial shared environmental influences on initiation of alcohol and tobacco use and small to moderate shared environmental effects on sensation seeking. Previously, we found no significant shared environmental effects on sensation seeking (Koopmans et al., 1995), although the pattern of twin correlations for Boredom Susceptibility and Disinhibition suggested some shared environmental influences. In the analyses reported in this paper, the addition of alcohol use and smoking to the multivariate genetic analysis may have increased the power to detect the shared environmental effects on Boredom Susceptibility and Disinhibition.

Part of the shared environmental influences on alcohol use and smoking are due to age of the twins. The effects of age contributes to differences between twin pairs and not to differences within twin pairs, thus increasing the estimates of the shared environmental factors. We did not account for the effects of age because there were no significant correlations between sensation seeking and age (Koopmans et al., 1995). Previously, we have found for both alcohol use and smoking, an increase in the prevalences with increasing age (Boomsma et al., 1994; Koopmans and Boomsma, 1996a). For initiation of alcohol use (Koopmans and Boomsma, 1996a), but not for smoking (Boomsma et al., 1994), there was evidence to suggest that there are different modes of inheritance in adolescents and young adults, with an increase of the genetic influences in young adults aged 17 years and older. In this study the sample was not divided into different age groups and there was not much evidence for a genetic influence on initiation of alcohol use in males. Because of this low heritability of alcohol use in males the association with sensation seeking could only be attributed to correlated shared environmental factors. It remains to be tested whether the genetic contribution to the association between alcohol use and sensation seeking increases in the young adult male twins.

In conclusion, there is evidence to suggest that sensation seeking mediates the genetic influences on initiation of alcohol use and smoking. Thus, one of the pathways to the genetic inheritance of initiation of substance use is through the inheritance of sensation seeking characteristics that predispose to substance use.

6

The Genetics of Initiation and Quantity of Alcohol and Tobacco Use

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Not much is known about the determinants of various aspects of substance use in adolescents. This study examined whether the inheritance of initiation of alcohol and tobacco use in adolescents is independent of the inheritance of level of consumption. Three alternative multifactorial threshold models were applied to data on alcohol and tobacco use in almost 1700 Dutch adolescent twin pairs. The three models that were considered are (i) single liability dimension (SLD); (ii) independent liability dimension (ILD); and (iii) combined model (CM). For both alcohol use and smoking, the combined model was the best fitting model. This model postulates that there are separate initiation and quantity dimensions, but allows for the possibility that there are some individuals who are so low on the liability to level of consumption that they are not using substances. Initiation of alcohol use in males was mainly due to shared environmental influences (92%). For females, shared environmental influences (54%) and genetic influences (41%) contributed to variance in initiation of alcohol use. The amount of alcohol consumption was influenced by genetic effects (32%) and shared environmental factors (44%), for both males and females. A small proportion of the abstainers were not drinking due to low exposure to the genetic and environmental risk factors which influence the amount of alcohol consumption. Smoking initiation was influenced by genetic factors (39%) and shared environmental influences (54%). The liability to quantity smoked was mainly influenced by genetic factors (86%). Less than 10% of the sample were potential smokers on the initiation dimension but became non-smokers due to their genetic predisposition on the quantity dimension.

Evidence from large scale population-based twin studies suggests that genetic factors contribute to individual differences in drinking behavior and smoking (e.g. Heath, 1995; Heath and Madden, 1995). An important issue, that most twin studies have not addressed, is whether the same or different genetic and environmental factors influence various aspects of substance use. For example, are initiation of alcohol use and level of consumption part of the same continuum of liability to alcohol use or are there independent genetic and environmental factors that determine initiation and the quantity of alcohol consumption? It is important to understand the determinants of different aspects of substance use because an incorrect definition of the phenotype can lead to biased estimates of the genetic and environmental factors (Heath et al., 1991a). If the same genetic and environmental factors determine whether or not a person is a drinker and how much alcohol is consumed, then exclusion of abstainers can lead to truncation of the distribution. In twin data this will lead to biased estimates of the heritability (Heath et al., 1991a; Neale et al., 1989). If the determinants of abstinence from alcohol are independent of the determinants of level of alcohol consumption then inclusion of abstainers in the analyses of consumption measures may confound two different modes of inheritance (Heath et al., 1991a). In his review of the genetic influences on drinking behavior, Heath (1995) discussed how different twin studies have used different definitions of abstinence, and have made different decisions about the inclusion of abstainers in analyses of quantity, frequency and total consumption measures.

Heath et al. (1991b) proposed three alternative multifactorial threshold models to test different assumptions about the determinants of initiation and quantity of alcohol use. Similar models were used to test whether the inheritance of smoking initiation was independent of the inheritance of smoking persistence (Heath and Martin, 1993) (formally, despite use of the same labels, the "combined" models used in the two papers make somewhat different assumptions). Briefly, these models are (i) single liability dimension (SLD) which assumes that the same genetic and environmental factors influence initiation and quantity of substance use, but to a different degree; (ii) independent liability dimension (ILD) which assumes that the genetic and environmental determinants of initiation of substance use are separate from the determinants of quantity consumed; and (iii) combined (CM) which postulates that there are separate initiation and quantity dimensions, but allows for the possibility that there are some individuals who are so low on the liability to level of consumption that they are not using substances. Up till now the application of these models required purpose-written software. In this paper we used Mx (Neale, 1995) to fit the multifactorial threshold models to contingency tables by method of maximum likelihood. Mx is a structural equation modeling package that is

specifically designed to fit genetic models to multiple groups.

Heath et al. (1991b) applied the models described above to data on alcohol use in adult Australian twins to test whether the inheritance of abstinence of alcohol is separate from that of quantity and frequency of alcohol consumption. Heath et al. found that there were separate dimensions for abstinence and for quantity and frequency, and showed that there were major shared environmental influences on abstinence of alcohol, and substantial genetic influences on both frequency and quantity of alcohol use. The best fitting model was the combined model, indicating that some individuals were abstaining due to the determinants of the quantity or frequency dimension. Similar models were applied to data on smoking initiation and smoking persistence in two cohorts of Australian twins (Heath and Martin, 1993). For the older cohort (aged 31 years and older) the independent liability dimension model gave the best fit to the data. The genetic effect on smoking persistence, explaining 53% of the total variance, was independent of the genetic and environmental effects on smoking initiation. For the young cohort (aged 18-30 years), Heath and Martin (1993) showed that the combined model gave the best description of the data, indicating that there were genetic and environmental factors which influenced both smoking initiation and smoking persistence and other factors which influenced only persistence. We will apply the three multifactorial threshold models to data on initiation and quantity of alcohol and tobacco use in a population based sample of Dutch adolescent twins.

There are three other twin studies that assessed adolescent alcohol use and smoking (Heath and Martin, 1988; Hopper et al., 1992; Maes et al., 1996a). None of these studies examined the inheritance of the level of consumption. In a study of 1400 adolescent Australian twin pairs, aged 11 to 18 years, twin associations for alcohol use and smoking were represented by log odds ratios (Hopper et al., 1992). Higher odds ratios in MZ male twins compared to DZ male twins, suggested that genetic factors played a role in determining alcohol use in male adolescents while for female twins, MZ and DZ odds ratios were equal, suggesting only shared environmental influences. For smoking, estimates indicated stronger genetic influences in males compared to females, although this difference was not formally tested. Retrospective information about abstinence from teenage alcohol use and age of onset of drinking was obtained from 1589 Australian twin pairs aged 20-30 years (Heath and Martin, 1988). Abstinence from teenage alcohol use was determined by both genetic and shared environmental factors, to differing degrees in males and females. Individual differences in age of onset of teenage drinking were explained by shared environmental influences (51%) in males and by genetic influences (44%) and shared environmental factors (14%) in females. The Virginia Twin Study of

Adolescent Behavioral Development assessed tobacco and alcohol use in 1412 twin pairs aged 8-16 years (Maes et al., 1996a). Maes et al. restricted the genetic analyses to twins aged 13-16 years and found that lifetime alcohol use was influenced by shared environmental factors (65%) while current use of alcohol was influenced by genetic factors (82%). For tobacco use, Maes et al. found that both lifetime and current use was explained for the most part by genetic factors (85 and 88%, respectively).

In our twin-family study of health-related behavior we have found previously that individual differences in initiation of alcohol and tobacco use could be attributed to shared environmental influences and small to moderate genetic influences (Boomsma et al., 1994; Koopmans and Boomsma, 1996a). In this paper the question is addressed whether the inheritance of initiation of alcohol and tobacco use in adolescents is independent of the inheritance of level of consumption. After identification of the correct liability model, the relative contribution of genetic and environmental factors to initiation and quantity of alcohol and tobacco use will be estimated.

Methods

Sample

This study is part of an ongoing twin family study on health-related behavior in a population based sample of Dutch adolescent and young adult twins (Boomsma et al., 1994; Koopmans and Boomsma, 1996a; Koopmans et al., 1995). The data were collected in 1991 from the first questionnaire on health and lifestyle that was mailed to 2375 adolescent twins and their parents. Completed questionnaires were returned by 1700 families. Age of the twins at the time of completing the questionnaire was between 12-24 years. Less than 4% of the sample was younger than 14 years and 7% was older than 21, the mean age was 17.7 years (± 2.26). Zygosity of the twins was determined by questionnaire items about physical similarity and frequency of confusion of the twins by family and strangers (Goldsmith, 1991; Magnus, Berg, and Nance, 1983). The sample was divided into five groups by sex and zygosity of the twins; 275 pairs of monozygotic males (MZM); 360 monozygotic female twins (MZF); 259 dizygotic males (DZM); 322 dizygotic females (DZF); 485 dizygotic opposite sex twins (DOS). There were 1592 twin pairs that provide complete data on alcohol use and 1676 twin pairs that provide complete data on smoking.

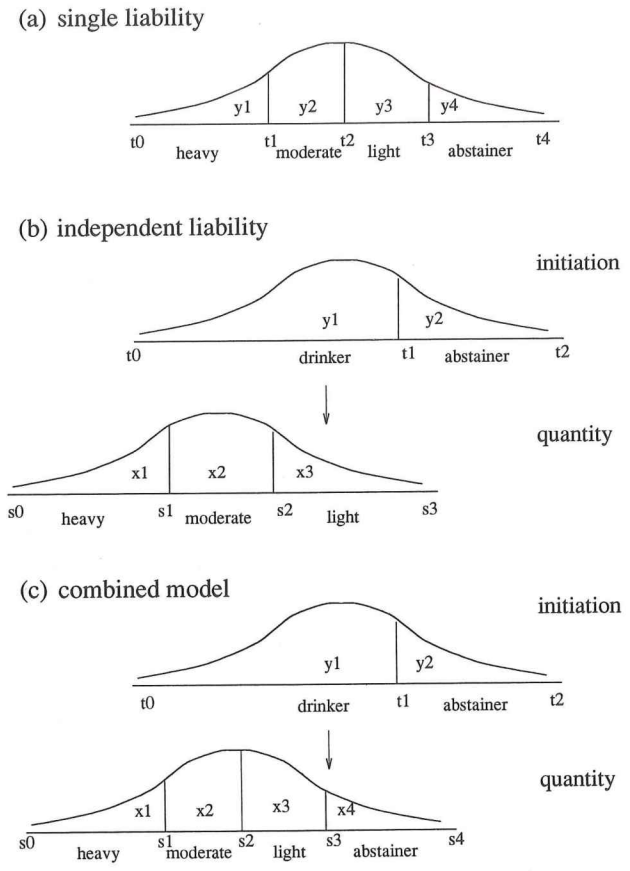

Figure 6.1 *Normal liability distribution for alcohol use under the single liability dimension (SLD) model (a) and normal liability distributions for initiation and quantity of alcohol use under the independent liability dimension (ILD) model (b) and the combined model (CM) (c).*

Measures

We asked twins whether they used or had used alcohol. The question could be answered with "No, seldom or never", "Yes, but not anymore" and "Yes". Those who answered "Yes, but not anymore (less than 2% of the sample) were classified as alcohol consumers. To assess the quantity of alcohol consumption, respondents were asked how many alcoholic drinks on average they used on normal weekdays and during the weekend. The total amount of alcohol consumed in a week was calculated by summing the number of drinks on weekdays and in the weekend. Those who answered "no, seldom or never" but indicated that they drank one or more glasses of alcohol in a week, were considered alcohol users. Smoking initiation was assessed with the questions "Have you ever smoked?" and "Are you a smoker?". Current smokers (17%) and former smokers (7.7%) were asked how many cigarettes, cigars or pipes on average they (had) smoked per day. Less than 1% of the sample reported that they smoked cigars or pipe. The twins were classified as nonsmokers if they answered no to the first question. Current and former smokers were classified according to the daily amount of cigarettes smoked. For each zygosity group two-way contingency tables were computed separately for alcohol consumption and smoking. To avoid empty cells, the quantity data were collapsed into three categories. Alcohol users were classified according to the number of drinks in a week; >10 drinks per week (heavy drinkers); 6-10 drinks per week (moderate drinkers); 1-5 drinks per week (light drinkers). Smokers were divided into heavy smokers (>10 cigarettes per day), moderate smokers (6-10 cigarettes per day) and light smokers (1-5 cigarettes per day).

Liability Models

Figure 6.1 shows three different models for the relationship between the genetic and environmental determinants of initiation and quantity of substance use. Heath et al. (1991b) postulated these three models to describe genetic and environmental influences on abstinence, frequency and quantity of alcohol consumption in adult Australian twins. In the following section we will describe the models for alcohol consumption, but the models equally apply to smoking initiation and quantity smoked. The single liability dimension (SLD) model (Figure 6.1a) assumes that the liability to alcohol use is unidimensional and is normally distributed and determines both initiation and quantity of alcohol consumption. Under this model the same genetic and environmental risk-factors predispose to initiation of alcohol consumption and to quantity consumed. Heavy drinkers are influenced by more extreme genetic or environmental factors than light drinkers or abstainers. The underlying normal

liability distribution is divided by thresholds into discrete categories which, in the case of the SLD model, corresponds to the observed categories. Individuals falling between threshold t_0 and t_1 will be heavy drinkers, those falling between t_1 and t_2 wil be moderate drinkers, etc. The probability that an individual falls in one of the four categories is given by y_1, y_2, y_3, and y_4 in Figure 6.1a and can be calculated by integrating a standardized normal distribution between the corresponding threshold values. The model predicts that the co-twins of heavy drinking twins are more likely to be heavy drinkers than are co-twins of light drinkers.

The independent liability dimension (ILD) model (Figure 6.1b) postulates two independent liability dimensions for initiation and quantity that are each determined by completely separate genetic and environmental factors. The initiation dimension determines whether a person will become a drinker or not. Individuals falling below the threshold t_1 are predicted to be drinkers. The quantity dimension determines whether an individual becomes a heavy, moderate or light drinker, given that he is a drinker, with conditional probabilities x_1, x_2, x_3 (see Figure 6.1b). The probabilities that an individual will be a heavy drinker, moderate drinker, light drinker or an abstainer are y_1x_1, y_1x_2, y_1x_3, y_2 , respectively, where y_1 and y_2 are the unconditional probabilities for initiating alcohol use, or remaining an abstainer, respectively. The ILD model predicts that the co-twin of an abstinent twin is more likely to abstain from alcohol, but if the co-twin of an abstinent twin is a drinker, he/she will not, on average, differ in the amount of alcohol consumption from drinking co-twins of drinking twins.

The combined model (CM) (Figure 6.1c) includes features of both the SLD and ILD models. The SLD and ILD models are nested under the more general combined model. Like the ILD model, the combined model allows for independent initiation and quantity dimensions, with different genetic and environmental factors that determines whether or not a person is a drinker and the total amount of alcohol consumption. However, like the SLD model, those on the quantity dimension can become abstainers due to low exposure to risk-factors which influence the amount of alcohol consumption. Thus, under the combined model there are two different routes to abstinence from alcohol. Under the combined model the co-twin of a drinking twin is more likely to become an abstainer than under the ILD model.

Model Fitting

For both alcohol use and smoking, substance use (heavy, moderate, light or abstaining) in the first twin was cross-classified with substance use in the second twin, resulting in 4×4 contingency tables for each zygosity group (see also Table 6.2 and 6.3). Models were fitted to the five contingency tables by method of maximum likelihood with Mx (Neale, 1995). Mx is a structural equation modeling package that is specifically designed to fit genetic models to multiple groups.

The analyses were based on the assumption that the observed discrete distribution (i.e. heavy, moderate, light drinker, abstainer) has an underlying continuous distribution that has been termed the liability (Falconer, 1989). Thresholds divide this normal liability distribution into discrete categories. The joint distributions of twin pairs for the liability dimensions are assumed to be bivariate normal, with correlation r_i being the correlation in liability between twins for the i-th zygosity group. For each of the liability dimensions the polychoric twin pair correlations and the thresholds were estimated by maximum likelihood. The thresholds were allowed to be different for males and females. Under the SLD model one twin correlation for each zygosity group and three thresholds for males (t_1, t_2, t_3) and females (t'_1, t'_2, t'_3) were estimated, with $t_0 = t'_0 = -\infty$ and $t_4 = t'_4 = \infty$ (see Figure 6.1a), giving in total 11 parameters to be estimated. Under the ILD and combined model separate twin correlations for the initiation and quantity dimensions were estimated for each zygosity group. For the initiation dimension two thresholds (t_1 and t'_1 were estimated, with $t_0 = t'_0 = -\infty$ and $t_2 = t'_2 = \infty$. Under the ILD model there was no abstinence category for the quantity dimension, leaving four thresholds to be estimated (s_1, s_2, s'_1, s'_2) with $s_0 = s'_0 = -\infty$ and $s_3 = s'_3 = \infty$. Under the combined model the same number of thresholds was estimated for the quantity dimension as for the SLD model (three thresholds for males and three for females). There were 16 parameters to be estimated under the ILD model, and 18 parameters under the combined model. The probability that a twin pair from the i-th zygosity group falls into the j,k-th cell of the i-th contingency table is calculated by

$$y(i,j,k) = \Phi(t_j, t_k) - \Phi(t_{j-1}, t_k) - \Phi(t_j, t_{k-1}) + \Phi(t_{j-1}, t_{k-1}) \qquad (6.1)$$

where $\Phi(t_j, t_k)$ represents the integrated bivariate normal density from $-\infty$ to t_j and from $-\infty$ to t_k with correlation r_i between twins. Equation 6.1 gives the unconditional probability y(i,j,k) for alcohol consumption (SLD model) or for initiation of alcohol use (ILD and combined models). For the quantity dimension of the ILD and combined models the conditional probability x(i,j,k) can be obtained by

$$x(i,j,k) = \Phi(s_j, s_k) - \Phi(s_{j-1}, s_k) - \Phi(s_j, s_{k-1}) + \Phi(s_{j-1}, s_{k-1}) \qquad (6.2)$$

where $\Phi(s_j, s_k)$ represents the integrated bivariate normal density from $-\infty$ to s_j and from $-\infty$ to s_k with correlation r'_i, and where r'_i is the twin correlation for liability to quantity.

Table 6.1 *Predicted probabilities for a twin pair under the single liability dimension (SLD), the independent liability dimension (ILD) and the combined model (CM).*

			twin2		
twin1	model	heavy	moderate	light	abstainer
heavy	SLD	y_{11}	y_{12}	y_{13}	y_{14}
	ILD	$y_{11}x_{11}$	$y_{11}x_{12}$	$y_{11}x_{13}$	$y_{12}x_{1.}$
	CM	$y_{11}x_{11}$	$y_{11}x_{12}$	$y_{11}x_{13}$	$y_{11}x_{14} + y_{12}x_{1.}$
moderate	SLD	y_{21}	y_{22}	y_{23}	y_{24}
	ILD	$y_{11}x_{21}$	$y_{11}x_{22}$	$y_{11}x_{23}$	$y_{12}x_{2.}$
	CM	$y_{11}x_{21}$	$y_{11}x_{22}$	$y_{11}x_{23}$	$y_{11}x_{24} + y_{12}x_{2.}$
light	SLD	y_{31}	y_{32}	y_{33}	y_{34}
	ILD	$y_{11}x_{31}$	$y_{11}x_{32}$	$y_{11}x_{33}$	$y_{12}x_{3.}$
	CM	$y_{11}x_{31}$	$y_{11}x_{32}$	$y_{11}x_{33}$	$y_{11}x_{34} + y_{12}x_{3.}$
abstainer	SLD	y_{41}	y_{42}	y_{43}	y_{44}
	ILD	$y_{21}x_{.1}$	$y_{21}x_{.2}$	$y_{21}x_{.3}$	y_{22}
	CM	$y_{11}x_{41} + y_{21}x_{.1}$	$y_{11}x_{42} + y_{21}x_{.2}$	$y_{11}x_{43} + y_{21}x_{.3}$	$y_{11}x_{44} + y_{21}x_{.4} + y_{12}x_{4.} + y_{22}$

Under the SLD model, y_{jk} = the probability that a twin pair falls in the j,k-th category of alcohol use. Under the ILD and combined model, y_{jk} = the probability that a twin pair falls in the j,k-th category of the initiation dimension; x_{jk} = the probability that a twin pair falls in the j,k-th category of the quantity dimension; $x_{j.}$ ='the probability that the first twin falls in the j-th category of the quantity dimension; $x_{.k}$ = the probability that the second twin falls in the k-th category of the quantity dimension.

The predicted probabilities for a twin pair under the three models are given in Table 6.1. Under the SLD model, y_{11} denotes the probability that both twins are heavy drinkers, y_{12} denotes the probability that the first twin is a heavy drinker and the second twin is a moderate drinker, and so on. Under the ILD and combined model, y_{11}, y_{22}, y_{12} and y_{21} denote the probabilities that twins both fall in the drinking category, both fall in the abstinent category, or are discordant for drinking status at the initiation dimension. The conditional probability that both twins are heavy

drinkers, the first twin is a heavy drinker and the second twin is a moderate drinker etc., is represented by x_{11}, x_{12} etc., $x_{j.}$ denotes the probability that the first twin falls into the j-th category of the quantity dimension, and $x_{.k}$ denotes the probability that the second twin falls into the k-th category of the quantity dimension. Under the combined model there are two routes to abstinence. For example, $y_{11}x_{14} + y_{12}x_{1.}$ gives the probability that both twins are drinkers on the initiation dimension (y_{11}) and the first twin is a heavy drinker while the second twin is an abstainer on the quantity dimension (x_{14}) plus the probability that the first twin is a drinker and the second twin is an abstainer on the initiation dimension (y_{12}) and the first twin is a heavy drinker ($x_{1.}$). Let p(i,j,k) denote the probability, under a given model, that a twin pair from the i-th zygosity group will fall in the j,k-th cell of the i-th contingency table. Under the SLD model, p(i,j,k) = y(i,j,k) in equation (1) for all i,j,k. Under the other two models, p(i,j,k) is the predicted probability as given in Table 6.1. The log-likelihood of a set of observations, under a given model, is given by

$$LL = \ln(c) + \Sigma\Sigma\Sigma\, f(i,j,k)\, \ln(p(i,j,k)) \qquad (6.3)$$

where c is a constant, and f(i,j,k) is the observed frequency of twin pairs from the i-th twin group in the j,k-th cell of the observed contingency table. Maximum likelihood estimates of the model parameters are obtained by maximizing this function with respect to the parameter values. The goodness-of-fit of nested models was assessed with likelihood-ratio chi-square tests.

Genetic Models

The three models were fitted to the data, estimating separate polychoric correlations for each zygosity group. For the model that gave the best description of the data, the twin correlations in liability were expressed as a function of genetic and environmental parameters based on the classical twin design (Neale and Cardon, 1992). For both the initiation and the quantity dimension, different genetic models were fitted. Under the full model (ACE), both additive genetic and shared environmental factors contribute to resemblances between twins. Sex-differences were tested by allowing the magnitude of the genetic and environmental effects to be different for males and females and by allowing the correlation between the shared environmental factors or the genetic factors in opposite-sex twins to be less than unity. If the phenotypic correlation in opposite-sex twins is lower than the same-sex dizygotic twin correlations this might be due to shared environmental effects that influence one sex but not the other, or genetic effects that are expressed in one sex but not in the other.

Table 6.2 *Twin concordance for average number of alcoholic drinks consumed in a week with proportions for first and second born twins of heavy, moderate, light drinkers or abstainers.*

	twin2	females					males				
twin1		>10	6-10	1-5	abst.	%	>10	6-10	1-5	abst.	%
MZ		n = 344					n = 259				
	>10	10	8	1	0	*5.5*	29	11	3	4	*18.1*
	6-10	5	23	12	8	*14.0*	11	20	5	7	*16.6*
	1-5	2	9	25	17	*15.4*	2	5	17	11	*13.5*
	abst.	2	7	12	203	*65.1*	3	11	10	110	*51.7*
	%	*5.5*	*13.7*	*14.5*	*66.3*		*17.4*	*18.1*	*13.5*	*51.0*	
DZ		n = 305					n = 230				
	>10	3	4	3	6	*5.2*	35	9	4	6	*23.5*
	6-10	6	15	7	8	*11.8*	7	15	9	7	*16.5*
	1-5	4	9	25	25	*20.7*	6	6	16	9	*16.1*
	abst.	2	7	19	162	*62.3*	6	6	7	82	*43.9*
	%	*4.9*	*11.5*	*17.7*	*65.9*		*23.4*	*15.7*	*15.7*	*45.2*	
DOS	fem.	n = 454									
male	>10	18	24	16	42	*22.0*					
	6-10	7	20	21	43	*10.6*					
	1-5	2	9	22	38	*15.6*					
	abst.	5	8	19	160	*42.3*					
	%	*7.1*	*13.4*	*17.2*	*62.3*						

If both additive genetic and shared environmental factors contribute substantially to individual differences in both males and females it is not possible to distinguish between these two effects with twin data (Eaves, 1977). Under the additive genetic (AE) model individual differences are explained by additive genetic influences and by environmental effects that are unique for an individual. Under the shared environmental (CE) model individual differences are explained by environmental influences that are shared between family members and by individual-specific environmental factors. For all models, different thresholds were estimated for males and females, allowing for differences in the prevalence of substance use between males and females.

Table 6.3 *Twin concordance for number of cigarettes smoked per day with proportions for first and second twins of heavy, moderate, light or non-smokers.*

	twin2	females					males				
twin1		>10	6-10	1-5	non	%	>10	6-10	1-5	non	%
MZ		n = 355					n = 272				
	>10	11	3	2	3	*5.4*	11	1	2	5	*7.0*
	6-10	4	7	3	3	*4.8*	4	8	2	4	*6.6*
	1-5	1	3	29	12	*12.7*	1	3	12	11	*9.9*
	non	2	4	12	256	*77.2*	3	4	7	194	*76.5*
	%	*5.1*	*4.8*	*13.0*	*77.2*		*7.0*	*5.9*	*8.5*	*78.7*	
DZ		n = 315					n = 252				
	>10	9	2	6	5	*7.0*	8	8	1	3	*7.9*
	6-10	1	1	1	8	*3.5*	4	4	5	8	*8.3*
	1-5	4	8	16	10	*12.1*	2	1	5	21	*11.5*
	non	6	9	19	210	*77.5*	7	6	8	161	*72.2*
	%	*6.3*	*6.3*	*13.3*	*74.0*		*8.3*	*7.5*	*7.5*	*76.6*	
DOS	fem.	n = 482									
male	>10	11	9	7	14	*8.5*					
	6-10	5	5	8	28	*9.5*					
	1-5	4	5	17	24	*10.4*					
	non	11	20	23	291	*71.6*					
	%	*6.4*	*8.1*	*11.4*	*74.1*						

Results

Table 6.2 shows the cross-classification of alcohol consumption in the first twin with alcohol consumption in the second twin. For opposite-sex twins the data were reordered so that alcohol consumption in male twins was cross-classified with alcohol consumption in the female cotwins. Table 6.2 also shows the proportions of heavy drinkers, moderate drinkers, light drinkers and abstainers for first and second born twins in each zygosity group. The proportion of drinkers is higher for males than for females, and males also consume more alcohol. Table 6.3 gives the contingency

tables for smoking. For smoking there are no sex differences in the proportion of smokers and non-smokers, nor in the quantity smoked.

The three different models of liability underlying the initiation and the quantity dimension were fitted to the data, estimating polychoric correlations for each zygosity group. Table 6.4 shows the estimated polychoric twin correlations for each zygosity group for the initiation and the quantity dimension under the full combined model. For initiation of alcohol use in males there was no difference between the MZ and DZ correlation, suggesting that there are no genetic influences but predominantly shared environmental influences on initiation of alcohol use in males. For initiation of alcohol use in females the MZ correlation was somewhat higher than the DZ correlation, indicating both genetic and shared environmental influences. The opposite-sex correlation was lower than the same-sex dizygotic twin correlations. This might be due to the different modes of inheritance for alcohol use in males and females. The pattern of twin pair correlations for quantity of alcohol consumed suggested both genetic and shared environmental influences. For smoking, the difference between the MZ and DZ correlations for the initiation dimension suggested that both shared environmental and genetic factors are important, whereas the pattern of correlations for the quantity dimension suggested that genetic factors are more important.

Table 6.4 *Estimated polychoric twin pair correlations (r) with 95% confidence intervals (CI) for the initiation and quantity dimensions under the full combined model and estimated thresholds.*

	alcohol				smoking			
	initiation		quantity		initiation		quantity	
	r	95%CI	*r*	95%CI	*r*	95%CI	*r*	95%CI
MZM	.92	.77 - .99	.78	.55 - .90	.91	.68 - .98	.84	.52 - .96
DZM	.91	.73 - .99	.71	.43 - .86	.76	.39 - .99	.65	.17 - .89
MZF	.95	.85 - .99	.75	.50 - .89	.94	.84 - .99	.88	.69 - .96
DZF	.84	.64 - .99	.56	.13 - .80	.82	.59 - 1.0	.44	-.09 - .79
DOS	.66	.43 - .92	.54	.23 - .74	.64	.40 - .71	.47	-.02 - .78
	initiation	quantity			initiation	quantity		
	t_1	s_1	s_2	s_3	t_1	s_1	s_2	s_3
males	0.31	-0.42	0.32	1.13	-0.44	-0.71	-0.05	0.78
females	-0.17	-1.11	-0.17	0.94	-0.55	-0.82	-0.25	0.94

Table 6.5 gives the goodness-of-fit for each liability model. For both alcohol use and smoking, the SLD model was rejected. The combined model gave the best description of the data. Thus, a person can be an abstainer or nonsmoker due to genetic and/or environmental factors that influence the initiation dimension or because that person is low on the quantity dimension that determines the amount of alcohol consumed in a week or the number of cigarettes smoked per day. The predicted marginal probabilities for alcohol use and smoking under the full combined model are represented in Figure 6.2. The percentage of alcohol abstainers in the total sample that comes from the quantity dimension is 8% (= 0.62x 0.13) in males (Figure 6.2a) and 7% in females (Figure 6.2b). For smoking, the percentage of non-smokers in the total sample that is low in liability on the quantity dimension is 7% in males (Figure 6.2c) and 5% in females (Figure 6.2d).

Table 6.5 *Goodness-of-fit of the single liability dimension (SLD), the independent liability dimension (ILD) and the combined model (CM) to the data on alcohol and tobacco use.*

		alcohol		smoking	
model	df	χ^2	p	χ^2	p
SLD	64	115.12	<0.001	116.87	<0.001
ILD	59	72.22	0.12	78.79	0.04
CM	57	48.97	0.77	67.68	0.16

Different genetic models were fitted both to the initiation dimension and to the quantity dimension under the combined model. The results for alcohol use are shown in Table 6.6. For the initiation dimension the full model with sex differences could not be reduced to the full model without sex differences (model 2) or to a simple additive genetic model (model 3) or a shared environmental model (model 4). All three models gave a significant reduction in the goodness of fit compared to the first model. Under the full model the additive genetic factor for the initiation dimension in males was estimated at zero. For the quantity dimension the full model without sex differences gave a good description of the data (model 5). The additive genetic model (model 6) and the shared environmental model (model 7) were rejected by the likelihood ratio test. The best fitting model was model 9. Under this model there were no genetic influences on initiation of alcohol use in males, both additive genetic and shared environmental effects on the initiation of alcohol use in females, and additive genetic and shared environmental influences that were sex-independent on the

quantity of alcohol consumed.

Table 6.7 gives the model fitting results for smoking. The initiation dimension was best described by a model without sex differences and with both additive genetic and shared environmental effects (model 2). For the quantity dimension the full model could be reduced to an additive genetic model without a significant increase of the chi-squared (model 6). Model 8, which fitted the full model without sex-differences to the initiation dimension and the additive genetic model to the quantity dimension, was the best fitting model.

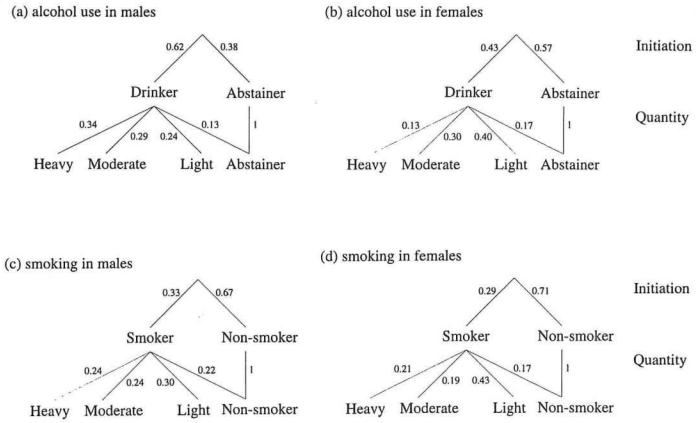

Figure 6.2 *Estimated probabilities under the full combined model for (a) alcohol use in males, (b) alcohol use in females, (c) smoking in males and (d) smoking in females.*

The parameter estimates for the best fitting models are given in Table 6.8. Shared environmental factors explained 92% of the total variance in the initiation of alcohol use in males. Individual differences in the initiation of alcohol use in females could be attributed to additive genetic factors (41%) and shared environmental effects (54%). The amount of alcohol consumed in a week was influenced by moderate genetic effects (32%) and shared environmental influences (44%) for both males and females. The magnitude of the genetic and environmental influences on smoking initiation and quantity smoked were the same for males and females. Individual differences in smoking initiation could be explained by shared environmental factors (54%) and moderate genetic influences (39%) whereas 86% of the total variation in the number of cigarettes smoked per day could be explained by genetic factors.

Table 6.6 *Model fitting results for alcohol use under the combined model (best fitting model is given in boldface).*

	genetic model					
	initiation	quantity	χ^2	df	*p*	AIC
1.	full	full	48.97	57	0.77	-65.03
2.	ACE	full	57.64	60	0.56	-62.38
3.	AE	full	82.95	61	0.03	-39.05
4.	CE	full	61.50	61	0.46	-60.50
5.	full	ACE	51.19	60	0.78	-68.81
6.	full	AE	63.96	61	0.37	-58.04
7.	full	CE	57.53	61	0.60	-64.27
8.	m = CE, f = ACE, r_c <1	ACE	51.19	61	0.81	-70.81
9.	idem, r_c = 1	ACE	**53.73**	**62**	**0.76**	**-70.27**

full = full model with sex-dependent effects and a correlation between the shared environmental factors in opposite-sex twins (= r_c) that is allowed to be less than 1; ACE = full model without sex differences; A = additive genetic factor; C = shared environmental factor; E = unique environmental factor; AE = additive genetic model; CE = shared environmental model; m = males; f = females; AIC = χ^2 - 2df, this is a measure of the parsimony of the model, a lower value of AIC indicates a more parsimonious model.

Table 6.7 *Model fitting results for smoking under the combined model (best fitting model is given in boldface).*

	genetic model					
	initiation	quantity	χ^2	df	*p*	AIC
1.	full	full	67.70	57	0.16	-46.30
2.	ACE	full	70.85	60	0.16	-49.15
3.	AE	full	86.13	61	0.02	-35.87
4.	CE	full	75.60	61	0.10	-46.40
5.	full	ACE	69.24	60	0.19	-50.76
6.	full	AE	70.34	61	0.19	-51.66
7.	full	CE	84.38	61	0.03	-37.62
8.	ACE	AE	**75.65**	**64**	**0.15**	**-52.35**

full = full model with sex-dependent effects and a correlation between the shared environmental factors in opposite-sex twins (= r_c) that is allowed to be less than 1; ACE = full model without sex differences; AE = additive genetic model; CE = shared environmental model. AIC = χ^2 - 2df, this is a measure of the parsimony of the model, a lower value of AIC indicates a more parsimonious model.

Table 6.8 *Proportions of the total variance in initiation and quantity of alcohol and tobacco use that are explained by additive genetic factors (h^2), shared environmental influences (c^2) and unique environmental effects (e^2) under the best fitting model (95% confidence intervals of the parameter estimates are given between parentheses).*

			h^2	c^2	e^2
alcohol	initiation	m	-	.92 (.81 - .98)	.08 (.02 - .19)
		f	.41 (.16 - .66)	.54 (.30 - .78)	.05 (.00 - .14)
	quantity		.32 (.00 - .70)	.44 (.09 - .72)	.24 (.14 - .39)
smoking	initiation		.39 (.00 - .68)	.54 (.25 - .95)	.07 (.02 - .16)
	quantity		.86 (.70 - .94)	-	.14 (.06 - .30)

m = parameter estimates for males; f = females

Discussion

Three different multifactorial threshold models were fitted to data on initiation and quantity of alcohol and tobacco use in adolescent twins. The results for alcohol use show that there is not one underlying continuum of liability to alcohol use. Initiation of alcohol use and the quantity of alcohol consumed are two independent dimensions that are each influenced by separate genetic and environmental factors. The combined model was the best fitting model. Under this model there are two routes to abstinence: a person can be an abstainer due to genetic and/or environmental factors that influence the initiation dimension or because that person is low on the quantity dimension that determines the amount of alcohol consumed in a week. Only a small proportion of the abstainers were not drinking alcohol due to low exposure to the genetic and environmental risk factors which influence the amount of alcohol consumption.

Why do adolescents start to use alcohol? Our results showed that for males, initiation of alcohol use is mainly due to shared environmental influences. For females, both shared environmental influences and moderate genetic influences contribute to variation in initiation of alcohol use. This is in line with a growing body of evidence that suggests that there is a major influence of the shared environment on onset of teenage drinking (Heath and Martin, 1988; Maes et al., 1996a) and on abstinence of alcohol in adults (Heath et al., 1991b; Prescott et al., 1994). Evidence from an adoption study by McGue et al. (1996) suggests that part of the shared environmental influences on adolescent alcohol use are due to sibling effects. Another aspect of the shared environment that has been shown to be inversely related to alcohol use in adolescents and adults is religious affiliation and religiosity (Heath and Martin, 1988; Kendler, Gardner, and Prescott, 1996; Maes et al., 1996a). In our sample of adolescent twins, religiosity of the mother was negatively associated with smoking in the twins but not with alcohol use (Rietveld et al., 1996). Religious involvement of the twins was found to be associated with alcohol use and smoking (Rietveld, 1996). Adolescents who were actively involved were less likely to smoke and drink than those who had a religious affiliation but were not actively involved.

Once an adolescent is a drinker, the amount of alcohol consumption is influenced by other genetic effects and shared environmental factors, that explain 32% and 44% of the variance in liability, respectively. For males, a genetic predisposition to alcohol consumption is expressed once drinking has started. For females, both initiation and level of alcohol consumption are influenced by genetic factors. Our model fitting results showed that these genetic factors are independent, although some of the genetic factors that contribute to quantity consumed might also

influence abstinence of alcohol in females, to some extent. The genetic influences on initiation of alcohol use in females might be mediated by heritable personality characteristics, such as unconventionality, sensation seeking and impulsivity (Eaves, Eysenck, and Martin, 1989; Koopmans et al., 1995), that are found to be associated with adolescent alcohol use (e.g. Bucholz, 1990; Zuckerman, 1994). It has been hypothesized that genetic factors that regulate the sensitivity to the pharmacological and toxicological effects of alcohol are involved in the individual differences in level of alcohol consumption (e.g. Collins, 1990a). Among individuals of Asian ancestry the alcohol-flush reaction, an unpleasant response to alcohol, is protective against heavy drinking and is associated with the mutant ALDH2*2 allele that produces an inactive aldehyde dehydrogenase enzyme (Thomasson et al., 1993). Caucasians do not have the heterogeneity at the ALDH2 loci found in Asians. It is still well established that there are substantial genetic influences on level of alcohol consumption in Caucasian adults (Heath, 1995; Heath et al., 1991b). The genetic mechanisms that are involved remain to be identified.

Smoking initiation was influenced by genetic and shared environmental factors that explain 39% and 54% of the variance in liability, respectively, for both males and females. Sensation seeking and other heritable personality traits that are associated with adolescent smoking might mediate the genetic influences on smoking initiation (Gilbert, 1995; Zuckerman, 1994). There is evidence to suggest that the same shared environmental factors influence smoking initiation and initiation of alcohol use (e.g. peers, siblings, religious affiliation) (Koopmans, van Doornen, and Boomsma, 1997).

The determinants of the liability to smoking initiation were independent from the genetic factors that influenced the quantity smoked. Less than 10% of the sample were potential smokers on the initiation dimension but became non-smokers due to their genetic predisposition on the quantity dimension. Our results suggest that once smoking is initiated, genetic factors determine whether an individual becomes a light, moderate or heavy smoker. These individual differences in the amount of tobacco use are most likely due to genetic differences in the sensitivity to nicotine, in the development of tolerance to nicotine and in the rewarding effects of nicotine (Collins and Marks, 1991; Pomerleau, 1995).

Our results show that future research into the genetic factors that determine individual differences in alcohol and tobacco use should make a distinction between different aspects of substance use and test whether the phenotypes under study are part of one underlying continuum of liability or whether there are independent liabilities. For both alcohol use and smoking, we have shown that there is not one underlying continuum of liability to initiation and quantity consumed.

7

Association between Alcohol Use and Smoking in Adolescent and Young Adult Twins: A Bivariate Genetic Analysis

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The association between alcohol use and smoking was examined in a large population-based sample of Dutch twins consisting of three age groups; young adolescent twins aged 12–14 years (n = 650 twin pairs), 15–16-years-old adolescent twins (n = 705 twin pairs), and young adult twins aged 17–25 years (n = 1266 twin pairs). For all three age groups, alcohol use and smoking were correlated (r = 0.5–0.6). Adolescents and young adults who smoked were more likely to drink alcohol than nonsmokers. The relation between alcohol use and smoking was also found within a twin pair; alcohol use in one twin was correlated with smoking in the cotwin. This finding suggested that familial factors contribute to the association between alcohol and tobacco use. With a bivariate genetic model, it was examined to what extent the comorbidity was due to genetic and environmental factors that predispose to both alcohol use and smoking. The genetic analyses showed that the underlying factors that influence alcohol and tobacco use and cause their association were different for adolescent and young adult twins. Initiation of alcohol use and smoking in adolescents (aged 12–16 years) was substantially influenced by the same shared environmental features. Alcohol and tobacco use in young adults were associated due to the same genetic risk factors.

Key Words: Alcohol Use, Smoking, Comorbidity, Twin Study, Bivariate Genetic Model.

ALCOHOL USE and smoking are associated—individuals who smoke are more likely to drink alcohol than nonsmokers.[1,2] Conversely, drinkers smoke more than abstainers. The link between drinking and smoking is found in both sexes and is consistent across different age groups and different nationalities.[1] The relationship between alcohol use and smoking is dose related in that heavy drinkers are heavy smokers and vice versa. Among alcoholics, over 90% were found to be smoking cigarettes and a substantial proportion of these alcoholics were heavy smokers.[2] In adolescents and young adults, the same association between drinking and smoking as in adults is found.[1,2] Not only are adolescents and young adults who drink more likely to smoke and vice versa, there is also a relationship between heavy drinking and heavy smoking in this age group. In an epidemiologic study of around 1000 young adults, dependent and nondependent smokers had an elevated risk for alcohol dependence compared with nonsmokers.[3] In a clinical sample of adolescents with alcohol or other drug problems (n = 166), 75% were daily smokers and 61% smoked half a pack of cigarettes or more per day, rates that are much higher than that of the general adolescent population.[4]

It is well known that chronic abuse of alcohol and smoking have negative health consequences[5] and that both are associated with increased mortality risks.[6,7] Furthermore, there is evidence that the combination of alcohol and tobacco use increases the risk for some diseases such as cancer of the mouth and throat.[2] Cigarette smoking also has health consequences in adolescents. It was found that smoking had negative effects on the level and growth of lung function in adolescents, with girls being more vulnerable than boys to the effects of smoking on the growth of lung function.[8] For prevention, it is important to gain insight into the factors that determine the initiation of alcohol use and smoking and the co-occurrence of these two behaviors during adolescence. Adolescence is a period of major transitions in which many adolescents start to experiment with both alcohol and cigarettes. Not much is known about the mechanisms underlying the association between smoking and drinking.[2,9] The comorbidity can be caused by genetic and/or environmental factors that predispose to both smoking and drinking. Environmental factors can be shared between family members (e.g., religious affiliation) or can be specific for an individual (e.g., stressful life events).

With a twin design, it is possible to disentangle the genetic and environmental contributions to the association between alcohol use and smoking. The rationale of the twin method is that monozygotic (MZ) and dizygotic (DZ) twins only differ in the extent to which they share their genes; MZ twins are genetically identical, whereas DZ twins have on average 50% of their genes in common. In the bivariate case, the correlation between trait A in one twin and trait B in the cotwin provides information about the underlying factors that contribute to the phenotypic association within a person. If genetic factors contribute to the association between alcohol use and smoking, the cross-trait correlation in DZ twins is expected to be about half the cross-correlation in MZ twins. If the cross-correlations are about

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equal for MZ and DZ twins then the association between alcohol use and smoking can be attributed to correlated shared environmental factors. If the association between alcohol use and smoking is induced by correlated unique environmental factors, the cross-trait cross-twin correlation is expected to be zero while the two traits are correlated within a person.[10]

Univariate twin and adoption studies have shown that individual differences in normal drinking behavior in adults are substantially influenced by genetic factors.[11] Genetic factors also contribute substantially to individual differences in various aspects of smoking behavior in adults.[12] Findings from twin studies of adolescent alcohol and tobacco use suggest that there are only small to moderate genetic influences on both drinking and smoking and that shared environmental influences are more important.[13–17] Although univariate results show that both smoking and drinking are influenced by genetic factors, the question is whether the comorbidity results from the same genes influencing both traits. For adults, there is indeed evidence from twin studies to suggest that correlated genetic factors contribute to the association between alcohol use and smoking.[18,19] Sher et al.[20] found among young adults evidence for a common vulnerability to alcohol use disorder and tobacco dependence. However, Sher et al. could not distinguish between a common genetic predisposition or common environmental influences to both dependencies. To our knowledge there are no published twin studies of the association between alcohol use and smoking during adolescence. The causes of comorbidity might be different for adolescents who experiment with alcohol and tobacco than for adults who may be regular smokers and drinkers.

In this paper, we explore the association between alcohol use and smoking in a population based sample of Dutch adolescent and young adult twins. Previously, we showed that 59% of the individual differences in smoking initiation could be attributed to environmental influences shared by twins and that genetic factors accounted for 31% of the total variance.[13] For alcohol use in adolescents aged 15–16 years, shared environmental factors (between 58 and 88%) were more important than genetic influences (ranging from 0 to 34%), whereas for young adults (aged 17 years and older), 43% of the variance in alcohol use could be attributed to genetic factors and 37% to shared environment.[16] Thus, we found that both individual differences in both alcohol and tobacco use among youngsters could be attributed to moderate genetic influences and to substantial shared environmental influences. These findings raise the question to what extent the same genetic and the same environmental factors influence alcohol use and smoking in adolescents and young adults.

METHODS

Subjects and Measures

This study is part of an ongoing twin-family study of health-related behavior.[13,16,21,22] Questionnaires on health and lifestyle were mailed in 1991 and 1993 to adolescent twins and their parents. Twin families were recruited by asking all city councils in The Netherlands for addresses of twins aged 13–22 years. An initial positive response was received from 252 city councils that supplied 3859 addresses; 177 addresses were available from other sources. After contacting these 4036 families by letter, 2375 twin families indicated that they were willing to complete a questionnaire on health and lifestyle and 1700 families returned these questionnaires in 1991. Data from three families were entered twice by mistake, leaving a total of 1697 families. In 1993, a second questionnaire was mailed to the 4036 families that had been contacted before and to 1987 new families. Additional addresses of new twin families were obtained from city councils that had reacted positively to our request, but were not able to furnish addresses in time for the first wave of data collection. The new addresses included several of the larger cities in the Netherlands. At the second measurement occasion, we obtained questionnaires from 1974 families; 959 families participated for the second time; 877 families came from the new addresses; 138 families were contacted before in 1991 but had not responded at the time. In total, we have studied 2712 families measured at two different occasions, with 959 families participating twice. Results are reported for the 1697 families that participated in 1991 and for the additional 1015 families that participated for the first time in 1993.

Age of the twins was between 12 and 25 years. The mean age of the twins at the first measurement occasion was 17.7 years (SD = 2.3), 4% of this sample was younger than 14 years and 7% was 21 years or older. The mean age of the twins that participated for the first time in 1993 was 16.0 years (SD = 2.7). In this group, 29% of the sample was younger than 14 years and 7% was 21 years or older.

Zygosity of the twins was determined by questionnaire items about physical similarity and frequency of confusion of the twins by family and strangers.[23,24] The classification of zygosity was based on a discriminant analysis, relating the questionnaire items to zygosity based on bloodgroup polymorphisms and DNA fingerprinting in a group of 131 same-sex adolescent twin pairs who participated in a study of cardiovascular risk factors.[25] In that sample, zygosity was correctly classified by questionnaire in 95% of the cases. A subsample of 96 same-sex twins, aged 16 years at the time, participated both in our study and in a longitudinal study of brain development.[26] For these same-sex twins, zygosity was based on blood polymorphisms. The agreement between zygosity based on the questionnaire and zygosity based on blood polymorphisms was 92%. Compared with the classification based on blood polymorphisms, there were 8 MZ twin pairs who were mistakenly assigned as DZ twins by the questionnaire. The total sample was divided into five groups by sex and zygosity; monozygotic males (MZM) and females (MZF), dizygotic males (DZM), and females (DZF) and dizygotic opposite sex twins (DOS).

The questionnaire contained questions about alcohol and tobacco use, sport activities, health, socioeconomic status, religion, and a number of personality factors. In the first questionnaire we asked the twins whether they used or had used alcohol. The question could be answered with "No, seldom or never," "Yes, but not any more" and "Yes." Less than 2% of the sample of twins answered "yes, but not any more." Therefore, the last two answers were collapsed into one category, leaving a dichotomous variable for alcohol use. Those who answered "No, seldom or never" but indicated that the quantity of alcohol they consumed in a week was one or more glasses, were considered alcohol users. Smoking was assessed with the question, "Have you ever smoked?" which could be answered with "No" or "Yes." In the second questionnaire, we asked, "Have you ever used alcohol?" and "Have you ever smoked?" The response categories were "No," "A few times just to try," and "Yes." Those who answered, "A few times just to try," were not considered as alcohol users or smokers. Thus, the variables under study are never used alcohol versus ever used alcohol and never smoked versus ever smoked. The data were analyzed for the 1697 twins that completed the first questionnaire and for the additional 1015 twin pairs that participated for the first time in 1993 at the second measurement occasion. In total, there were 2612 twin pairs available for analyses with complete data for both smoking and alcohol use.

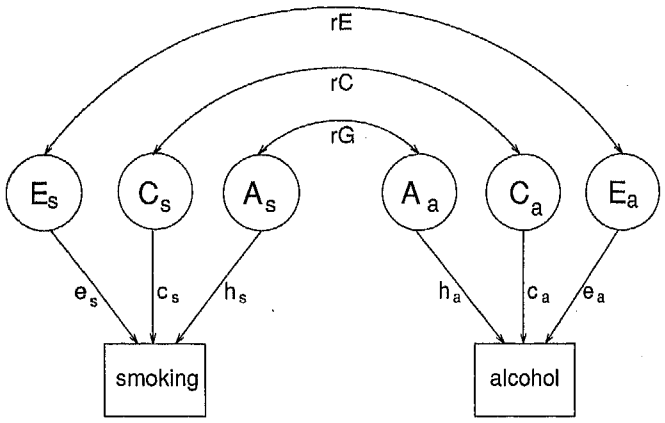

Fig. 1. Path diagram of the bivariate genetic model. Circles represent the latent variables and squares the observed variables. A_s and A_a represent the additive genetic influences on smoking and alcohol use, respectively, C_s and C_a the shared environmental effects, and E_s and E_a the unique environmental influences. The influence of the latent factors on smoking and alcohol use is given by path coefficients h, c, and e, with the subscripts *s* and *a* standing for smoking and alcohol use, respectively. The path coefficients equal the standardized regression coefficients and must be squared to equal the proportion of variance accounted for in the observed variable. The phenotypic correlation between alcohol use and smoking is decomposed into that due to the correlation between the genetic factors (rG), the correlation between the shared environmental effects (rC) and the correlation between the unique environmental factors (rE). The phenotypic correlation can be expressed as $rP = h_s\, rG h_a + c_s\, rC c_a + e_s\, rE e_a$.

Statistical Analysis

Quantifying the genetic and environmental factors that contribute to a dichotomous variable is possible by assuming that the variable has an underlying continuous distribution.[27] This underlying continuous variable has been termed the liability. The liability can be due to multiple genetic and environmental influences, giving a normal distribution in liability. A threshold divides the distribution into two classes, e.g., smokers and nonsmokers. The correlation in liability, between two family members for example, is called the tetrachoric correlation. We used PRELIS2[28] to estimate the tetrachoric correlations between twins. For each pair of variables (e.g., drinking in twin 1 and drinking in twin 2; smoking in twin 1 and drinking in twin 2), a two-by-two contingency table was obtained from which the maximum likelihood estimate of the tetrachoric correlation was computed by PRELIS2, under the assumption that the two variables have a bivariate normal distribution. Putting these correlations together results in a four-by-four correlation matrix, giving the correlations between alcohol use and smoking of first and second born twins. The matrix of tetrachoric correlations was computed for each zygosity group. For opposite-sex twins correlations between males and females were computed. The correlation matrices and their asymptotic weight matrices were used for genetic analyses.

A general bivariate genetic model was fitted to the data to test for the genetic and environmental contributions to the variance and covariance of alcohol use and smoking.[10,29] Figure 1 represents the path diagram of the full bivariate model. The variation in alcohol use and smoking is decomposed into genetic effects, environmental effects shared by siblings growing up in the same family, and individual specific environmental effects. The phenotypic correlation between alcohol use and smoking can be decomposed into three parts: a correlation between the genetic factors that influence alcohol use and smoking (rG); a correlation between the shared environmental influences on alcohol use and smoking (rC); and correlated individual specific environmental influences for alcohol use and smoking (rE). Under the full model, the genetic and the two environmental correlations were estimated. Several submodels were fitted to the data by constraining one or more correlations between the latent factors to zero. For example, the hypothesis that the correlation between alcohol use is induced by correlated environmental factors was tested by constraining the genetic correlation (rG) to zero. The hypothesis that alcohol use and smoking are correlated due to correlated genetic factors can be tested by constraining both the shared environmental correlation (rC) and the unique environmental correlation (rE) to zero. Sex differences were assessed by estimating different parameters for males and females and by estimating in opposite-sex twins the correlation between the shared environmental factors that influence males and the shared environmental factors that influence females. If this correlation is less than unity, this implies that different environmental factors influence alcohol use and smoking in males and females, at least to some extent. The bivariate genetic models were fitted to the data by weighted least squares using Mx.[30] The weight matrices, which are required for weighted least squares estimation, were computed with PRELIS2 and consisted of the asymptotic covariance matrix of the observed correlations. For each model an overall χ^2 test of the goodness-of-fit of the model was obtained. The goodness-of-fit of each submodel was compared with the fit of the full model by likelihood ratio χ^2 tests, with degrees of freedom equal to the number of parameters that are fixed to zero. For each parameter estimate Mx computed likelihood based confidence intervals.[31]

RESULTS

Most adolescents take up the habits of drinking and smoking between ages 15 and 16. Figure 2 shows that the percentage of adolescent boys and girls who have used alcohol increased after the age of 14 and stabilized after the age of 17. The percentage of adolescents who reported that they had ever smoked is shown in Figure 3. The number of smokers increased from around 15% at age 15–16 to around 35% after the age of 17. Based on these age differences in the prevalence of alcohol use and smoking, the sample was divided into three age groups: 12- to 14-year-old twins (n = 650 twin pairs); 15- to 16-year-old twins (n = 705); and 17- to 25-year-old twins (n = 1266; mean age 19.44, SD = 1.56).

Table 1 shows the percentages of alcohol users and smokers for males and females in these three age groups. Alcohol use is more common in males than in females. Between the ages of 15 and 16 years, 46% of the males and 38% of the females stated that they had used alcohol. After the age of 17 years, around 78% of the males and 55% of the females had used alcohol. For all three age groups, the sex differences in alcohol use were highly significant [χ^2 (1) = 5.87, p = 0.02 for 12–14 years olds; χ^2 (1) = 9.02, p = 0.003 for 15–16 years olds; χ^2 (1) = 142.39, $p < 0.001$ for 17–25 year olds]. For smoking, there were fewer differences between males and females. In the youngest group, 9% of the males and females had ever smoked. In the 15- to 16-year-old group, more females (21%) than males (17%) stated that they had smoked, but this difference was not significant [χ^2 (1) = 3.10, p = 0.08]. In the oldest group, more males (38%) than females (32%) had smoked [χ^2 (1) = 9.93, p = 0.002].

The association between alcohol use and smoking is shown in Table 2. For all three age groups, alcohol use and smoking were highly associated. The odds ratios were significant and ranged from 4.28 in young adult females to 8.89 in young adolescent boys. The relation between alcohol use and smoking can also be expressed as the tetra-

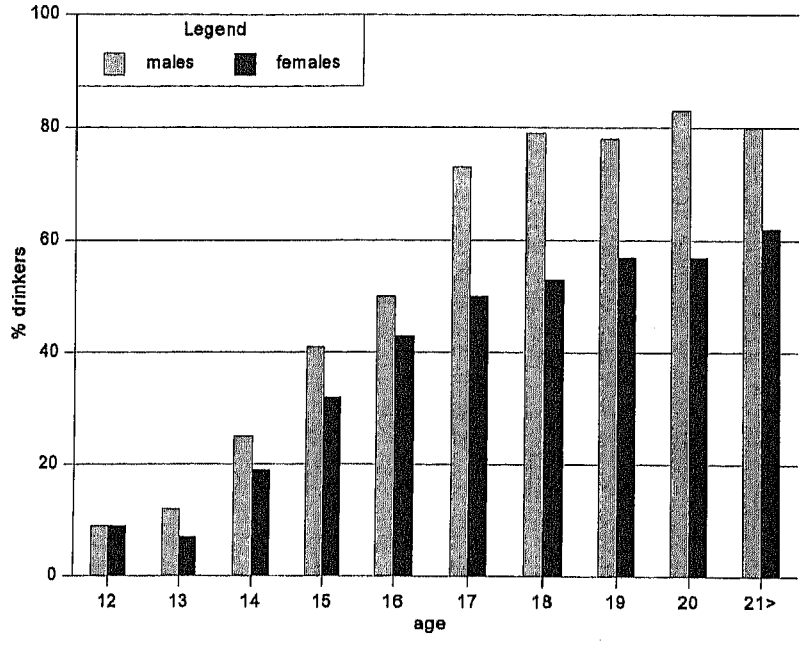

Fig. 2. Percentage alcohol users as a function of age.

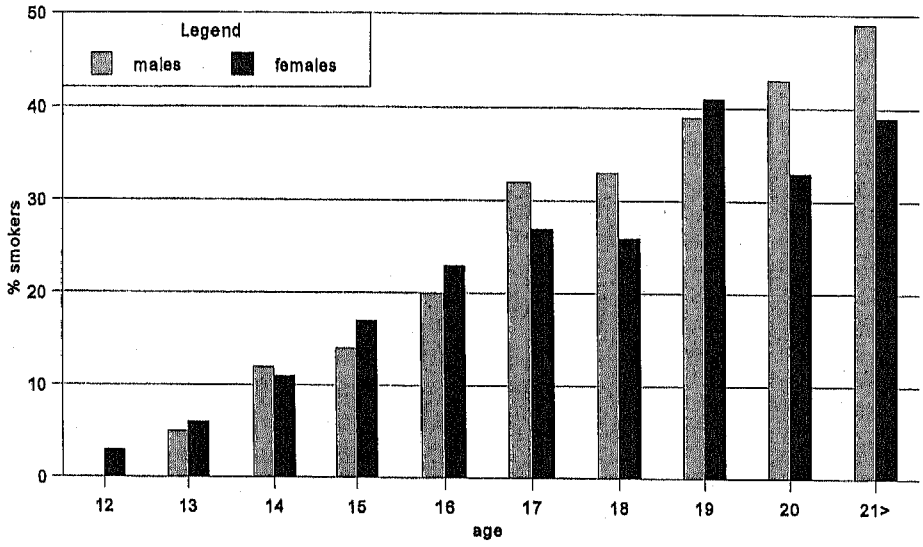

Fig. 3. Percentage smokers as a function of age.

Table 1. Percentage Alcohol Use and Smoking for Males and Females in Three Different Age Groups

	Males			Females		
Age (yr)	*n*	Alcohol use	Smoking	*n*	Alcohol use	Smoking
12–14	573	19.0	8.9	727	14.0	8.8
15–16	667	45.6	16.8	743	37.7	20.5
17–25	1154	77.7	38.2	1378	55.1	32.2

n, number of individuals, based on pairwise deletion.

choric correlation, i.e., the correlation in liability. This correlation was between 0.5 and 0.6 for all three age groups (Table 2). The question was addressed whether this phenotypic correlation between alcohol use and smoking could be attributed to correlated genetic factors and/or correlated environmental factors.

Table 3, 4, and 5 give for each age group the matrices of tetrachoric correlations between alcohol use and smoking of the first and second born twin. As explained in the introduction, the cross-correlations between the liability in alcohol use in one twin and liability in smoking in the cotwin (or vice versa) can give a first indication of the underlying factors that explain the observed correlation between alcohol use and smoking. For 12- to 14-year-old twins (Table 3) and 15- to 16-year-old twins (Table 4), there was not much difference between the cross-correlations for

Table 2. Magnitude of the Association between Alcohol Use and Smoking for Three Different Age Groups

	Males			Females		
Age (yr)	OR	95% CI	*r* (SE)	OR	95% CI	*r* (SE)
12–14	8.89	4.83–16.37	0.61 (0.07)	6.63	3.83–11.46	0.54 (0.07)
15–16	6.15	3.77–10.02	0.55 (0.06)	4.78	3.27–6.99	0.52 (0.05)
17–25	5.68	3.85–8.37	0.53 (0.04)	4.28	3.31–5.52	0.50 (0.04)

OR, odds ratio; CI, confidence interval; *r*, tetrachoric correlation; SE, standard error.

Table 3. Tetrachoric Correlations for Alcohol Use and Smoking for Each Zygosity Group in 12- to 14-year-old twins

		Males				Females			
		Alcohol		Smoking		Alcohol		Smoking	
		Twin 1	Twin 2	Twin 1	Twin 2	Twin 1	Twin 2	Twin 1	Twin 2
MZ		*n* = 112 pairs				*n* = 159 pairs			
Alcohol	Twin 1	1.00				1.00			
	Twin 2	**0.79**	1.00			**0.93**	1.00		
Smoking	Twin 1	0.60	0.51	1.00		0.24	0.34	1.00	
	Twin 2	0.83	0.68	**0.95**	1.00	0.53	0.69	**0.66**	1.00
DZ		*n* = 88 pairs				*n* = 118 pairs			
Alcohol	Twin 1	1.00				1.00			
	Twin 2	**0.73**	1.00			**0.75**	1.00		
Smoking	Twin 1	0.57	0.62	1.00		0.55	0.52	1.00	
	Twin 2	0.45	0.60	**0.95**	1.00	0.61	0.54	**0.88**	1.00
DOS		*n* = 173 pairs							
Alcohol	Male	1.00							
	Female	**0.45**	1.00						
Smoking	Male	0.60	0.32	1.00					
	Female	0.37	0.61	**0.71**	1.00				

Twin pair correlations for alcohol use and for smoking are given in boldface.

Table 4. Tetrachoric Correlations for Alcohol Use and Smoking for Each Zygosity Group in 15- to 16-year-old Twins

		Males				Females			
		Alcohol		Smoking		Alcohol		Smoking	
		Twin 1	Twin 2	Twin 1	Twin 2	Twin 1	Twin 2	Twin 1	Twin 2
MZ		*n* = 127 pairs				*n* = 162 pairs			
Alcohol	Twin 1	1.00				1.00			
	Twin 2	**0.74**	1.00			**0.93**	1.00		
Smoking	Twin 1	0.56	0.16	1.00		0.33	0.41	1.00	
	Twin 2	0.56	0.45	**0.75**	1.00	0.35	0.64	**0.92**	1.00
DZ		*n* = 103 pairs				*n* = 106 pairs			
Alcohol	Twin 1	1.00				1.00			
	Twin 2	**0.86**	1.00			**0.82**	1.00		
Smoking	Twin 1	0.67	0.39	1.00		0.53	0.28	1.00	
	Twin 2	0.26	0.57	**0.65**	1.00	0.50	0.39	**0.79**	1.00
DOS		*n* = 207 pairs							
Alcohol	Male	1.00							
	Female	**0.61**	1.00						
Smoking	Male	0.57	0.36	1.00					
	Female	0.24	0.61	**0.32**	1.00				

Twin pair correlations for alcohol use and for smoking are given in boldface.

MZ and DZ twins. For 17- to 25-year-old twins (Table 5) the DZ cross-correlations were on average lower than the MZ cross-correlations. Thus, for the youngest twins it is expected that the association between alcohol use and smoking is explained by correlated shared environmental factors, whereas for the oldest twins correlated genetic factors are expected. The pattern of twin pair correlations within a trait gives a first impression of the factors that contribute to the familial resemblances. For 12- to 14-year-old twins and 15- to 16-year-old twins, there were only small differences between the MZ and DZ twin pair correlations for alcohol use and for smoking (Table 3 and 4). This finding suggests that for these two age groups shared environmental factors are the most important influences on both alcohol use and smoking. For 17- to 25-year-old twins the pattern of twin pair correlations suggests that both

Table 5. Tetrachoric Correlations for Alcohol Use and Smoking for Each Zygosity Group in 17- to 25-year-old Twins

		Males				Females			
		Alcohol		Smoking		Alcohol		Smoking	
		Twin 1	Twin 2	Twin 1	Twin 2	Twin 1	Twin 2	Twin 1	Twin 2
MZ		*n* = 197 pairs				*n* = 266 pairs			
Alcohol	Twin 1	1.00				1.00			
	Twin 2	**0.78**	1.00			**0.81**	1.00		
Smoking	Twin 1	0.45	0.43	1.00		0.47	0.42	1.00	
	Twin 2	0.39	0.47	**0.83**	1.00	0.44	0.50	**0.88**	1.00
DZ		*n* = 202 pairs				*n* = 245 pairs			
Alcohol	Twin 1	1.00				1.00			
	Twin 2	**0.58**	1.00			**0.61**	1.00		
Smoking	Twin 1	0.57	0.33	1.00		0.43	0.30	1.00	
	Twin 2	0.24	0.56	**0.57**	1.00	0.24	0.44	**0.77**	1.00
DOS		*n* = 356 pairs							
Alcohol	Male	1.00							
	Female	**0.38**	1.00						
Smoking	Male	0.56	0.32	1.00					
	Female	0.21	0.56	**0.51**	1.00				

Twin pair correlations for alcohol use and for smoking are given in boldface.

Table 6. Model Fitting Results for 12- to 14-year-old twins

Model	*df*	χ^2	*p*	Δdf	$\Delta\chi^2$	*p*
1. Full sex-dependent model	14	19.84	0.14			
2. rE = 0 for males and females	16	23.25	0.11	2	3.41	NS
3. rC = 0 for males and females	16	77.94	0.00	2	58.10	< 0.01
4. rG = 0 for males and females	16	20.35	0.21	2	0.51	NS
5. rG = 0 and rE = 0 for m&f	18	23.51	0.17	4	3.67	NS
6. Model 5 with rc_{mf} = 1	20	27.67	0.12	2	4.16	NS
7. Model 5 without sex differences	25	44.18	0.01	7	24.34	< 0.01

rc_{mf}, correlation between shared environmental factors in opposite-sex twins.

genetic and shared environmental influences contribute to the familial resemblances in alcohol use and smoking (Table 5).

Genetic Analyses

For each age group, bivariate genetic models were fitted to the data to test whether correlated genetic factors and/or correlated environmental factors contributed to the observed phenotypic correlation between alcohol use and smoking. The models allowed for sex differences by estimating different factor loadings for males and females and by estimating the correlation between the shared environmental factors in opposite-sex twins. Under the full model genetic, shared environmental and unique environmental correlations were estimated. For each latent factor, the correlation was first fixed to zero for males and females separately. Model fitting results report the fixation of a correlation in both sexes unless the conclusion about the significance of a correlation was different for males and females.

Table 6 summarizes the model fitting results for the 12- to 14-year-old twins. Without a significant deterioration in the goodness-of-fit, the unique environmental correlation (model 2) and the genetic correlation (model 4) could be set to zero. By constraining the shared environmental correlation to zero (model 3), the χ^2 increased significantly ($\Delta\chi^2$ (2) = 58.10, $p < 0.01$). Thus, a model that explained the correlation between alcohol use and smoking by correlated shared environmental factors gave the best description of the data (model 5). The correlation between the shared environmental factors in opposite-sex twins could be set to unity (model 6), indicating that the same environmental factors influence smoking and drinking in males and females. However, a model that constrained the magnitude of the factor loadings to be equal for males and females gave a significantly worse fit, indicating that males and females differ in the extent to which they are influenced by genetic and shared environmental factors. The estimates of the genetic and environmental variances for alcohol use and smoking in 12- to 14-year-old males and females are given in Table 7. For both alcohol use and smoking, there is not much evidence for genetic variance. The confidence intervals showed that only the estimate of the heritability for alcohol in females (48%) was significantly different from zero. Shared environmental influences accounted for 78% and 48% of the total variance of alcohol use in males and females, and for 97 and 84% of the total variance of smoking in males and females. The correlation between the shared environmental factors that influenced alcohol use and the shared environmental factors that determined smoking was estimated at 0.88 in males and 0.86 in females (Table 7). For smoking in males, the unique environmental

Table 7. Parameter Estimates for Alcohol Use and Smoking with 95% Confidence Intervals in Italics

		12–14 years		15–16 years		17–25 years	
		Male	Female	Male	Female	Male	Female
Alcohol	h^2	0.01	0.48	0.01	0.10	0.48	0.75
		0.00–0.24	*0.19–0.74*	*0.00–0.21*	*0.00–0.32*	*0.27–0.91*	*0.46–0.92*
	c^2	0.78	0.48	0.84	0.86	0.32	0.10
		0.59–0.92	*0.23–0.74*	*0.68–0.94*	*0.65–0.99*	*0.00–0.52*	*0.00–0.36*
Smoking	h^2	0.03	0.01	0.00	0.27	0.66	0.33
		0.00–0.17	*0.00–0.36*	*0.00–0.45*	*0.00–0.62*	*0.43–0.86*	*0.21–0.54*
	c^2	0.97	0.84	0.71	0.67	0.19	0.57
		0.83–1.00	*0.61–0.95*	*0.34–0.87*	*0.33–0.96*	*0.04–0.39*	*0.38–0.69*
	rG	—	—	—	—	0.91	0.98
						0.63–1.00	*0.73–1.00*
	rC	0.88	0.86	0.52	0.67	—	—
		0.77–1.00	*0.67–1.00*	*0.37–0.77*	*0.49–0.98*		
	rE	—	—	0.97	1.00	—	—
				0.47–1.00	*0.14–1.00*		

h^2, proportion of total variance due to additive genetic factors; c^2, proportion of total variance due to shared environmental factors; total variance, $h^2 + c^2 + e^2 = 1$; the proportion of total variance due to unique environmental factors is e^2, $1 - (h^2 + c^2)$; rG, genetic correlation; rC, shared environmental correlation; rE, unique environmental correlation.

Table 8. Model Fitting Results for 15- to 16-year-old twins

Model	*df*	χ^2	*p*	Δdf	$\Delta\chi^2$	*p*
1. Full sex-dependent model	14	22.85	0.06			
2. rE = 0 for males	15	31.09	0.01	1	8.20	< 0.01
3. rE = 0 for females	15	24.60	0.06	1	1.75	NS
4. rE = 0 for males and females	16	33.25	0.01	2	10.40	< 0.01
5. rC = 0 for males and females	16	35.97	0.00	2	13.12	< 0.01
6. rG = 0 for males and females	16	25.41	0.06	2	2.56	NS
7. rG = 0 for males rG = 0 and rE = 0 for females	17	29.63	0.03	1	4.22	0.04
8. Model 6 with $rc_{mf} = 1$	18	33.83	0.01	2	8.42	< 0.05
9. Model 6 without sex-differences	24	56.91	0.00	7	27.28	< 0.01

rc_{mf}, correlation between shared environmental factors in opposite-sex twins.

variance was estimated at zero. The unique environmental variance not only consists of individual specific influences but also includes variance due to measurement errors. Thus, the unique environmental variance is expected to be greater than zero. The low estimate of the unique environmental variance is probably due to the high concordance for not smoking in same-sex male twins (r = 0.95; SE = 0.05 for both MZ and DZ twins). Because of the low rate of smoking in this age group, there were only a few discordant pairs in which one twin was a smoker and the other was not. In sum, the association between alcohol use and smoking in 12- to 14-year-old adolescents is to a large extent due to the same shared environmental influences, both in males and females.

The model fitting results for 15- to 16-year-old twins are shown in Table 8. The unique environmental correlation could be fixed to zero in females (model 3) but not in males (model 2). When the unique environmental correlation was constrained to be zero in both males and females (model 4), the goodness of fit was significantly worse than that of the full model. The shared environmental correlation was also significant, the model that fixed it to zero (model 5) was rejected by the likelihood-ratio test. Without a significant deterioration in the goodness of fit, the genetic correlation could be set to zero (model 6). Model 6, in which the correlation between alcohol use and smoking was explained by correlated shared environmental factors and correlated unique environmental factors, was the best fitting model. The model in which both the genetic and the unique environmental correlations were constrained to be zero for females (model 7) fitted the data less well. The sex differences were significant (model 8 and model 9). The correlation between the shared environmental influences in opposite-sex twins was estimated at 0.34 for alcohol use and 0.69 for smoking. This finding suggests that environmental effects on males are (to some extent) different from the environmental influences on females. Table 7 shows the parameter estimates for alcohol use and smoking in 15- to 16-year-old twins. Shared environmental influences were the most important factor, explaining 84 and 86% of the individual differences of alcohol use in males and females and 71 and 67% of the total variance in smoking in males and females. The confidence intervals showed that the lower bounds of the heritability estimates were all zero. The upper range of the confidence intervals suggested only small genetic influences, except for smoking in females. The association between alcohol use and smoking in 15- to 16-year-old twins was explained by correlated shared environmental factors in males and females, and by correlated unique environmental factors in males (Table 7). Although

Table 9. Model Fitting Results for Twins Aged 17 Years and Older

Model	*df*	χ^2	*p*	Δdf	$\Delta\chi^2$	*p*
1. Full sex-dependent model	14	4.25	0.99			
2. rE = 0 for males and females	16	7.44	0.96	2	3.19	NS
3. rC = 0 for males and females	16	7.07	0.97	2	2.82	NS
4. rG = 0 for males and females	16	12.53	0.71	2	8.28	0.02
5. rC = 0 and rE = 0 for m&f	18	9.50	0.95	4	5.25	NS
6. Model 5 with rc_{mf} = 1	20	13.23	0.88	2	3.73	NS
7. Model 5 without sex-differences	25	24.91	0.48	7	15.41	0.03

rc_{mf}, correlation between shared environmental factors in opposite-sex twins.

the unique environmental correlation for females is estimated at unity, the unique environmental factors explain only 6 and 4% of the total variance of smoking and drinking, respectively, and thus does not contribute much to the phenotypic correlation between alcohol use and smoking in females.

Table 9 gives the model fitting results for the 17- to 25-year-old twins. The full model gave an excellent fit to the data. In this age group, both the unique environmental correlation (model 2) and the shared environmental correlation (model 3) could be fixed to zero, while the genetic correlation was significant (model 4). The best fitting model was a model that explained the correlation between alcohol use and smoking by correlated genetic factors (model 5). The correlation between the shared environmental factors in opposite-sex twins could be set to unity without a significant loss of fit (model 6). The sex differences in the magnitude of the genetic and environmental influences were significant (model 7). For the 17- to 25-year-old twins the genetic factors were more important compared with the two younger age groups for both alcohol use and smoking (Table 7). The heritability for alcohol use was 48% in males and 75% in females and the heritability for smoking was 66% in males and 33% in females. Shared environmental factors contributed 32 and 10% to the variance of alcohol use in males and females and 19 and 57% to the variance in smoking. The confidence intervals showed that the estimates of the shared environmental influences on alcohol use were not significantly different from zero. There was an almost perfect correlation between genes that affect alcohol use and genes that affect smoking for both males and females.

DISCUSSION

The causes of the association between alcohol use and smoking in Dutch adolescents and young adults were analyzed. The question was addressed to what extent genetic and environmental factors contribute to the comorbidity of alcohol use and smoking. The twin sample was divided into three groups; young adolescent twins aged 12–14 years, 15- to 16-year-old adolescent twins, and young adults aged 17–25 years. For all three age groups, alcohol use and smoking were highly associated (r = 0.5–0.6). Adolescents and young adults who smoked were much more likely to drink alcohol than nonsmokers. The correlation between alcohol use and smoking was also found across twins; the liability to alcohol use in one twin was correlated with the liability to smoking in the cotwin. This suggests that familial factors are important. Genetic analyses showed that the underlying factors that cause the relationship between alcohol and tobacco use were different in adolescents and young adults.

Initiation of alcohol and tobacco use in adolescents aged 12–16 years are both substantially influenced by shared environmental factors. Not much evidence was observed for the influence of genetic factors. The estimates of the heritabilities ranged between 0 and 10%, with the exception of alcohol use in 12- to 14-year-old females (48%) and smoking in 15- to 16-year-old females (27%). A retrospective study on age of onset of teenage drinking in adult Australian twins aged 20–30 years showed that early versus late onset of drinking was more influenced by genetic factors in females, but by shared environmental influences in males.[14]

Alcohol use and smoking in young adults are largely due to genetic influences and to a less extent to shared environmental effects. For smoking in young adult females, more moderate genetic influences and substantial shared environmental effects were found. Findings from surveys of adult twins consistently show a significant genetic contribution to abstinence of alcohol use and smoking initiation in males and females.[11,12]

Although there is some evidence for genetic influences on alcohol use and smoking in adolescent females, shared environmental factors are most important in the risk of initiation of alcohol and tobacco use in both males and females. The genetic analyses for the adolescent twins showed that the association between drinking and smoking could be explained by shared environmental factors that predispose to both behaviors. For young adult twins, we found that the same genetic factors increase the risk of alcohol use and smoking in both males and females. The findings suggest that once an individual is exposed to the effects of alcohol or nicotine, genetic factors come into play and only those individuals with a certain set of genes will persist in using the substances.[32]

Which shared environmental features might be involved in the association between alcohol use and smoking? Probably most important is the influence of peers. Numerous studies have found that peer influence is one of the most important determinants of the initiation of both cigarette

smoking and alcohol use.[33–40] The peers who encourage the initiation of alcohol use are most likely the same peers who are involved in the onset of smoking. For example, in a prospective study of 2159 nonsmoking secondary schoolchildren aged 11–13, it was shown that the uptake of smoking was associated with having a boyfriend or a girlfriend who drank.[34]

Another aspect that comes to mind when we think of environmental features that are shared between twins is the influence of parents. Positive family relationships and parental monitoring were found to be protective factors for the onset of smoking and drinking.[39,41] However, parenting behavior is not merely an environmental factor. It is possible that parenting behavior is influenced by genetic factors and that these genetic factors are associated with the genetic vulnerability for substance (ab)use. For example, Kendler et al.[42,43] found, in a population based sample of female adult twins, that both the association between depression and alcoholism, and the association between depression and smoking could be explained by common genetic risk factors. In this way, parents at high genetic risk for depression not only are more likely to show negative parenting behavior, they can also transmit their genetic predisposition for substance abuse to their children.

The association between alcohol use and smoking in young adults is due to the same genetic risk factors. A significant genetic correlation between smoking and drinking was also found in a study of older adult male twins.[18] A preliminary analysis of smoking and alcohol problems in two cohorts of Australian female twins (aged 18–25 and 25–89 years) suggested that the same genetic factors predispose to both disorders.[19] Additional evidence that there is a genetic link between smoking and drinking comes from animal studies. It has been demonstrated that there is common genetic control of sensitivities to ethanol and nicotine.[44] Mouse lines that were selectively bred for differential sensitivity to ethanol also differed in sensitivity to nicotine. Other evidence that the same mechanisms are involved in alcohol use and smoking comes from animal studies of cross-tolerance. Chronic treatment with nicotine in mice resulted in the cross-tolerance to some of the effects of ethanol and chronic ethanol-treated animals were cross-tolerant to some of the effects of nicotine.[2,9]

In conclusion, we showed that alcohol use and smoking are associated due to a common set of environmental factors in adolescents and a common set of genes in young adults. Prevention and intervention programs should be aware of the relation between drinking and smoking and should be targeted at both.

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8

Summary and Discussion

Alcohol use, smoking and physical inactivity all have distinct effects on health. They all exhibit significant familial aggregation. The extent to which genetic and environmental factors contribute to these familial resemblances in health-related behavior was examined in a large population-based sample of Dutch adolescent twins and their parents. Health-related behaviors and personality were assessed by questionnaire at three waves of data collection in 1991, 1993 and 1995. In total 2712 families participated in this Dutch twin-family study. The results that are reported in this thesis were based on the questionnaires from 1700 families that were collected in the first wave of data collection. In chapter 6, data from the first and second wave were combined. A summary of the results is given in Table 8.1, depicting the relative contributions of genetic and environmental influences on individual differences in sports participation, alcohol use and smoking.

Parents and children may resemble each other because they share genes and because they share environmental influences. From the simultaneous analysis of twin and parent-offspring data it is possible to disentangle genetic influences from environmental influences that parents and children have in common and environmental influences that are specific for a generation. We have found that the resemblances between parents and children for alcohol use, smoking and sports participation can be attributed to their genetic relatedness (Chapters 1 and 2). Children from the same family resemble each other for these health-related behaviors because of their genetic resemblance and because they have environmental influences in common. The contribution of the genetic factors is only modest compared to the substantial shared environmental influences on health-related behavior (Table 8.1). Surprisingly, these environmental influences are not due to the effects of parental behavior.

Sensation seeking is one of the personality characteristics that is associated with adolescent alcohol use and smoking. The variance in sensation seeking during adolescence is due to genetic factors and to environmental factors that are unique for each individual (Chapter 3). Boredom Susceptibility and Disinhibition are the two dimensions of sensation seeking that show the highest association with adolescent alcohol and tobacco use. A genetic predisposition to Boredom Susceptibility and Disinhibition seems to increase the risk of initiation of alcohol and tobacco use (Chapter 4).

A stated, initiation of alcohol and tobacco use is modestly influenced by genetic factors and substantially by shared environmental factors. Once smoking is initiated, genetic factors determine to a large extent the quantity that is smoked (Chapter 5). These genetic influences are different from the genetic influences on smoking initiation and explain 86% of the individual differences (Table 8.1). The amount of alcohol consumed is influenced both by genetic (32%) and shared environmental

Table 8.1 *Overview of the heritabilities (expressed as percentage of total variance) for health-related behavior.*

		h^2	c^2	r_c	n
sport (parent-offspring)		45	44	0.0	1294[a]
smoking (parent-offspring)	parent ever smoker	32	61	0.6	1324[a]
	parent current smoker	30	62	0.6	1324[a]
smoking initiation		39	54	1.0	1676
quantity smoked		86	0	1.0	1676
smoking initiation males	12-14 years	3	97	1.0	650
	15-16 years	0	71	0.7	705
	17-25 years	66	19	1.0	1266
smoking initiation females	12-14 years	1	84	1.0	650
	15-16 years	27	67	0.7	705
	17-25 years	33	57	1.0	1266
alcohol use (parent-offspring)	15-16 years	34	58	0.5	403[a]
		0	88	0.4	403[b]
	17-25 years	43	37	0.4	805[a]
initiation alcohol use	males	0	92	1.0	1592
	females	41	54	1.0	1592
amount of alcohol		32	44	1.0	1592
initiation alcohol use males	12-14 years	1	78	1.0	650
	15-16 years	1	84	0.3	705
	17-25 years	48	32	1.0	1266
initiation alcohol use females	12-14 years	48	48	1.0	650
	15-16 years	10	86	0.3	705
	17-25 years	75	10	1.0	1266

r_c = correlation between shared environmental factors in opposite-sex twins; n = total number of twin pairs used for analyses; [a] = number of twin-families; [b] = models fitted equally well

factors (44%). As was the case for smoking, these factors are different from the factors that influence initiation of alcohol use (Chapter 5).

Alcohol use and smoking are associated in adolescents and young adults. Those twins who have started to use alcohol are at increased risk to take up smoking and vice versa. The underlying factors that cause this association are different for adolescents and young adults (Chapter 6). For these analyses the sample of twins was divided into three different cohorts: 12 to 14 year old twins, 15 and 16 year old twins and young adult twins aged 17 years and older. In adolescents (12 to 16 years), the same shared environmental factors influence initiation of alcohol use and smoking. In young adults (aged 17 to 25 years), the same genetic risk factors influence the initiation of alcohol and tobacco use. Table 8.1 shows the age specific estimates of the genetic and shared environmental effects on alcohol use and smoking. For females, the results consistently show both genetic and shared environmental influences on alcohol use and smoking. For males, genetic factors seem to be more important in young adults than in adolescent and young adolescent males.

In sum, the familial resemblance in health-related behavior is caused by modest genetic influences and by substantial contributions of shared environmental factors. The environmental influences that children from the same family have in common are not shared with their parents. In the next paragraphs the results for sports participation, smoking and alcohol use and their relation with sensation seeking are discussed in more detail.

Sports Participation

For sports participation, a more substantial effect of genetic factors was found than for the other lifestyle factors. The contribution of genetic and shared environmental factors to sports participation was about equal, explaining 45% and 44% of the total variance, respectively. There were somewhat more males than females who participated in sports. However, the relative importance of the genetic and shared environmental factors was the same for males and females. How can genetic factors be involved in the regulation of sports participation? There is evidence to suggest that individual differences in the increase in aerobic fitness in response to the same amount of exercise is largely genetically determined (Bouchard and Perusse, 1994). Other determinants of athletic ability, like motor development and performance, composition of muscle fibre and maximal cardiac output are also under genetic control (Bouchard et al., 1986; Fagard, Bielen, and Amery, 1991; Maes et al., 1996b;

Malina and Bouchard, 1986). Thus, a possible mechanism linking genes to sports participation might be that persons with a favorable genetic endowment for sports are more attracted to participate in sports. It can be further hypothesized that persons whose cardiovascular system adapts quickly to training are more likely to adhere to a regular exercise training program. In our laboratory, data have been collected on baseline heart rate and respiratory sinus arrhythmia in a sample of adult and a sample of adolescent twins (Boomsma, 1992; Snieder, 1996). In these data we will test a possible causal influence of these cardiovascular traits on sports participation. A second question to be addressed in future studies is whether the same genetic and environmental factors determine whether or not someone is involved in sports and at what intensity level someone is performing these sporting activities. This question will be addressed with the multifactorial threshold models that were developed for initiation and quantity of alcohol and tobacco use.

One of the other determinants of participation in sports that might explain some of the genetic variance is personality (Dishman, 1988). We have analyzed the association between sports participation and personality characteristics (results are not described in this thesis). In our sample of adolescent twins, sports participation was modestly and positively correlated with extraversion ($r = 0.13$) and with thrill and adventure seeking ($r = 0.26$), a sensation seeking characteristic. Furthermore, those who participated in sports were less withdrawn, less depressed and had less social problems (Boomsma and Koopmans, 1994), as assessed with the Young Adult Self Report (YASR) for problem behavior (Achenbach, 1990). However, the nature of the association between personality characteristics and sports participation remains to be identified.

In addition to the genetic influences, there were substantial shared environmental influences on sports participation. We found that the parent-child correlations for sports participation ($r = 0.3$) were lower than the correlations between spouses ($r = 0.5$) and between DZ twin pairs ($r = 0.4$-0.7). This pattern of higher resemblance within generations (spouses and siblings) than between generations (parent-offspring) strongly suggests that there are environmental factors that are common to members of the same generation (Perusse, Leblanc, and Bouchard, 1988). The results from the parent-offspring models indeed showed no vertical cultural transmission for sports participation. The environmental influences that children from the same family have in common are not influenced by sports participation of their parents. The resemblance between parents and children for sports participation is attributable to their genetic relatedness. Thus, when parents and children both participate in sports this is not because children imitate the behavior of their parents but because they share a genetically determined physical constitution that is favorable for sports participation.

The environmental factors that influence sports participation differed between males and females. Male and female siblings from opposite-sex twins were less alike for sports participation than siblings from same-sex DZ twin pairs. This lower resemblance was explained by shared environmental factors that influence sports participation in males but not in females. The findings imply that health promotion campaigns should be targeted at specific generations and at males and females separately, at least partly.

Health risk behaviors are interrelated and this clustering starts early in adolescence (Marti and Vartianen, 1989; Pate et al., 1996). We observed sports participation to be inversely related with alcohol use and smoking. Not participating in sports increased the risk of taking up the smoking habit or vice versa. For males, the relative risks was somewhat higher (RR = 1.96; 95%CI = 1.5-2.5) than for females (RR = 1.68; 95%CI = 1.3-2.1). Sports participation also seemed to protect against alcohol use in males (RR = 1.37; 95%CI = 1.1-1.7) but not in females (RR = 1.04; 95%CI = 0.8-1.3). The factors that cause this association will be addressed in future studies. Prevention programmes might consider the positive effects that sports participation can have on other health risk behaviors.

Smoking

Why do some adolescents start to smoke while others do not? Smoking initiation is moderately influenced by genetic factors (30-39%) and substantially by shared environmental factors (54-62%). This pattern was the same for males and females. Adolescent males and females did not differ in the prevalence of smoking initiation. However, there was evidence that the shared environmental influences on smoking initiation in males were to some extent different from those in females. This was derived from the imperfect correlation between the shared environmental factors in opposite-sex twins.

The results from the simultaneous analyses of twin and parent-offspring data showed that the familial resemblance for smoking behavior could not be attributed to vertical cultural transmission. We have analyzed both the association between smoking behavior in the children and current smoking in their parents and the association between smoking in the children and ever smoking in their parents. The resemblance between parents and children for smoking was not systematically higher for currently smoking parents compared to parents who ever smoked. This strongly suggests that children do not imitate smoking behavior of their parents. If children

model the behavior of their parents, they should have been more similar to parents who are currently smoking than to parents who have ever smoked. Our findings imply that, children of parents who are current or former smokers all have a genetically determined risk to become smokers.

The liability to smoking initiation is influenced by shared environmental factors and to a lesser extent by genetic factors. We have investigated the extent to which the genetic influences on smoking initiation are mediated by sensation seeking characteristics. The genetic influences on smoking initiation could entirely be attributed to the genetic variance in sensation seeking. Thus, one of the pathways to the genetic inheritance of smoking initiation is through the inheritance of sensation seeking characteristics that predispose to smoking. The sensation seeking characteristic that showed the highest genetic correlation with smoking initiation was Boredom Susceptibility, i.e. a genetic predisposition to Boredom Susceptibility increases the risk of initiation of tobacco use.

Once smoking is initiated, genetic factors determine to a large extent whether an individual becomes a light, moderate or heavy smoker. These genetic factors are different from the genetic factors that influence smoking initiation. The magnitude of the genetic influences on quantity smoked was the same for males and females, explaining 86% of the individual differences. The individual differences in the quantity smoked are likely to be due to genetic differences in the sensitivity to nicotine, in the development of tolerance to nicotine and in the rewarding effects of nicotine (Collins and Marks, 1991; Pomerleau, 1995).

When age is taken into consideration, the results suggest that for young adolescent males, shared environmental factors are the most important contributors to the risk of smoking initiation, while for young adult males, genetic factors are more important. A limitation of this conclusion is that in the youngest age group the prevalence of smoking is rather low (9%) and the sample was relatively small (650 twin pairs in total). For a binary trait (e.g. ever smoked) with a low prevalence, very large sample sizes are needed to have enough power to detect moderate genetic influences (Neale and Cardon, 1992). It may be that the power to detect genetic influences on smoking initiation in the youngest age groups was too small. The 95% confidence intervals around the heritability estimates, that are reported in chapter 6, showed that the heritability may lie between 0 to 17% in 12 to 14 year old males, and 0 to 36% in 12 to 14 year old females, indicating that there might be moderate genetic influences. The influences of shared environmental factors on initiation of smoking behavior in adolescents are more substantial than commonly found in studies of adult twins (Heath and Madden, 1995). This may reflect age cohort, but also cultural differences. In the first case it illustrates the importance of assessing initiation of smoking behavior when adolescents actually take up the smoking habit in stead of assessing smoking initiation retrospectively as most studies of adult twins have done.

Alcohol Use

Initiation of alcohol use is largely determined by shared environmental factors. These environmental factors are shared between twins from the same family but not between parents and children. As for smoking, the resemblance between parents and children for alcohol use can be explained by their genetic resemblance and not by vertical cultural transmission. For 15 and 16 year old twins and their parents, the results are less conclusive, but even for this age group horizontal cultural transmission is far more important than vertical cultural transmission.

Alcohol use is more frequent in adolescent males than in adolescent females. There are also different determinants of alcohol use in males and females. In males, the initiation of alcohol use is not influenced by genetic factors but by shared environmental factors. In females, there are both substantial shared environmental factors and genetic factors that influence the initiation of alcohol use. When age is taken into consideration the results suggest that for young adult males genetic factors are more important in the initiation of alcohol use than shared environmental influences.

The genetic influences on the initiation of alcohol use in females are to some extent mediated by sensation seeking characteristics. Boredom Susceptibility and Disinhibition were both associated with alcohol use. There is a common set of genes that influence Boredom Susceptibility and alcohol use and there is a common set of genes that influence Disinhibition and alcohol use in females. Once girls have started to drink alcohol, other genetic and shared environmental factors influence the amount of alcohol consumed. For males, a genetic predisposition to level of alcohol consumption is expressed once drinking has started. Although adolescent males consume on average more alcoholic drinks in a week than females, the relative importance of the genetic and shared environmental influences on the amount of alcohol consumed is the same for adolescent males and females, explaining 32% and 44% of the individual differences, respectively.

The influence of genetic factors on the amount of alcohol consumption in adolescents is much lower than the genetic influence on quantity smoked. A possible explanation is that there is less inter-individual variation in the weekly amount of alcohol consumption than in the number of cigarettes smoked. Adolescents mostly drink alcohol only during the weekends. Adult drinkers are more likely to drink

alcohol during weekdays and thus show more individual differences in alcohol consumption patterns. It is expected that the individual differences in alcohol consumption patterns will increase as the adolescent twins grow older, and that the genetic factors will become more important in the contribution to individual differences in the quantity of alcohol use.

There has been some debate about the extent to which genetic factors play a role in the inheritance of alcoholism in women (e.g. Kendler et al., 1992; McGue, Pickens, and Svikis, 1992). Recently, in a review of gender differences in the genetic contribution to alcoholism risk, Heath et al. (1995) concluded that there is not much evidence for a higher heritability of alcoholism in men than in women. For drinking patterns in adults it has also been found that genetic influences are at least as important in women as in men (Heath, 1995). We have shown that there are no differences between adolescent males and females in the genetic contribution to individual differences in alcohol consumption. Besides the significant genetic influences on adolescent alcohol use, we observed more substantial influences of shared environmental factors than commonly found for the inheritance of drinking behavior in adults (Heath, 1995). With longitudinal data on alcohol use, smoking and sports participation we will address the question to what extent the same determinants of health-related behavior in adolescence are also of influence in early adulthood.

Association between Alcohol Use and Smoking

Adolescent and young adult twins who have started to drink alcohol are at increased risk to take up the smoking habit and vice versa. The factors that cause this association differ for adolescents and young adults. For adolescents, alcohol use and smoking are correlated due to shared environmental factors that predispose to both behaviors. For young adults, the association between alcohol use and smoking is due to common genetic factors. One of these genetic factors may be the genetic predisposition to Boredom Susceptibility and Disinhibition. However, the results that we found for the relation between sensation seeking, alcohol use and smoking are based on the analyses of the total sample that was not divided into different age groups. Further analyses are needed to explore whether the mediational effects of sensation seeking on the initiation of alcohol use and smoking are different in adolescents and young adults.

Personality

Personality characteristics, such as extraversion, neuroticism, impulsivity and sensation seeking are associated with smoking and alcohol use (Gilbert, 1995; Zuckerman, 1994). Moreover, impulsivity and sensation seeking enhance the risk for developing alcoholism (Cloninger, Sigvaardsson, and Bohman, 1988; McGue, 1995). We also observed sensation seeking to be associated with alcohol use and smoking. Specifically, Boredom Susceptibility and Disinhibition showed the highest association with adolescent alcohol and tobacco use.

Individual differences in sensation seeking were attributable to genetic factors and to environmental factors that are unique for an individual. Four dimensions of sensation seeking were assessed: Thrill and Adventure Seeking, Experience Seeking, Boredom Susceptibility and Disinhibition. Genetic factors explained between 48 and 63% of the variance in these scales. The magnitude of the genetic and unique environmental effects was equal for males and females. Furthermore, there was no evidence that there are sex-specific genes that influence sensation seeking behavior in males and females. The four subscales are intercorrelated and a common set of genes seems to contribute to the correlations between the sensation seeking subscales.

We have also collected data on several other personality traits, such as extraversion, neuroticism, anxiety, depression, anger and type-A behavior. Behavioral problems were measured with the YASR (Achenbach, 1990) that assesses a broad range of adolescent and young adult psychopathologies. For all these personality characteristics, we have found that between 40 and 50% of the individual differences are due to genetic factors (Boomsma and Koopmans, 1994; Boomsma and Koopmans, 1996; Koopmans et al., 1993). Multivariate genetic analyses for anxiety, neuroticism and depression showed that most of the heritability in these traits could be explained by a common set of genes. The genes that contribute to a quantitative trait, such as sensation seeking, are called quantitative trait loci (QTL) (Lander and Botstein, 1989). With the availability of polymorphic DNA markers spanning the entire human genome and improved linkage methodology, it has become possible to localize the QTL's for personality traits. Recently, a specific genetic locus was identified that contributes to variation in sensation seeking. Two independent studies found an association between polymorphisms in the D4 dopamine receptor gene (D4DR) and variation in Novelty Seeking (Bejamin et al., 1996; Ebstein et al., 1996). The extensive data on symptoms of anxiety/depression in twin-families that we have collected during this project, will be used as a starting point in an international collaborative linkage study to identify the QTL's for anxiety and depression.

No Vertical Cultural Transmission for Health-Related Behaviors

Parents and children may resemble each other because of the effects of cultural transmission or because of their genetic relatedness. For alcohol use, smoking and sports participation the same conclusion emerged: there is no evidence for vertical cultural transmission. In other words, health-related behavior of the parents has no direct effect on health-related behavior of the children. Thus, children do not seem to imitate health-related behavior of their parents. The associations between parents and children for alcohol use, smoking and sports participation are due to genetic inheritance.

We modeled vertical cultural transmission as a direct effect of the parental phenotype (e.g. alcohol use) on the children. There may though be other aspects of parental behavior that indirectly influence health-related behavior in their offspring. For example, parents who are not physical active anymore due to a lack of time, might transmit a positive attitude towards sports participation to their children. Several studies found that parental attitudes towards adolescent alcohol use (Ary et al., 1993), parental monitoring and positive family relations (Cohen, Richardson, and LaBree, 1994; Dielman, Butchart, and Shope, 1993), and religious involvement (Kendler, Gardner, and Prescott, 1996; Maes et al., 1996a) are protective factors for the onset of adolescent alcohol use and smoking. However, all of these aspects of parental behavior are not necessarily transmitted culturally. Martin et al. (1986) found genetic influences and no vertical cultural transmission for social attitudes in Australian and British twins and spouses (cf. Plomin and Bergeman, 1991). Moreover, these aspects of parental behavior are also associated with alcohol use and smoking in the parents themselves. Parents with a positive attitude toward adolescent alcohol use are more likely to drink alcohol themselves. Thus, parents with a permissive attitude towards adolescent alcohol use, not only transmit their attitudes but also their genetic liability to alcohol use to their children. An adoption study of 653 U.S. adopted families (McGue, Sharma, and Benson, 1996) showed that the correlation between family functioning and adolescent alcohol involvement was much weaker for adoptive as compared to birth offspring. Based on these findings McGue et al. (1996) concluded that genetic factors mediate the relationship between ratings of family functioning and adolescent alcohol use.

One of the few characteristics that is transmitted culturally, is religious involvement (Eaves, Eysenck, and Martin, 1989; Kendler, Gardner, and Prescott, 1996). Kendler et al. (1996) concluded that religiosity may be one of the more important shared environmental aspects that influence the risk for substance use and dependence. In our own sample of adolescent twins, religious involvement of the

mother seem to be a protective factor for the onset of smoking, but not for initiation of alcohol use in the children (Rietveld et al., 1996). Religious involvement of the offspring themselves was also found to be negatively associated with alcohol use and smoking (Rietveld, 1996). Twins who were actively involved were less likely to smoke and drink than those who had a religious affiliation but were not actively involved.

Shared Environmental Influences

The resemblance between children from the same family for alcohol use, smoking and sports participation could be attributed to shared genes and to shared environmental influences. The environmental influences that children from the same family have in common are not shared with their parents. For successful prevention it is important to concentrate on the identification of these environmental factors. One of these factors might be the influence that siblings can have on each other. For example, smoking by one twin can stimulate the experimentation with cigarettes by the cotwin. It is possible to determine whether smoking by one twin has a direct environmental effect on the probability that the co-twin will also become a smoker. If there are both genetic influences and sibling interaction effects, a difference in the prevalence of a trait is predicted between MZ versus DZ twin pairs (Carey, 1992). We have analyzed sibling interaction models for alcohol use, smoking and sports participation to assess the extent to which shared environmental influences are due to the effect of the behavior of one twin on the behavior of the cotwin and vice versa. Preliminary results suggest that there are sibling interaction effects (Koopmans and Boomsma, 1996b). The sibling interaction effects were cooperative, e.g. smoking of one twin stimulates the onset of the smoking habit in the cotwin. However, it was not possible to distinguish between a model with genetic and shared environmental factors and a model with genetic factors and sibling interaction effects. There was not enough power to distinguish between sibling interaction effects and other features of the shared environment. Evidence for sibling environmental effects on alcohol use comes from an adoption study by McGue et al. (1996) that showed that same-sex similar aged adopted siblings were more similar for alcohol involvement ($r = 0.45$) than opposite-sex siblings of dissimilar age ($r = 0.05$).

Another important environmental factor that is shared between twins but not between parents and children is the influence of peers. Numerous studies found that peer influence is one of the most important determinants of the initiation of both cigarette smoking and alcohol use (Ary et al., 1993; Chassin and Presson, 1984; Dielman, Butchart, and Shope, 1993; Duncan, Duncan, and Hops, 1994; McNeill et

al., 1988; Swan, Creeser, and Murray, 1990). The influence of peers can be one of the shared environmental factors that contribute to the association between alcohol use and smoking. For sports participation, there is also evidence for peer influences (Lewko and Greendorfer, 1988). We found for all three health-related behaviors that there are shared environmental factors that are specific for males and females. Thus, there must be environmental factors shared by males, but not by females, that influence their drinking and smoking behavior. One of these factors might be same-sex peers. The association between adolescent health-related behavior and peers may also reflect assortative friendship (Heath and Martin, 1988), which is the active selection of friends with a behavior pattern that is similar to oneself. For example, it can be that individuals with heritable personality characteristics such as sensation seeking that increase the risk of harmful behavior, tend to select friends with similar behaviors. This is a form of active genotype-environment correlation (Scarr and McCartney, 1983), where individuals at high genetic risk also expose themselves to high risk environments (Heath, 1995). We have collected data on health-related behavior of peers. For example, we have asked the twins to rate the health-related behaviors of their best friend. Moreover, in the third wave of data collection, one or two siblings of the twins were asked to complete the same questionnaire on health-related behavior as their twin siblings. The data that we collected on siblings and peers of the twins will be analyzed in future studies. This will extend our knowledge about the environmental influences that are shared within this generation of adolescent and young adult twins.

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Samenvatting

Samenvatting

Het is bekend dat familieleden vaak op elkaar lijken in leefgewoonten die voor gezondheid van belang zijn, zoals roken, drinken en sportdeelname. De vraag is hoe deze overeenkomsten tussen familieleden ontstaan. Met behulp van tweelingonderzoek kan worden nagegaan in hoeverre gelijkenis in gedrag samenhangt met genetische verwantschap en met gemeenschappelijke omgevingsinvloeden. Door ouders van de tweelingen bij het onderzoek te betrekken kan er onderscheid worden gemaakt tussen genetische en culturele transmissie van ouders op kinderen. In dit project zijn tweelingen, hun ouders en hun broers/zusters onderzocht. Vragenlijsten over leefgewoonten en persoonlijkheid zijn in 1991, 1993 en 1995 verstuurd naar in totaal 2712 gezinnen met een tweeling tussen de 12 en 25 jaar.

Het clusteren van individuele verschillen in roken, alcoholgebruik en sportparticipatie binnen families blijkt voor een deel door genetische en voor een deel door omgevingsfactoren te worden verklaard. De invloed van genetische factoren op beginnend alcohol en nicotinegebruik is klein. De invloed van met name gemeenschappelijke omgevingsfactoren is groot. De overeenkomsten tussen ouders en kinderen voor alcoholgebruik, roken en sportdeelname kunnen worden toegeschreven aan hun genetische verwantschap en niet aan culturele transmissie: De leefgewoonten van ouders zijn niet direct van invloed op de leefgewoonten van hun kinderen.

Voor persoonlijkheid werd daarentegen geen invloed van gedeelde omgevingsfactoren gevonden. Verschillen in persoonlijkheid bij jongeren worden voor ongeveer 50% verklaard door genetische factoren en voor ongeveer 50% door persoonsgebonden omgevingsinvloeden. Er zijn aanwijzigingen dat erfelijke persoonlijkheidseigenschappen voor een deel het beginnen met roken en drinken bepalen. Beginnen met roken en drinken gaan vaak samen. Bij jongeren tussen de 12 en de 16 jaar blijken omgevingsfactoren die van invloed zijn op het beginnen met drinken ook van invloed te zijn op het beginnen met roken. Bij jong-volwassenen (17 jaar en ouder) zijn het met name dezelfde genetische factoren die het risico op het roken en drinken beïnvloeden. Als men eenmaal begonnen is met roken, blijkt het aantal sigaretten dat men rookt voornamelijk door genetische factoren te worden bepaald. Hoeveel wordt gedronken, hangt af van zowel genetische als gedeelde omgevingsfactoren. Deze factoren zijn onafhankelijk van de determinanten van beginnen met roken en drinken.

Genetische en culturele transmissie spelen dus een kleine rol in het verklaren van verschillen tussen jongeren in leefgewoonten. Bij jong-volwassenen die al roken en drinken verklaren genetische factoren in toenemende mate hoeveel er wordt gedronken en gerookt.

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Dankwoord

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List of Publications

List of Publications

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