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The genetic and environmental architecture of substance use development from early adolescence into young adulthood: a longitudinal twin study of comorbidity of alcohol, tobacco and illicit drug use

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ABSTRACT

Aims To investigate how use of alcohol, illicit drugs and tobacco come from substance-specific pathways and from pathways general to all three substances through adolescent development. **Design** Analysis of population-based survey. Adolescent twins reported alcohol use (AU), tobacco use (TU) and illicit drug use (IDU) in three waves (2006, 2008, 2010). Restructuring data by age allowed for variance decomposition into age- and substance-specific and common genetic and environmental variance components. **Setting** Norway. **Participants** Seven national twin birth cohorts from 1988 to 1994, totalling 1483 pairs (558 monozygotic; 925 dizygotic, same and opposite sex). **Measurements** Six-point Likert scores of AU, TU and IDU on items from the Monitoring the Future Study. **Findings** Substance use was found to be highly heritable; a^2 = 0.73 [95% confidence interval (CI) = 0.61–0.94] for AU, a^2 = 0.36 (CI = 0.18–0.52); d^2 = 0.49 (95% CI = 0.29–0.62) for IDU and a^2 = 0.46 (95% CI = 0.23–0.54); d^2 = 0.05 (95% CI = 0.00–0.07) for TU during the whole adolescence period. General substance use (GSU) was also highly heritable at each age and averaged a^2 = 0.57 (95% CI = 0.48–0.66). There was a high genetic carry-over from earlier age to later age. Genetic effects on GSU at ages 12–14 years were still detectable 4 years later. New substance (general and specific)-genetic effects also appeared. IDU demonstrated significant non-additive genetic effects (ages 12–14 years). Shared environment had a small impact on AU only. There was almost no non-shared environmental carry-over from age to age, the effect probably due partly to reliability deficiency. Common genetic effects among substance and substance-specific genetic effects were observed at each age-period. **Conclusions** Among Norwegian adolescents, there appear to be strong genetic effects on both substance-specific and comorbid use of alcohol, illicit drugs and tobacco; individual differences in alcohol use can be explained partially by family background.

Keywords Adolescence, alcohol use, comorbidity, heritability, illicit drug use, longitudinal, substance use, tobacco use, twin study.

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INTRODUCTION

Adolescence is the peak period for the onset of using substances. The median age of onset for alcohol and tobacco use is 16–18 years world-wide, and somewhat later for illicit drug use such as marijuana (18–19 years) and cocaine (21–24 years) [1]. Low use of alcohol or tobacco are the most prevalent patterns [2]. Using multiple substances and including illicit drugs [3]) is associated with different predictors and more problematic outcomes [4].

The causal mechanisms behind substance use in adolescence are still largely unknown, but genetic influences are indicated. Molecular studies have shown several genetic variants associated with substance use (individual effect sizes typically low [5,6]), some also pointing to a more non-specific liability for abuse and dependence among substance types [7,8].

Genetically informative designs (twin and extended family studies), estimating the total effect of genetic and environmental influences in complex traits, have proved very useful in studying the structures behind substance use, abuse and dependence [9]. Twin studies have demonstrated heritabilities of 40–70% for alcohol and illicit drug dependence [9,10]. The heritability of substance use is smaller [11]. Genetic sources explained approximately half the variation in life-time use of any substance in young twins [12]. An additive genetic component explaining approximately 60% of the common liability factor concerning alcohol, tobacco and cannabis dependence [13] showed moderate, correlated genetic influences at two consecutive waves into young adulthood [14]. However, results concerning substance abuse and dependence may not apply for substance use, and underlying structures may differ in adults and adolescents. A few studies have reported increasing heritability estimates for substance use and abuse from adolescence to adulthood [15–17], although there is a paucity of studies investigating the development of comorbid drug use from early adolescence into young adulthood within genetically informative designs.

Using a population-based community sample of twins followed longitudinally throughout adolescence to young adulthood answering questionnaires about recent substance use at ages 12–14, 15–17 and 18–22 years, the aim of the present study was to (1) investigate how use of alcohol, illicit drugs and tobacco come from substance-specific pathways and (2) investigate the role of any general liability to using these substances.

METHOD

To investigate how—throughout adolescence—individual differences in alcohol, illicit drugs and tobacco use depend upon substance-common and substance-unique genetic and environmental factors, a repeated-measures twin study was used. This allowed us to decompose the observed variance into latent genetic and environmental variance components [18], which is possible as twins comprise two types: monozygotic (MZ) twins, who share 100% of their genetic variance, and dizygotic (DZ) twins, who share on average 50% of segregating genes. The use of repeated measures makes it possible to investigate stability and change in those environmental and genetic variance components across time or age.

Design

This study used a multivariate repeated-measures twin design. Adolescent MZ and DZ twins (see sample description) reported alcohol, tobacco and illicit drug use (see measures) in three waves (in 2006, 2008, 2010). For statistical analyses these data were restructured according to age (more details below), such that the genetic and environmental variance components could be decomposed further into age-specific and age-common variance components.

Participants

The sample of MZ and DZ twins was recruited as follows: information concerning all multiples born in Norway between 1988 and 1994 (n = 5374 multiple births, 10 748 individual twins) and their parents was provided by the Norwegian Medical Birth Register. A postal invitation to participate was sent to the 4669 twin pairs who were still alive and residing in the country (elective pairs) when the study started. Of those pairs, 2486 pairs gave informed consent. Surveys were sent to a total of 1393 pairs (29.8% of the elective pairs) who participated in the first wave, 1065 (22.8%) in the second wave and 883 (18, 9%) in the third wave. Based on questionnaire-signed response dates, the median time span between waves 1 and 2 was 1.8 years (94.4% between 1.5 and 2.5 years); 2.6 years between waves 2 and 3 (99, 6% between 2.0 and 3.0 years); and 4.4 years between waves 1 and 3 (96, 7% between 4.0 and 5.0 years). The number of pairs with a response from at least one of the twins on at least one of the measurement occasions on at least one measure of substance use was 1483 (32% of elective pairs). Of these, 558 were monozygotic and 928 were dizygotic, same and opposite sex. In 428 pairs, both twins gave valid answers on all three substance measures at all waves (complete pairs). Comparisons between the 'complete' and 'incomplete' pairs indicated lower rates of substance use for complete pairs. Further analyses on longitudinal attrition indicated that there were, in general, no differences in zygosity and sex distribution between the complete pairs and the pairs including those without a co-twin (any pairs: complete plus incomplete pairs) for all waves (for details, see Supporting information, Table S1).

Generally, the percentages of males and opposite-sex pairs decreased from the first to third waves. All relevant cross-sectional and longitudinal within- and between-twin correlations were calculated separately for the 'complete pairs' and 'any pairs'. Only small differences between the corresponding correlations were observed for these two samples. Their averages were also almost identical (0.41 versus 0.43). For further details on recruitment, participation and dropout rates, see Waaktaar & Torgersen [19].

Measures

At each wave, substance use was assessed by youths' self-report and parents' report using items from the Monitoring the Future study [19]. For statistical analyses, we selected responses on the self-reports on the three items that asked how many times participants used (1) tobacco, (2) alcohol

Table 1 Descriptive statistics (95% confidence intervals between square brackets; percentages between round brackets).

	Ages 12–14			*Ages 15–17*			*Ages 18–22*		
	Alcohol use	*Illicit drug use*	*Tobacco use*	*Alcohol use*	*Illicit drug use*	*Tobacco use*	*Alcohol use*	*Illicit drug use*	*Tobacco use*
n	1299	1300	1296	2111	2110	2113	1227	1228	1226
np MZm (%comp)	100 (95.0%)	100 (95.0%)	100 (94.0%)	162 (93.2%)	162 (93.8%)	162 (93.8%)	98 (72.4%)	98 (71.4%)	98 (72.4%)
np MZf (%comp)	149 (97.3%)	149 (97.3%)	149 (96.6%)	243 (94.2%)	243 (94.6%)	243 (94.2%)	171 (80.1%)	171 (80.1%)	171 (80.1%)
np DZm (%comp)	100 (92.0%)	100 (92.0%)	100 (92.0%)	160 (93.1%)	160 (92.5%)	160 (93.8%)	85 (74.1%)	85 (75.3%)	84 (75.0%)
np DZf (%comp)	117 (98.3%)	117 (99.1%)	117 (99.1%)	212 (91.5%)	212 (91.5%)	212 (91.5%)	146 (77.4%)	146 (77.4%)	146 (76.7%)
np DZo (%comp)	201 (92.0%)	201 (92.0%)	200 (92.0%)	320 (90.9%)	320 (90.3%)	320 (90.9%)	206 (66.5%)	206 (70.0%)	206 (70.0%)
Mean	0.16 (0.13, 0.19)	0.01 (0.00, 0.01)	0.02 (0.01, 0.03)	1.75 (1.66, 1.84)	0.08 (0.06, 0.10)	0.22 (0.19, 0.26)	3.86 (3.75, 3.97)	0.26 (0.20, 0.31)	0.42 (0.36, 0.48)
Mean of males	0.17 (0.13, 0.21)	0.01 (0.00, 0.02)	0.02 (0.01, 0.03)	1.91 (1.80, 2.01)	0.08 (0.05, 0.11)	0.23 (0.19, 0.27)	3.92 (3.79, 4.05)	0.23 (0.17, 0.30)	0.43 (0.36, 0.50)
Mean of females	0.15 (0.11, 0.19)	0.00 (0.00, 01)	0.02 (0.00, 0.03)	1.56 (1.44, .167)	0.08 (0.05, 0.11)	0.22 (0.17, 0.26)	3.78 (3.63, 3.94)	0.30 (0.21, 0.38)	0.38 (0.31, 0.49)
SD	0.49 (0.44, 0.51)	0.09 (0.08, 0.10)	0.15 (0.13, 0.15)	1.65 (1.48, 1.71)	0.47 (0.42, 0.48)	0.65 (0.59, 0.67)	1.62 (1.46, 1.70)	0.86 (0.77, 0.90)	0.90 (0.81, 0.95)
Min	0	0	0	0	0	0	0	0	0
Max	6	2.5	2	6	6	4	6	6	5
Mode	0	0	0	0	0	0	4	0	0

n = number of individual observations; np = number of twin pairs; %comp = percentage complete twin pairs; MZm = monozygotic male; MZf = monozygotic female; DZm = dizygotic male; DZf = dizygotic female; DZo = dizygotic opposite sex; SD = standard deviation of the variable; min = minimum observed score on the variable; max = maximum observed score on the variable

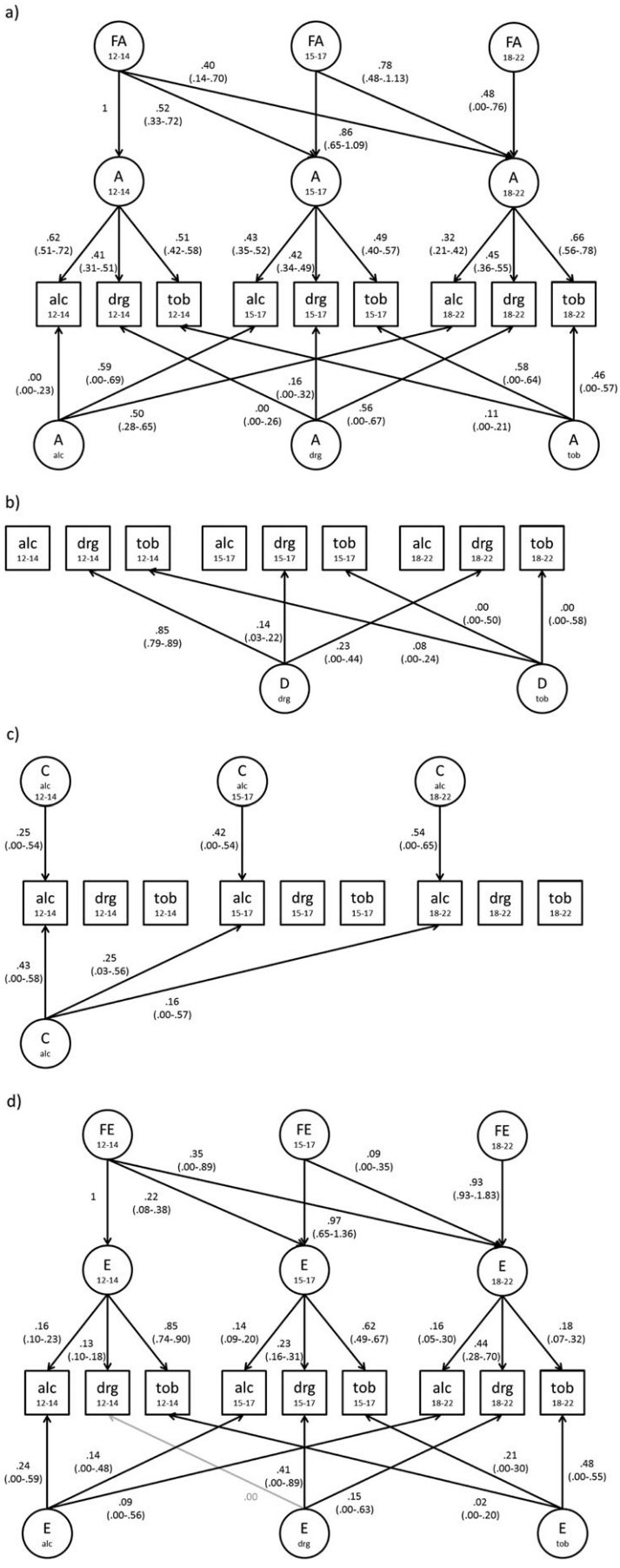

Figure 1 Results of the biometric model-fitting analyses, showing the standardized path coefficients (and their 95% confidence intervals) in the adjusted developmental model. To avoid clutter, the coefficients are shown separately for the additive genetic factors (a), non-additive genetic factors (b), shared environmental factors (c) and (d) non-shared environmental factors (d) that influence alcohol use (alc), drug use (drg) and tobacco use (tob) at ages 12–14, 15–17 and 18–22. The path in grey represents the path coefficient that was fixed to 0. Measurement-specific residual E is omitted.

and (3) illicit drugs during the past 12 months. The measurement of illicit drug use at wave 1 (ages 12–14) was an exception; here, the twins were asked how many times they had used illicit drugs in their entire life. Response options were 'never' (coded 0); '1–2 times' (coded 1); '3–5 times' (coded 2); '6–9 times' (coded 4); '10–19 times' (coded 5); '20–39 times' (coded 6) and '40 or more times' (coded 7).

Zygosity was determined through a combination of questionnaire data on twin physical similarity and DNA secured through cheek swabs from a subsample of the participants. For details, see Waaktaar & Torgersen [19] and Torgersen [20].

Statistical analysis

As the data were obtained in waves rather than age, data were first restructured according to age using three bins: ages 12–14, 15–17 and 18–22. Whenever two measures fell in the same bin, these were averaged. Descriptive statistics of the restructured data are provided in Table 1 (centrality and dispersion measures) and Supporting information, Tables S3 (age bin–age bin correlations) and S4 (I and II) (twin correlations). The relationships between wave, cohort and age bin are provided in Supporting information, Table S5.

From the twin correlations it can be derived that phenotypical similarity of DZ twins was generally close to half that of the of MZ twins, suggesting that genetic effects on substance abuse were mainly additive (A) and environmental effects between twins non-shared (E). However, for alcohol use, the DZ correlations were clearly more than half the MZ correlations, while for tobacco use and illicit drug use they tended to be less than half the MZ correlations. This suggested the presence of additional shared environmental effects (C) on alcohol use (but not on tobacco use and illicit drug use), and the possible presence of non-additive genetic effects (D) on drug use and illicit drug use (but not on alcohol use).

To incorporate all effects, we constructed the statistical model displayed graphically in Fig. 1. It describes how observed variance in the observed variables was split into substance-common and substance-specific variance components at each age (bin), and how those components related across age. More specifically, the model distinguishes at each age between substance-common and substance-specific additive genetic variance components (depicted as first-order latent A factors) and substance-common and substance-specific non-shared environmental variance components (first-order latent E factors) on which the observed variables alcohol, illicit drugs and tobacco use were regressed. In addition, the alcohol use measures were regressed on age-specific and age-common environmental components (alcohol-specific latent C factors), while the tobacco and illicit drug use scores were regressed on age-common and age-specific non-additive genetic variance components common to tobacco and illicit drug use (depicted as latent D factors).

Statistical overlap (correlations) among the three substance-common, age-specific A factors was dealt with by adding three latent A factors at the second order and by regressing the first-order substance-common A factor at a given age on (1) the second-order A factor at that age and (2) any such factors on previous ages. Statistical overlap among the three substance-common, age-specific E factors was modelled accordingly.

The model was implemented in R, package OpenMx [21], using full information maximum likelihood. To lower the computational burden, the observed variables were treated as continuous. As the number of categories of the observed variables was larger than five, in many cases this is not problematic [22]. We note, however, that standard errors (of large factor loadings especially) might be underestimated (and that model comparison can therefore be problematic); for example, as the observed variables were skewed to the left. Our results should thus be interpreted with some degree of caution. However, we stress that our focus was not so much on individual parameters of the model or on deriving a best-fitting model. Rather, we were interested in the (potentially different) roles of genetic and environmental sources of individual differences in a model that can be regarded as being as saturated as possible.

Because qualitative and quantitative sex differences in genetic and environmental effects are rare [23] and have not been detected in earlier studies into substance use [24], we assumed that nor were such differences present in the present sample. Importantly, this assumption increased the power to detect possible C and D effects substantially. However, as per Del Boca's recommendation [25], we allowed for sex differences; namely, in the observed means, as in the frequency of substance use (even though the descriptives suggested that such sex differences were small and probably insignificant). This was accomplished by including sex as a covariate (definition variable in OpenMx), i.e. as a predictor of the observed variables tobacco use, alcohol use and illicit drug use.

RESULTS

The model as described above turned out to be non-identified empirically, but by fixing the near-zero loading of illicit drug use on the age-common D factor to 0, this issue was solved. Figure 1 includes the standardized path coefficients (and their 95% confidence intervals) that followed.

The additive genetic pathways (Fig. 1a) show that the substance-common additive genetic effects present at ages 12–14 were also present at later ages, because the second-order factor at ages 12–14 (which is identical to the first order factor at ages 12–14) predicted significantly the first-order factors at ages 15–17 and 18–22. Significant new substance-common additive genetic effects also emerged at ages 15–17. Substance-specific additive genetic effects were generally not significant, with the exception of additive genetic effects on alcohol use at ages 18–22. In conclusion, additive genetic effects contributed mainly to comorbidity, and to comorbid stability as well as comorbid change. Additive genetic influences do not provide a good explanation of why some individuals are inclined to use alcohol, while others use tobacco or illicit drugs.

The non-additive genetic effects on tobacco use and drug use (Fig. 1b) could not be dropped from the model without a significant decrease in model fit (see Supporting information, Table S2 for fit statistics of nested models), yet such effects must be considered limited, as the only significant effect (at $\alpha = 0.05$) was on drug use at ages 12–14. From ages 15 to 17 onwards, significant non-additive effects were absent. Thus, if not indicating a false positive (as mentioned, standard errors can be underestimated), these results suggest that in contrast to additive genetic effects, any genetic effects vanish, and quickly so.

The shared environmental pathways on alcohol use (Fig. 1c) could not be dropped either. Only at ages 17–22 was there a significant, moderate contribution (of the age-common C factor). However, the sum of the age-specific and age-common contributions appeared significant at each age, suggesting that shared environmental effects were present throughout the whole age span, but that we lacked power to distinguish between age-specific and age-common effects.

From the non-shared environmental pathways (Fig. 1d), we observed that substance non-shared environmental effects were largely age-specific, implying that these effects contributed mainly (although not only) to change. An important distinction here is between age-specific substance-specific non-shared environmental effects and age-specific substance-common non-shared environmental effects. The former includes (and may be largely comprised of) the effects of measurement error. The latter do not include effects of measurement error, and represent actual environmental effects that contribute to comorbidity. The pathways from the second-order factors to the first-order components show that such environmental effects did not explain comorbid stability greatly, but rather comorbid changes, as the pathways from first-order variables to previous second-order variables were insignificant.

In summary, the results suggest that (a) stability in comorbidity was due mainly to additive genetic effects, (b) while changes in comorbidity are due mainly to non-shared environmental effects, and (c) substance-unique variance was from various sources and showed little carry-over, perhaps except for the contribution of shared environmental effects on alcohol use.

Apart from studying the pathways, and thus the qualitative roles of genetic and environmental effects in explaining stability and change, we also calculated the

Table 2 Heritability coefficients [and their 95% confidence intervals (CI)] as obtained from the best-fitting adjusted developmental (ADCE) model.

Age (years)	*Trait*	a^2	*95% CI*	d^2	*95% CI*	c^2	*95% CI*	e^2	*95% CI*
12–14	Comorbidity	0.51	0.44–0.60	–	–	–	–	0.49	0.40–0.56
	Alcohol use	0.39	0.26–0.52	–	–	0.25	0.16–0.34	0.36	0.29–0.44
	Drug use	0.17	0.10–0.26	0.72	0.63–0.78	–	–	0.11	0.09–0.14
	Tobacco use	0.27	0.18–0.35	0.01	0.00–0.06	–	–	0.73	0.64–0.81
15–17	Comorbidity	0.57	0.48–0.66		–	–	–	0.43	0.34–0.52
	Alcohol use	0.53	0.42–0.65	–	–	0.24	0.14–0.34	0.23	0.19–0.27
	Drug use	0.20	0.13–0.29	0.02	0.00–0.05	–	–	0.78	0.70–0.85
	Tobacco use	0.57	0.28–0.63	0.00	0.00–0.31	–	–	0.43	0.37–0.49
18–22	Comorbidity	0.75	0.57–0.86	–	–	–	–	0.25	0.14–0.43
	Alcohol use	0.35	0.16–0.52	–	–	0.32	0.18–0.47	0.33	0.27–0.40
	Drug use	0.51	0.48–0.63	0.06	0.00–0.19	–	–	0.43	0.36–0.51
	Tobacco use	0.65	0.40–0.78	0.09	0.00–0.34	–	–	0.26	0.22–0.32
12–22	General substance use	0.57	0.48–0.66	–	–	–	–	0.43	0.34–0.52
	Alcohol use	0.73	0.61–0.94	–	–	0.19	0.00–0.26	0.08	0.01–0.22
	Drug use	0.36	0.18–0.52	0.49	0.29–0.62	–	–	0.14	0.02–0.40
	Tobacco use	0.46	0.23–0.54	0.05	0.00–0.27	–	–	0.50	0.42–0.57
	Alcohol use-specific	0.62	0.44–0.94	–	–	0.29	0.00–0.43	0.09	0.00–0.27
	Drug use-specific	0.26	0.09–0.42	0.60	0.34–0.76	–	–	0.14	0.00–0.44
	Tobacco use-specific	0.60	0.19–0.72	0.10	0.00–0.61	–	–	0.30	0.20–0.44

relative, quantitative contributions of genetic (and shared and non-shared environmental) variance to total (phenotypical) variance and covariance at each specific age and across age. These contributions ('heritability coefficients') are provided in Table 2. Their standard errors and confidence intervals should be interpreted with caution. Again, the pattern in these results is more important than single heritability estimates. This pattern suggests that heritability of substance use is moderate to high, providing evidence that the genetic effects on influences on all alcohol use, tobacco use and drug use were substantial throughout the entire age span and that the same holds for the accumulated effects of all the influences that contribute to comorbid substance use.

DISCUSSION

Corroborating previous findings, our model showed that comorbid substance use is moderately to highly heritable from early adolescence into young adulthood. The comorbidity factor in alcohol, tobacco and illicit drugs use had a heritability of 0.57 throughout the age span, varying from 0.51 (in early adolescence) to 0.75 (in young adulthood). Comparable estimates were reported on the liability for comorbid alcohol, tobacco and cannabis DSM-IV life-time dependence symptoms in young people [13]. Genetic effects throughout adolescence are also supported by molecular genetic studies on substance use [6] and dependence [8].

Our longitudinal design showed that genetic and environmental factors have different roles in explaining stability and change over time. Stability in comorbidity was due primarily to genetic effects, while the environmental influences on comorbidity lead to comorbid change. An earlier study on adolescents' substance use covering a narrower age span also found a common genetic factor accounting for stability in comorbid tobacco, alcohol and drug use [24]. While they reported shared environmental effects contributing substantially to comorbid continuity, in our study these were small and specific to alcohol use. We lacked power to determine whether these effects were the same shared environmental effects throughout development; however, our results fit with estimates reported on alcohol disorders [26].

A novel finding is that illicit drug use was driven by partly non-additive genetic (dominance or epistasis) influences. Clear genetic dominance effects were documented recently in molecular genetic studies of substance dependence [27], supporting the relevance of such models in twin designs. However, non-additive genetic influences were substance-specific changes at specific ages. Within the context of the full model, they did not contribute to comorbidity or stability. After age 18 these effects had disappeared. Large-scale extended family designs are needed to explore further the relative roles of C and D modelled together.

It is noteworthy that the importance of genetic effects in explaining comorbid stability does not exclude additive genetic effects (also) explaining change. In fact, the additive genetic effects that lead to change in the present study merely tended to accumulate, whereas all effects of genetic dominance, shared environment and non-shared environment were idiosyncratic. Thus, some additive genetic effects do not vanish while all other effects do. Those additive genetic effects that do not vanish all contribute to comorbidity.

Finally, a highly interesting finding is that the comorbidity of adolescents' substance use is due mainly to a common genetic liability, while genetic specificity for alcohol, drugs and tobacco become more prominent in young adulthood. This is supported in a study reporting decreasing common genetic liability and increasing substance-specific genetic effects in regular smoking, alcohol intoxication and illicit drug use throughout adolescence [24]. A longitudinal twin study of comorbid alcohol, tobacco and marijuana dependence [28] found a genetic component of approximately 70% in the common comorbidity factor at 17 years, deceasing to less than 50% by age 29 years. There, the non-shared environmental influence increased accordingly, explaining more of the differentiation between substances than substance-specific genetic liabilities. Conversely, others [29] have reported that comorbidity of substance use in adolescents was caused mainly by common shared environmental influences, while comorbidity in young adults was caused by common genetic sources. Although results from studies throughout adolescence differ markedly on the relative importance of common and substance-specific causation, perhaps indicating a cultural tunnelling of the expression of genetic effects on substance use, increasing differentiation from adolescence to adulthood has also been found in other studies of externalizing symptomatology. Thus, in early adolescence, the subjective response to the different drugs differs very little among substances [30], an effect that is influenced partly by a general genetic liability among substances [31]. Some [32] have reported non-specific genetic vulnerability among substances, while others [33] have found common genetic sources as well as substance-specific sources in substance use disorders in adults. Similar results have been reported in molecular genetic studies on adult life-time substance dependence [8].

The present results have several implications for molecular genetic studies. They demonstrate that genes are highly influential in explaining variance in substance use —not only substance abuse and dependence—throughout adolescence and early adulthood. Common and substance-specific genetic sources should be investigated among age groups as potential causal agents behind both stability and change in these phenotypes.

STRENGTHS AND LIMITATIONS

Major advantages of the present study are the longitudinal genetically informative twin design, the population-based sample, use of adolescents' self-report on behaviours under normative and legal restrictions and the wide age span included. Some basic assumptions inherent in the classical twin design, e.g. that the same amount of environmental variation is affecting MZ and DZ twins (equal environments), and that there is no genetic correlation between the parents (random mating) [34], were not tested specifically. Results from other studies indicate a low threat on assumptions for the phenotypes studied here [35–38]. As we assumed, rather than tested for, qualitative and quantitative sex differences in genetic and environmental effects, we cannot exclude that such effects were actually present. If so, our results should be interpreted as averaged among the sexes. Above, we have mentioned that sex effects are rare [23] and have not been detected in earlier studies into substance use [24], but they may be small, so that they went undetected in previous studies due to a lack of power. In line with Del Boca's recommendation [25], we therefore advise future (large-scale) studies to (re)address possible qualitative and quantitative sex differences in any phenotype in general and in substance abuse in particular [25].

As we were focusing upon stability and change in interindividual differences in substance use, in this study initiation and progression were taken together. Twin studies separating initiation and progress [39] may provide further insight.

Attrition may constitute a threat to representativeness. Earlier analyses indicated somewhat higher parental socioeconomic status (SES) among the participating families compared to the national mean [19]. Norway is a highly egalitarian society [40], and SES-based differences in parental and young people's health-related behaviour are generally small compared to other European countries [41,42]. However, further studies on more SES-diverse samples are warranted. Analyses did not indicate marked effects of systematic attrition in an association between variables longitudinally.

CONCLUSION

Our results indicate that, within the Norwegian population and society, individual differences in substance use (alcohol, tobacco and illicit drugs) are driven in large part by stable genetic sources. Environmental influences (including measurement error) are, in large part, the drivers of time and/or substance-specific use. Shared environmental effects are limited to alcohol use.

Declaration of interests

None.

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Supporting Information

Additional Supporting Information may be found online in the supporting information tab for this article.

Table S1 Numbers of incoming questionnaires, valid responses and percentages of complete and any (complete plus incomplete) pairs by each wave.
Table S2 Model-fitting results. The results of the preferred model are shown in bold type.
Table S3 Within individual correlations among use of substance types, estimates and 95% confidence intervals.
Table S4 (I) Estimated monozygotic (MZ) intrapair correlations, estimates and 95% confidence intervals.
Table S4 (II) Estimated dizygotic (DZ) intrapair correlations, estimates and 95% confidence intervals.
Table S5 Relationship between waves and age bins.