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The gene–environmental architecture of the development of adolescent substance use

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Original Article

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Abstract

Background. Using a longitudinal twin design and a latent growth curve/autoregressive approach, this study examined the genetic–environmental architecture of substance use across adolescence.
Methods. Self-reports of substance use (i.e. alcohol, marijuana) were collected at ages 13, 14, 15, and 17 years from 476 twin pairs (475 boys, 477 girls) living in the Province of Quebec, Canada. Substance use increased linearly across the adolescent years.
Results. ACE modeling revealed that genetic, as well as shared and non-shared environmental factors explained the overall level of substance use and that these same factors also partly accounted for growth in substance use from age 13 to 17. Additional genetic factors predicted the growth in substance use. Finally, autoregressive effects revealed age-specific non-shared environmental influences and, to a lesser degree, age-specific genetic influences, which together accounted for the stability of substance use across adolescence.
Conclusions. The results support and expand the notion that genetic and environmental influences on substance use during adolescence are both developmentally stable and developmentally dynamic.

Introduction

Although adolescent substance use has declined modestly during the past decade, it remains a serious public health concern in most Western nations. Substance use typically emerges during early adolescence and linearly increases – both in terms of prevalence rates and frequency of use – until late adolescence, when a majority of adolescents report prior use of alcohol or illicit drugs (Duncan & Duncan, 1996; Miech *et al.* 2017). Although some degree of experimentation with alcohol and marijuana may be considered normative (Johnston *et al.* 2015), there is evidence that high levels (i.e. quantity or frequency) of substance use or a sharp increase in substance use during adolescence are associated with adverse social, academic, behavioral, and mental health outcomes (Hingson *et al.* 2006; Jacobus *et al.* 2009; Peleg-Oren *et al.* 2009).

Behavioral genetic research based on twin designs indicates that both genetic and environmental factors influence substance use during adolescence, and that they are, to a large extent, the same across different substances (Han *et al.* 1999; Kendler *et al.* 2003; Young *et al.* 2006; Sartor *et al.* 2010). Nevertheless, the relative contribution of genetic and environmental influences on adolescent substance use seems to differ with age. Substance use during early adolescence seems to be primarily influenced by shared social and familial environmental factors, whereas substance use during middle and late adolescence seems to be primarily influenced by genetic factors (for a review, see Hopfer *et al.* 2003; Lynskey *et al.* 2010). However, most evidence for age differences rests on (a) studies using retrospective data, which are sensitive to memory problems or reconstruction biases (e.g. Kendler *et al.* 2008; Long *et al.* 2017) or (b) prospective longitudinal studies with a limited number of data points, often during late adolescence or early adulthood (Koopmans *et al.* 1997; Viken *et al.* 1999; Malone *et al.* 2004). Only one prospective study has examined the relative contribution of genetic and environmental factors from age 13 to 20 (Baker *et al.* 2011). Results from a Cholesky decomposition of the longitudinal data indicated that genetic and shared environmental factors on general substance use were substantial and stable with age, although some evidence for genetic innovation emerged. Shared environmental influences were also stable over time, whereas unique environmental influences were largely age-specific. Similar to previous work on the topic, this prospective study examined the extent to which repeated measures of substance use have a shared and/or independent etiology; it did not examine whether the same or different genetic and environmental factors influence the level and the growth of substance use at different ages, which is best addressed with latent growth curve modeling. To address this limitation, the present study examines the extent to which genetic and/or environmental factors contribute to the level and rate of change in substance use from early to late adolescence.

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Adopting the recommendations of Gillespie *et al.* (Gillespie *et al.* 2015; Long *et al.* 2017), the present study combined a latent growth curve approach with an autoregressive approach, in order to disentangle different mechanisms of change. A latent growth model assumes that the level (i.e. intercept) and rates of change (i.e. linear or non-linear slope) in substance use results from the unfolding of inherent, random effects over time that can be decomposed into genetic and environmental sources of variance. An autoregressive model (also known as a simplex/transmission model) assumes that genetic (and/or environmental) variance increases are due to the progressive accumulation of age-specific genetic influences (Eaves *et al.* 1986; Boomsma & Molenaar, 1987). The two models are not incompatible. For example, genetic influences may account for individual differences in the overall level and rate of change in substance use from early to late adolescence (as indicated by growth models), whereas environmental influences may account for individual differences in the persistence of substance use across different ages (as indicated by autoregressive effects). A mixed-model approach, known as a 'dual change score model', integrates a latent growth curve model and an autoregressive model (McArdle, 2009; Eaves *et al.* 2016).

Objective of the present study

The present study examines the relative role of genetic and environmental sources of influence on individual differences in the development of substance use between early adolescence (i.e. age 13) and late adolescence (i.e. age 17). To this end, an ACE decomposition was applied to a dual change score model to (a) examine genetic and environmental effects on the stability of substance use from early to late adolescence and (b) assess the contribution of genetic and environmental factors to the overall level and the rate of change of adolescent substance use from age 13 to 17. We first assessed substance use at age 13, a time considered early onset of use (Swendsen *et al.* 2012), because it is the age when our participants entered high school. With the exception of age 16, we tracked substance use annually up to age 17, an age when most adolescents report at least some substance use (Martino *et al.* 2008).

Methods

Participants

Participants consisted of 476 twin pairs (475 boys, 477 girls) drawn from an ongoing longitudinal study of a population-based sample of 662 monozygotic (MZ) and dizygotic (DZ) twin pairs (1324 individuals) recruited from the Québec Newborn Twin Registry, which identified all twin births occurring in the Province of Québec between 1995 and 1998 (Boivin *et al.* 2013). Zygosity was assessed by genetic marker analysis of 8–10 highly polymorphous genetic markers; twins were diagnosed as MZ when concordant for every genetic marker. When genetic material was insufficient or unavailable (43% of cases), zygosity was determined on the basis of physical resemblance questionnaires at 18 months and age 9 (Goldsmith, 1991). The comparison of zygosity based on genotyping with zygosity based on physical resemblance in a subsample of 237 same-sex pairs revealed a 94% correspondence rate, which is similar to rates obtained in other studies (Spitz *et al.* 1996; Magnusson *et al.* 2013).

Demographic characteristics of the final sample were similar to those of a representative population-based birth sample of singletons assessed in 1998 by the Quebec Ministry of Health and Social Services. Most participants were of European descent (78.8%; $n = 750$); the remainder were of African descent (2.3%; $n = 22$), Asian descent (2.3%; $n = 22$), Native North American descent (1.2%; $n = 10$), other descents (2.3%; $n = 22$), or did not specify their ethnicity (13.2%; $n = 126$). At the outset, 95% of parents lived together. Roughly 17% of mothers and 14% of fathers had not finished high school; 28% of mothers and 27% of fathers held a university degree; 83% of the parents were employed; and 10% of the families received social welfare or unemployment insurance.

Of the 662 twin pairs recruited at birth, 397 (60.0%), 389 (58.8%), 391 (59.0%), and 368 (55.6%) participated in data collection at ages 13, 14, 15, and 17, respectively. A total of 263 twin pairs participated in four waves of data collection, 114 participated in three waves, 54 participated in two waves, and 45 participated in one wave. The final sample (187 MZ twin pairs, 144 same-sex DZ twin pairs, and 145 mixed-sex DZ twin pairs; $M_{age} = 13.1$, S.D. = 0.30 years) included dyads with valid data for at least one wave. Compared with those who did not participate at ages 13–17, the final sample reported significantly higher family income [$t(613) = 3.67$, $p < 0.01$] and maternal education [$t(635) = 2.52$, $p = 0.01$]. They did not differ in terms of paternal education [$t(587) = 0.44$, $p = 0.66$], family structure [$t(649) = 0.09$, $p = 0.93$], child inattention [$t(603) = 0.37$, $p = 0.72$], or child hyperactivity [$t(603) = 0.84$, $p = 0.40$] during the preschool period. Both concurrently and over time, same- and mixed-sex DZ twins displayed no differences in their means, variances, and co-variances [$\chi^2(7–20) = 3.48–26.71$, $p > 0.14$], so the 145 mixed-sex DZ twin pairs were included in the analyses.

Procedure

Data collection at each wave was approved by the Sainte-Justine Hospital Research Centre ethics committee. Informed active parental consent and child assent for participation was obtained.

Missing data accounted for an average of 20.8% of reports (range 17.54–24.68%). Missing data were handled with full information maximum-likelihood estimation, which allowed participants with incomplete data to be included in the models. Little's test indicated that data were missing completely at random, $\chi^2(238) = 244.52$, $p = 0.37$.

Measures

Substance use

Frequency of substance use was assessed with the Personal Experience Screening Questionnaire (Henly & Winters, 1989; Winters *et al.* 1990–91) which consisted of three items (alcohol use, marijuana use, and binge drinking). Participants rated the frequency of substance use over the past 12 months on a scale ranging from 1 (*never*) to 7 (*daily*) (mean Cronbach's $\alpha = 0.69$). Item scores were averaged to create scale scores. Table 1 presents means and standard deviations for annual substance use. Table 1 also presents number of participants who used alcohol or marijuana at least once at each data point. Substance use increased steadily: 21.3% (at age 13) to 82.3% (at age 17) of participants reported experience with at least one substance at least once. The logs of substance use scores were calculated in order to correct for positively skewed distributions.

Plan of analysis

In the first step, we estimated a phenotypic dual change score model (Gillespie *et al.* 2015; Long *et al.* 2017) to describe the

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Table 1. Means, standard deviations, item frequencies, and intra-class correlations

	13 years	14 years	15 years	17 years
Means (s.d.)				
MZ	1.17 (0.39)	1.37 (0.66)	1.85 (1.02)	2.58 (1.23)
DZ	1.17 (0.37)	1.41 (0.63)	1.88 (1.00)	2.76 (1.29)
Item frequencies for any substance use (% of respondents)				
Alcohol	166 (21.1)	258 (34.2)	439 (57.8)	577 (80.5)
Intoxication	45 (5.7)	102 (13.5)	233 (30.7)	431 (60.1)
Marijuana	10 (1.3)	55 (7.3)	141 (18.6)	289 (40.3)
MZ/DZ intra-class correlations				
	0.56**/0.20**	0.50**/0.29**	0.60**/0.37**	0.62**/0.37**

Note. $N = 717–785$. ** $p < 0.01$.

phenotypic development of substance use from age 13 to 17. Dual change score models are well suited for segregating autoregressive effects from overall levels of a variable, and from the linear and non-linear inter-individual changes in a variable over time. A two-group model was estimated with 374 MZ twins and 578 DZ twins. The dual change score model tested whether (a) there were significant linear or non-linear increases in substance use, (b) there were autoregressive effects from one time point to the next, and (c) whether the results differed by zygosity. Both linear and non-linear growth curves were initially explored. However, the latter was omitted because it did not show a significant mean or variance in either MZ or DZ pairs. Factor loadings were orthonormalized. Only significant autoregressions were retained. Non-significant residual variances were fixed to 0. Across-zygosity constraints were retained if they did not significantly worsen model fit.

In the second step, we conducted an ACE decomposition of the dual change score model, which allows for the partitioning of effects that are 'time-specific' and that contribute to inter-individual differences in the stability of substance use, from effects that directly contribute to inter-individual differences in 'unfolding' growth. A Cholesky decomposition of the growth curve portion of the model allowed us to (a) estimate the relative contribution of genetic factors, shared environmental factors, and non-shared environmental factors to the intercept (i.e. overall level) and the slope (i.e. linear rate of change) of substance use, and (b) determine whether different genetic and environmental factors contributed to the intercept and the slope of substance use.

By comparing within-pair correlations for MZ twins (who are genetically identical) to those of DZ twins (who on average share only half of their genes), sources of variability in the intercept, slope, and time-specific portions of substance use can be estimated as latent additive genetic (*A*), latent shared environmental (*C*), and latent non-shared environmental (*E*) factors (Neale & Cardon, 1992). Within-twin pair correlations of the latent genetic factors (*A*) are fixed to 1.0 for MZ twins and to 0.5 for DZ twins. Within-twin pair correlations of the latent shared environmental factors (*C*) are fixed to 1.0 for both MZ and DZ twins. Within-twin pair correlations of the latent non-shared environmental factors (*E*) are fixed to 0 for both MZ and DZ twins. The estimated coefficients *a*, *c*, and *e* are fixed to be equal across the two members of a twin pair and across MZ and DZ twins. The estimated coefficients are factor loadings that provide information about the relative contribution of the latent factors *A*, *C*, and *E* to the total variance V_T of each phenotype ($V_T = a^2 + c^2 + e^2$).

Analyses were conducted with MPlus v7.4 (Muthén & Muthén, 1998–2017), applying maximum likelihood estimation with robust standard errors procedure. Standardized estimates for factor loadings are presented in text and in figures; 95% confidence intervals are presented in brackets. Proportions of variances explained are calculated by squaring the standardized factor loadings.

Results

Preliminary analyses

Two sets of nested χ^2-difference tests examined sex and zygosity differences in substance use. Boys reported higher substance use than girls at age 17 only [$\chi^2(1) = 9.14$, $p < 0.01$]. MZ and DZ twins did not differ on substance use at any age. Table 1 presents intra-class correlations for MZ and DZ twins. At ages 13 and 14, MZ correlations were roughly double those of DZ correlations, suggesting significant additive genetic effects (Falconer, 1960). At ages 15 and 17, MZ correlations were less than double those of DZ correlations, suggesting that shared environmental effects became more prominent at these ages. Table 2 presents phenotypic correlations of adolescent substance use.

Univariate ACE models were estimated to decompose the variance of substance use – separately at each age – into additive genetic (*A*), shared environmental (*C*), and non-shared environmental (*E*) factors. Results are presented in Table 3. At each age, significant ($p < 0.001$) loadings were identified on additive genetic factors [$\gamma_A = 0.68–0.72$ (0.40–0.98)], and on non-shared environmental factors [$\gamma_E = 0.61–0.70$ (0.50–0.83)], respectively, accounting for 46–52% and for 37–49% of the variance in substance use. Loadings for shared environmental factors were identified at ages 15 and 17 [$\gamma_{C15} = 0.34$(0.00–0.73), $p = 0.091$; $\gamma_{C17} = 0.42$ (0.11–0.74), $p = 0.009$], accounting for 11 and 18% of variances in substance use.

Dual change score model without ACE decomposition

The freely estimated two-group dual change score model was acceptable, $\chi^2(6) = 8.81$, $N = 945$, $p = 0.18$, comparative fit index (*CFI*) = 0.99, root mean error of approximation (*RMSEA*) = 0.03.

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Table 2. Phenotypic correlations between variables

Variable	1 [95% CI]	2 [95% CI]	3 [95% CI]	4 [95% CI]
1. Substance use age 13	—	0.46** [0.35–0.57]	0.27** [0.17–0.36]	0.20** [0.09–0.28]
2. Substance use age 14	0.34** [0.21–0.47]	—	0.51** [0.43–0.59]	0.37** [0.32–0.48]
3. Substance use age 15	0.26** [0.15–0.37]	0.57** [0.48–0.66]	—	0.51** [0.44–0.59]
4. Substance use age 17	0.15* [0.02–0.28]	0.41** [0.34–0.52]	0.55** [0.46–0.64]	—

Note. $N = 601–672$. MZ twins are below the diagonal, DZ twins are above the diagonal; 95% confidence intervals are presented in brackets. * $p < .05$, ** $p < 0.01$.

A scaled χ^2 difference test revealed that constraining the model parameters to be equal across zygosity groups did not significantly worsen model fit [$\chi^2(11) = 9.65$, $p = 0.56$].

The final, constrained two-group dual change score model fit the data, $\chi^2(17) = 18.23$, $N = 945$, $p = 0.37$, $CFI = 1.00$, $RMSEA = 0.01$. Results are depicted in Fig. 1. The intercept [I = 2.06 (2.01–2.12)], the slope [$S = 0.44$ (0.41–0.47)], and their correlation [$r_{IS} = 0.85$ (0.77–0.93)] were significantly different from zero ($p < 0.001$). Substance use significantly increased, in a linear fashion, from age 13 to 17. Intra-class correlations for the intercept and slope of substance use were statistically significant ($p < 0.001$), and were higher for MZ twin pairs [$r_{II} = 0.68$ (0.58–0.76), $r_{SS} = 0.67$ (0.56–0.76)] than DZ twin pairs [$r_{II} = 0.45$ (0.35–0.54), $r_{SS} = 0.43$ (0.33–0.53)]. There were statistically significant ($p < 0.001$) autoregressions from substance use at age 13–14 [$\beta = 0.17$ (0.12–0.23)], and from age 14 to 15 [$\beta = 0.19$ (0.13–0.25)], but not from age 15 to 17.

Dual change score model with ACE decomposition

The next step was to conduct an ACE decomposition of the dual change score model. To this end, the variances and the covariance of the intercept and slope of substance use were decomposed into common and unique genetic (*A*), shared environmental (*C*), and non-shared environmental (*E*) sources of influence. The model fit the data, $\chi^2(63) = 86.92$, $N = 476$, $p = 0.02$, $CFI = 0.96$, $RMSEA = 0.04$. Results are depicted in Fig. 2. Significant genetic, shared environmental, and non-shared environmental factors were identified for the intercept [$\gamma_{\text{IAshared}} = 0.68$ (0.43–0.93), $\gamma_{\text{ICshared}} = 0.59$ (0.36–0.82), $\gamma_{\text{IEshared}} = 0.43$ (0.29–0.57), $p < 0.001$], which, respectively, explained 47, 35, and 18% of the variance.

Genetic factors also affected the slope of substance use but these genetic factors were partly different from the ones associated with the intercept. More precisely, 24% of the slope variance was explained by genetic factors common to the intercept [$\gamma_{\text{SAshared}} = 0.49$ (0.14–0.84), $p < 0.001$], whereas another 34% of the variance was explained by different genetic factors [$\gamma_{\text{SAunique}} = 0.58$ (0.44–0.72), $p = 0.006$]. Shared environmental and non-shared environmental effects, respectively, accounted for 30% and 12% of the slope variance [$\gamma_{\text{SCshared}} = 0.55$ (0.25–0.84), $p < 0.001$; $\gamma_{\text{SEshared}} = 0.35$ (0.13–0.58), $p = 0.002$]. The environmental effects on the slope were the same as those that influenced the intercept of substance use.

The remaining variance in substance use not captured by the intercept and growth functions of the dual change score model was decomposed into latent variables representing age-specific additive genetic (*A*13–*A*17), shared environmental (*C*13–*C*17), and non-shared environmental influences (*E*–*E*17). At ages 14 and 15, age-specific genetic factors accounted for 27% and 30% of the variance, respectively, in substance use [$\gamma_{A14} = 0.52$ (0.41–0.63), $\gamma_{A15} = 0.55$ (0.44–0.65)]. At ages 14, 15, 16, and 17, age-specific non-shared environmental factors accounted for 47, 41, 34, and 22% of the variance, respectively, in substance use [$\gamma_{A13} = 0.69$ (0.56–0.81), $\gamma_{A14} = 0.64$ (0.55–0.74), $\gamma_{A15} = 0.59$ (0.49–0.68), $\gamma_{A17} = 0.47$ (0.36–0.58)]. Age-specific genetic factors at ages 14 and 17, as well as age-specific shared environmental factors at all ages, did not reach conventional levels of statistical significance.

The final analyses examined the extent to which age-specific genetic and non-shared environmental sources of influence explained the significant autoregressions identified in the baseline dual change score model. Only autoregressions involving significant age-specific variances were estimated. Results revealed significant associations between the age-specific genetic factors at age 14 and those at age 15, $\beta = 0.38$ (0.13–0.64), $p = 0.003$, between the age-specific non-shared environmental factors at age 13 and those at age 14, $\beta = 0.22$ (0.05–0.38), $p = 0.010$, and between the age-specific non-shared environmental factors at age 14 and those at age 15, $\beta = 0.22$ (0.05–0.40), $p = 0.014$.

Discussion

Consistent with previous studies, alcohol and marijuana use increased in a linear fashion from early to late adolescence

Table 3. Univariate ACE decompositions of substance use at age 13, 14, 15, and 17

	Model fit			Standardized factor loadings		
Adolescent substance use	S-B χ^2	RMSEA	CFI	*A* [95% CI]	*C* [95% CI]	*E* [95% CI]
Age 13	5.55	0.02	0.97	0.71** [0.59–0.83]	0.00 [0.00–0.00]	0.70** [0.58–0.83]
Age 14	5.11	0.01	1.00	0.69** [0.40–0.98]	0.17 [0.00–0.77]	0.70** [0.60–0.80]
Age 15	1.33	0.00	1.00	0.72** [0.48–0.96]	0.34† [0.00–0.73]	0.61** [0.51–0.71]
Age 17	1.90	0.00	1.00	0.68** [0.43–0.93]	0.42** [0.11–0.74]	0.60** [0.50–0.70]

Note: $N = 370–397$ dyads. For all models, df = 5; 95% confidence intervals are presented in brackets. S-B χ^2 = Satorra–Bentler scaled χ^2; RMSEA, root mean error of approximation; CFI, comparative fit index. † $p = 0.09$, * $p < 0.05$, ** $p < 0.01$.

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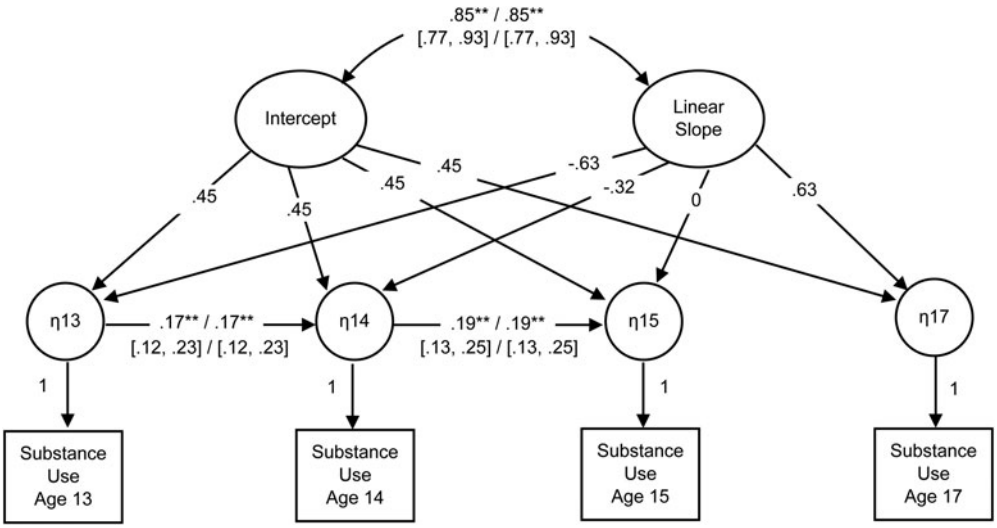

Fig. 1. Dual change score model of adolescent substance use from age 13 to 17. Note: $N = 373$ MZ and 572 DZ twins. Unstandardized factor loadings for the intercept and growth terms were orthonormalized. Standardized estimates are presented for autoregressions and for the intercept/slope correlations. Ninety-five percent confidence intervals are presented in brackets. Estimates for MZ twins are presented to the left of the slash and estimates for DZ twins are present to the right of the slash. Non-significant autoregressions were omitted from the model. $^{**}p < 0.01$.

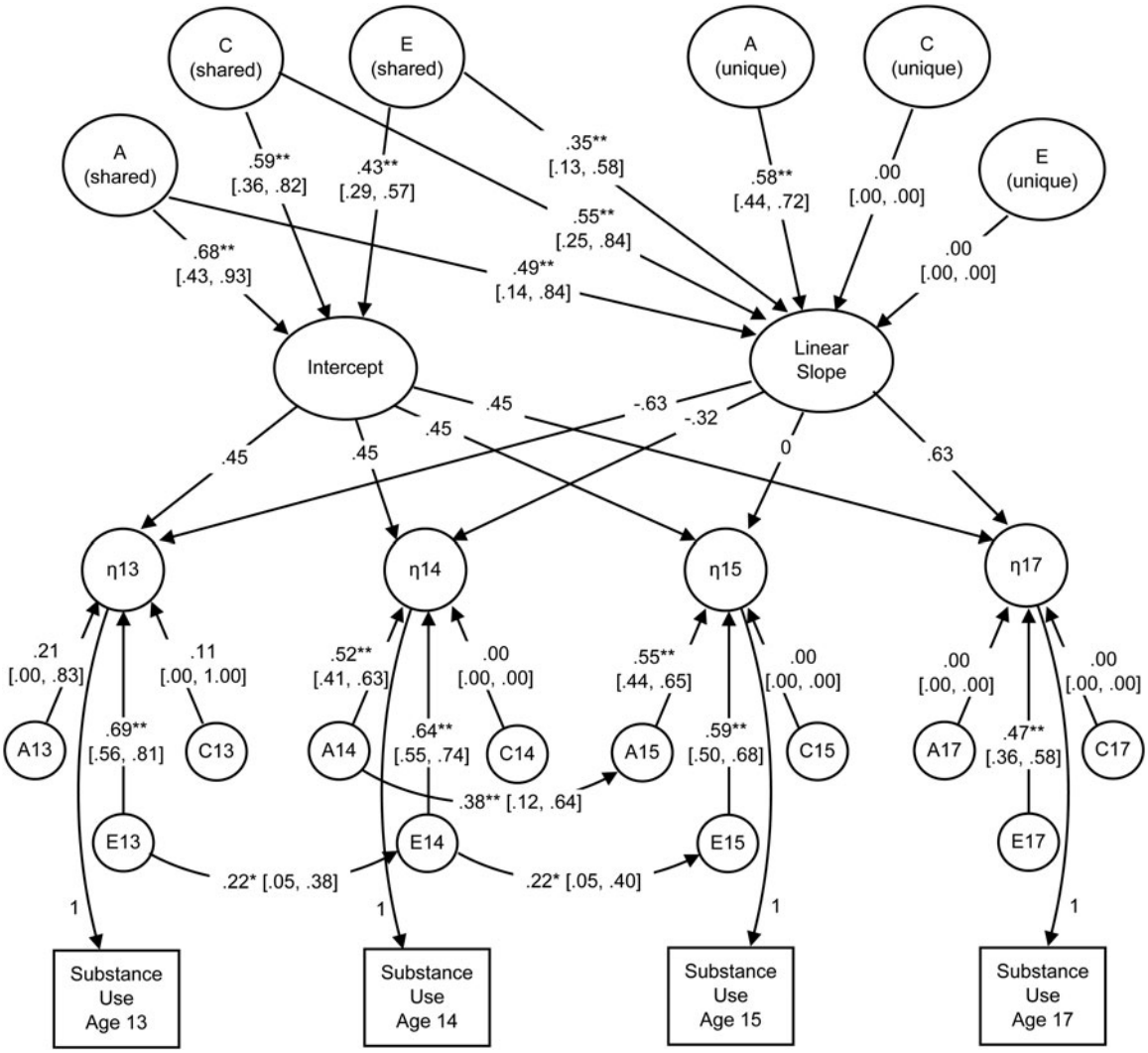

Fig. 2. ACE decomposition of the dual change score model of adolescent substance use from age 13 to 17. Note: $N = 187$ MZ and 289 DZ twin dyads. Unstandardized factor loadings for the intercept and growth terms were orthonormalized. Standardized estimates are presented for autoregressions and for all additional factor loadings. Ninety-five percent confidence intervals are presented in brackets. $^{*}p < 0.05$, $^{**}p < 0.01$.

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(Duncan & Duncan, 1996). However, both the general level of use and the rate of growth varied from one individual to another. Genetic as well as shared and non-shared environmental factors explained the general level of substance use; these same factors also partly accounted for inter-individual differences in growth in substance use from age 13 to 17. Importantly, our analyses also revealed genetic influences that are unique to the growth in substance use. These unique genetic effects were not accounted by autoregressive effects, which were also significant from age 13 to 14 and from age 14 to 15. Some of the inter-individual temporal stability of substance use, as indicated by these autoregressive paths, resulted from carry-over effects of time-specific non-shared environmental influences. However, the stability of substance use from age 14 to 15 was mostly explained by carry-over effects of time-specific genetic influences. Globally, these results are in line with the 'dual change score model' (McArdle, 2009; Eaves *et al.* 2016).

Latent growth effects

Genetic as well as shared and non-shared environmental factors affected both the general level of substance use and rates of change in substance use from age 13 to 17. The genes that might be responsible for this double effect from early to late adolescence may be the same as the genes related to heritable personal characteristics such as sensation seeking or hyperactivity–impulsivity that have been found to predict the amount and the rate of change in substance use during adolescence in non-genetically informed studies (Duncan & Duncan, 1996; Colder *et al.* 2002; Sartor *et al.* 2007). Attitudes toward substance, acquired from parents or the community, may be responsible for shared environmental influences over the level and the growth in substance use across adolescence. In other studies (e.g. Baker *et al.* 2012), perceived household substance use and parent attitudes towards substance use account for a portion of the shared environmental variance in substance use. Finally, idiosyncratic experiences with peers or others could account for non-shared environmental experiences that influence the overall level and the growth in substance use from early to late adolescence.

It is noteworthy that individual rates of change (i.e. the slope) were influenced by the unfolding of genetic factors, some of which differ from the genetic factors that influence the overall level of substance use. A similar finding emerged from the only other study of growth modeling of the development of alcohol use from age 15 to 25 (Long *et al.* 2017). In contrast to that study, however, no quadratic component was found in the present study, possibly because of the younger developmental period under examination here (i.e. the shifting point in genetic influences was age 18 in the Gillespie *et al.* study). The linear unfolding of genetic influences at different rates across individuals may reflect differential acceleration in the degree of autonomy adolescents gain across adolescence, but it could also reflect differential acceleration in maturational processes.

The possibility that genetic influences unfold at different rates for different individuals has important consequences: first, it suggests that age groups should not be collapsed. Individual growth should be considered apart from stability of substance use. Second, it suggests that prevention programs targeting same-age adolescents should account for variability in rates of change. These tentative conclusions are further accentuated by the fact that new genetic and environmental influences were also found in the autoregressive part of the model.

Autoregressive effects

Autoregressive effects partially accounted for the stability of non-shared environmental effects from age 13 to 14 and from age 14 to 15, but not from age 15 to 17. The latter null effect may have been because of the 2-year time interval. Autoregressive effects also accounted for age-specific effects at each time period. Non-shared environmental influences may be confounded with measurement error, which could explain some of the autoregressive and the time-specific effects. However, time-specific effects may also reflect environmental experiences that differ as adolescents grow older. For example, youth may not necessarily maintain the same friends over the course of adolescence. Changes in the friendship group may be reflected in emerging non-shared environmental influences. Yet despite changes in the composition of the peer network, new friends may nevertheless behave similar to old friends (e.g. they may all show high levels of substance use), which may explain the persistent effects of time-specific non-shared environmental influences that account, at least partly, for the stability of substance use from ages 13 14 and from ages 14 to 15.

Interestingly, new genetic factors emerged to influence the variability in substance use at ages 14 and 15 and they accumulated across the two ages. These new genetic factors seem to be expressed when substance use is on the rise (i.e. ages 14 and 15), but before substance use becomes normative by age 17. As suggested by Edwards & Kendler (2013), these age-specific genetic factors might represent a liability specific to substance use. In contrast, persistent genetic effects on substance use may reflect general dispositions to impulsivity, risk taking and problem behaviors (Krueger *et al.* 2002). Together, these findings help explain the increasing importance of genetic influences from early to late adolescence (e.g. Kendler *et al.* 2007; Baker *et al.* 2011). Yet, the absence of new genetic effects by age 17 is not in line with earlier studies (i.e. Kendler *et al.* 2007; Baker *et al.* 2011). These different results could be explained by the use of different instruments to assess substance use or by changing societal norms with respect to substance use. To illustrate, the retrospective assessment of substance use in the Kendler *et al.* (2008) study included substances such as caffeine and tobacco and referred to a period of time between the late 60s and the early 90s. At that time, attitudes toward substances such as alcohol and marijuana were less liberal than today (Miech *et al.* 2017). Different findings for new genetic effects at age 17 could also be explained by the fact that previous studies did not use a model that allowed for the segregation of factors driven by genetic and environmental time-specific effects from those that directly contribute to the unfolding of growth.

Strengths and limitations

The present study offers several important advantages over previous studies, including the use of a prospective longitudinal design that spans a critical period for the development of substance use and the adoption of a dual change model. Despite these merits, the present study also has limitations. First, our focus was on the frequency of substance use and not on substance-related problems. Although use by early adolescence and high involvement throughout adolescence are established precursors of later problems, caution should be exercised in generalizing our findings to the etiology of addictions. Second, we note our exclusive reliance on self-reports to assess substance use. Although adolescents' self-reports are reliable and valid, a multi-informant approach would have been preferable (Winters *et al.* 1990–91). Third, the relatively small sample size precluded the examination of possible

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sex differences. Finally, results are restricted to twins born in Quebec between 1996 and 1998.

We close with two tentative conclusions. First, it is important to determine whether specific endophenotype(s), which may themselves be heritable, mediate the genetic influences on the general level and the growth in substance use during adolescence. The identification of such phenotypes could be useful both for early screening of at-risk individuals and as a potential target for preventive interventions. As mentioned, sensation seeking/hyperactivity–impulsivity could play a role (Bezdjian *et al.* 2011), but other endophenotypes such as reward dependence/delayed discounting (i.e. how much a reward loses value based on its distance in time) (MacKillop, 2013) or a more general externalizing problem syndrome (Krueger *et al.* 2007) could be involved. Second, prevention programs in early adolescence that target personal and familial risk or beneficial factors linked to substance use may not be optimally effective, unless they are complemented by modules that specifically target later risk factors reflected in age-specific genetic and non-shared environmental influences.

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