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The Long Arm of Adolescence: School Health Behavioral Environments, Tobacco and Alcohol Co-Use, and the *5HTTLPR* Gene

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Abstract

Although sociologists, demographers, and others have thoroughly studied contextual and life-course influences on tobacco and alcohol use in adolescence and young adulthood, far less attention has been paid to the determinants of tobacco and alcohol *co-use*. This is important to remedy because co-use has non-additive effect on long-term health. In this paper, we use nationally representative, longitudinal data from adolescence to young adulthood to examine patterns of joint tobacco and alcohol use behaviors across the life course. Importantly, we describe how these trajectories are linked to their high school's joint profile of tobacco and alcohol use, measured two ways: the proportion of tobacco and alcohol co-users, and as the 'excess proportion' above that expected based on the marginal probabilities of smoking and drinking in that school. Joint tobacco and alcohol use is associated with both measures, emphasizing the 'long arm' of adolescent contexts. Furthermore, we extend previous research to assess whether there is a gene-environment interaction between this school-level measure, *5HTTLPR*, and tobacco and alcohol co-use, as suggested by recent work analyzing drinking and smoking separately. We find evidence of such a pattern, but conclude that it is likely to be due to population stratification or other forms of confounding.

Introduction

Cigarette smoking and alcohol abuse are important behavioral determinants of long-term health prospects (World Health Organization 2012, Nelson et al. 2013), especially when used together (Castellsague et al. 1999, Kalman et al. 2010). Because co-use is particularly common in adolescence and young adulthood (Grant 1998, Koopmans, vanDoornen, and Boomsma 1997, Levine et al. 2011, Weitzman and Chen 2005), it is important to consider the mechanisms responsible for the development of smoking *and* drinking as well as each separate behavior. Research on substance use frequently adopts a life course perspective that emphasizes behavioral transitions and how earlier contexts shape later-life outcomes. During adolescence, substance use and other health behaviors are closely regulated by parents (Johnston et al. 2008a, Johnston et al. 2008b, Beasley, Hackett, and Maxwell 2004, White et

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al. 2006). As individuals enter young adulthood, peers eclipse parents as the primary agents of socialization (Frech 2012, Van Ryzin, Fosco, and Dishion 2012, McDermott, Dobson, and Owen 2006), and rates of substance use and other unhealthy behaviors increase as parental control wanes (Beasley, Hackett, and Maxwell 2004, Frech 2012, Harris et al. 2006, White et al. 2006, Johnston et al. 2008a, Johnston et al. 2008b). Despite these changes in life circumstances, however, young adult health behaviors are not decoupled from the past. In general, early life conditions predict later health outcomes (Hayward and Gorman 2004, Umberson, Crosnoe, and Reczek 2010) as individuals draw on resources from earlier life stages to navigate their current circumstances (Crosnoe and Elder 2002). Accordingly, early life health behaviors are highly predictive of later-life behaviors (Lau, Jacobs Quadrel, and Hartman 1990, Telama et al. 1997). Less research has explored the specific contexts that shape health behavior trajectories during the transition to adulthood, however, with the exception of research on the independent effects of early life socioeconomic status (Lindstrom, Moden, and Rosvall 2013, Pampel, Mollborn, and Lawrence 2014, Poulton et al. 2002, Yang et al. 2007).

Research has linked tobacco and alcohol use in adolescence and adulthood to school and neighborhood characteristics cross-sectionally, however. Rates of cigarette smoking and alcohol consumption vary across schools (Aveyard, Markham, and Cheng 2004, Cleveland and Wiebe 2003, Ennett et al. 1997, Lovato et al. 2013, Maes and Lievens 2003, O'Malley et al. 2006, Rose et al. 2003, Sabiston et al. 2009, Sellstrom and Bremberg 2006) and neighborhoods (Galea et al. 2007, Karriker-Jaffe 2011, Snedker, Herting, and Walton 2009). However, the aggregate-level characteristics that may explain these patterns remain unclear. Some emphasize the role of composition (Aveyard, Markham, and Cheng 2004, Maes and Lievens 2003, O'Malley et al. 2006) and norms (Botticello 2009). A great deal of research examines the relationship of substance use rates and socioeconomic disadvantage, but varies in the direction of this association (Boardman et al. 2001, Hoffman, Welte, and Barnes 2001, Reboussin et al. 2010, Ennett et al. 1997, Galea et al. 2007, O'Malley et al. 2006). Finally, the rate of smoking in a school itself may be self-perpetuating, as peer substance use rates (Alexander et al. 2001, Eitle and Eitle 2004, Ellickson et al. 2003) and perceived rates (Chassin et al. 1984, Henry, Slater, and Oetting 2005) predict substance use initiation.

In contrast, far less research has examined the co-use of tobacco and alcohol and the potential role of school variation in predicting this key outcome. Most research on this topic has examined the relationship between these two behaviors at the individual level, showing that the two are positively related (Brener and Collins 1998, Johnson et al. 2000, Topolski et al. 2001, Orlando et al. 2005). This research concludes that the association runs more strongly in one direction than the other; i.e., far more adolescents drink without smoking than smoke without drinking (Jackson et al. 2002, Orlando et al. 2005). Approximately 22% of adolescents co-used tobacco and alcohol in the past year (Hoffman, Welte, and Barnes 2001), and rates of co-use increase with advancing age in adolescence and young adulthood (Connell et al. 2010, Costello et al. 2012, Leatherdale and Ahmed 2010). Finally, recent research (Daw, Nowotny, and Boardman 2013) demonstrates that the linkage between these two behaviors has strengthened over time even as their prevalence has declined. However, no previous research has examined the contextual determinants of tobacco and alcohol co-use, either cross-sectionally or longitudinally.

Finally, relatively little research incorporates information on both genetic influences on tobacco and alcohol use and the social environment to understand these patterns. *Gene-environment interactions* (G×Es) hold the potential to elucidate how combinations of social circumstances and genetic variation interact to predict important behaviors. Although a large number of genes (Munafo et al. 2004, Young-Wolff, Enoch, and Prescott 2011) and social influences have been linked to tobacco and alcohol use, relatively little research investigates multilevel gene-environment interactions for these outcomes, and none have taken such an approach to studying tobacco and alcohol co-use. However, outside of substance use research, a large body of research has demonstrated the potential importance of *5HTTLPR* (a polymorphic region in the SLC6A4 gene) with a large number of outcomes such as psychopathy (Fowler et al. 2009), impulsivity (Gerra et al. 2004), alcoholism (Wu et al. 2008), and violence (Liao et al. 2004, Retz et al. 2004).

This polymorphic region has played a particularly crucial role in research on gene-environment interactions. Previous research has demonstrated that individuals vary in their environmental susceptibility, which is associated with demographic characteristics like age and gender (Duncan et al. 2005, Sumter et al. 2009), but also potentially related to genetic variation. The *differential susceptibility hypothesis* (Belsky and Pluess 2009, Conley, Rauscher, and Siegal 2013, Ellis and Boyce 2008) posits that *5HTTLPR* genotype is related to environmental sensitivity, such that persons with more copies of the short (S′) allele may have very opposite outcomes depending on their environmental context. If the dependent variable is health, this hypothesis predicts that persons with more copies of the S′ allele will have better health in more favorable environments compared to others, and worse health in more unfavorable environments compared to others. In this way, persons with more copies of the S′ allele may be considered ‘orchids’ whose outcomes depend strongly on their soil, while those with more copies of the long (L′) allele may be considered ‘dandelions’ whose outcomes are comparatively insensitive to their soil (Conley, Rauscher, and Siegal 2013). In this vein, previous research has found gene-environment interactions for *5HTTLPR* for tobacco and alcohol use (Daw et al. 2013), depression (Caspi et al. 2003), physiological dysregulation (Brody et al. 2013), and juvenile delinquency (Aslund et al. 2013, Simons et al. 2011, Vaughn et al. 2009), among other outcomes. However, no research has investigated whether this model potentially applies to tobacco and alcohol co-use.

In this paper, we employ two novel measures of the school health behavioral environment (the proportion of co-users and the ‘excess proportion’ thereof), establish their associations with subsequent joint tobacco and alcohol use behaviors and behavioral transitions, and assess their role in tobacco and alcohol co-use from a gene-environment interaction perspective. Given the importance of earlier-life contexts and peer behaviors for health behavioral trajectories, and previous work relating gene-environment interactions to substance use, this research is a natural and important extension of previous work on this crucial topic. Our findings emphasize the ‘long arm’ of adolescence in predicting health behaviors years into the future, but find only questionable evidence of a gene-environment interaction between the school health behavior environment, *5HTTLPR*, and tobacco and alcohol co-use.

Analytical Strategy

The primary goal of this analysis is to investigate longitudinal patterns of tobacco and alcohol co-use in adolescence and young adulthood from a life course and gene-environment interaction perspective. Tobacco and alcohol co-use may be more likely through two separate proximate determinants: (a) the independent prevalences of tobacco and alcohol use; and (b) a tobacco-alcohol use association. For instance, if half the students at a school use alcohol and half use tobacco, even without an association one would expect that one-fourth of the students would use both alcohol and tobacco. Any proportion higher than one-fourth – i.e., an 'excess proportion' (EP) – would indicate an association between the two behaviors. More formally, one can determine the association between these two behaviors by comparing the prevalence of tobacco-and-alcohol co-use to that expected if the behaviors were independent (Daw, Nowotny, and Boardman 2013):

$$p_{ej} = p_{cj} - p_{sj}p_{dj}, \quad (1)$$

where p_{cj} is the prevalence of co-use in school j, p_{sj} is the prevalence of smoking, and p_{dj} is the prevalence of drinking. Under the assumption of independence, $p_{sj}p_{dj}$ is the expected proportion of co-users of tobacco and alcohol. Therefore p_{ej} is the 'excess' proportion of tobacco-and-alcohol co-use above that expected if the two behaviors were independent. The proportion of co-use itself (p_{cj}) is also of independent interest, since it may simply be the prevalence of co-use behavior, rather than the association between the two behaviors, that influences co-use outcomes.

We hypothesize that students attending schools with higher proportions of co-users and higher excess proportions of co-use are more likely to co-use tobacco and alcohol in subsequent. While the proportion of students at a school who use tobacco and use alcohol are separate indicators of the school health behavioral environment, the proportion of co-users and the excess proportion provides information on whether tobacco and alcohol use are *linked* at the school.

We test this hypothesis by examining over-time patterns of tobacco use, alcohol use, and their co-use; the relationship between these patterns and school-level indicators (using multinomial logistic regression and logistic regression models); and the interactive relationship between school indicators, *5HTTLPR*, and tobacco and alcohol co-use (using logistic and conditional logit regression models). This last gene-environment interaction step requires some additional exposition. A crucial methodological issue when conducting genetic research in heterogeneous populations is *population stratification*, which creates a spurious relationship between the gene and the dependent variable (Cardon and Palmer 2003). This occurs when allele frequencies vary across socially-defined groups and, for causally-unrelated reasons, significantly different levels of the dependent variable than others. The most common methods for addressing this concern require genome-wide data that are not available to us for this analysis (Price et al. 2006, Pritchard et al. 2000), and merely controlling for race/ethnicity is inadequate since these grouping mask considerable heterogeneity by ancestry group (Ramachandran et al. 2005). Instead, since population stratification occurs at the ancestry group level, we reason (like others: Conley and Rauscher

2013, Daw et al. 2013, Guo et al. 2007) that full siblings uniformly share this characteristic, since they share two parents and their implied lineages. Therefore, we address population stratification concerns using a *sibling conditional logit* model in which only within-pair differences are used to estimate these effects. Compared to the full sample logistic regression models, these models reduce the likelihood of Type I error by eliminating a large number of potential confounders, including population stratification. However, as a result of the smaller analytical sample, non-representativeness of that sample, and discarded variance, this comes at the cost of an increased likelihood of Type II error.

Data, Measures, and Analysis

Data

Data for this study come from the National Longitudinal Study of Adolescent Health (Add Health), a nationally representative dataset on secondary school attendees in 132 schools in 1994. There are currently five waves of Add Health data: the in-school survey, and four waves of in-home interviews with a subset of the attendees of those schools (Harris et al. 2009). The in-school survey offers far less depth than the in-home surveys, but has the benefit of surveying everyone at each of these schools on a moderate range of behavioral, attitudinal, and other social measures. Crucially, the in-school survey asked students to report their cigarette smoking and alcohol drinking, producing data on the health behaviors of more than 90,000 students in 132 schools, which we used to measure the school health behavioral environment. Furthermore, the longitudinal follow ups of a subset of these students (more than 15,000 in waves 3 and 4) permit study of the long-term influences of this association on co-use. In wave 4, genetic data was collected on all consenting participants using Oragene genetic data collection kits, and genotype calls were made for the *5HTTLPR* gene. As described elsewhere (Smolen et al. 2013), 15,140 (96%) of the Wave 4 Add Health Sample consented to the collection of Oragene saliva samples but only 12,234 (78%) agreed to archive their genotypes for future analyses. Archive rates varied slightly by racial and ethnic groups in which non-Hispanic blacks rate of archival (72%) was lower than that of non-Hispanic white (82%) respondents. Smolen et al. (2013) also present the Hardy Weinberg Equilibrium (HWE) estimates for all study participants and show no deviations from HWE for the *5HTTLPR* for non-Hispanic and white respondents but significant deviations among non-Hispanic and black respondents. We recalculated HWE based on the genotype frequencies presented in Table 1 which are based on the updated *5HTTLPR* genotype and we continue to see significant deviations from HWE (Chi-squared = 13.25, 1 df, $p<.001$). We largely attribute these differences to population stratification rather than genotyping errors which is largely confirmed by ancillary analyses in which HWE was met for four of the five major racial/ethnic groups. The exception was African-American respondents (HWE = 8.08, $p< .004$).

In this analysis, the Add Health data is subset to those who are the typical ages for their grades in wave I (11-12 for 6^{th} grade, 17-18 for 12^{th} grade, etc.). This results in an analytical sample size of 13,773, who are followed-up in each wave. One further characteristic of the Add Health data is crucial for present purposes. The *sibling subsample* in Add Health takes advantage of the fact that siblings frequently attend the same schools to obtain crucial data

for genetic research (Harris et al. 2013). In the in-school survey, all respondents were asked if they had a twin; Add Health sought to recruit all persons who responded affirmatively into the in-home sample. Additionally, other types of siblings were both recruited into the in-home sample by chance. As a result, the sibling subsample includes data on 289 identical twin pairs, 452 fraternal twin pairs, 1,251 full sibling pairs, and 442 half sibling pairs. For our sibling fixed effects regression models, we analyze the all full sibling and fraternal twin pairs (who share two biological parents and 50% of their genes by descent) in order to address population stratification concerns.

Measures

In-school tobacco and alcohol use measures—The school health behavior environment indicators are calculated using in-school measures of tobacco and alcohol use. The in-school tobacco use measure is constructed using the question, “During the past twelve months, how often did you smoke cigarettes?” Responses were measured ordinally on a 0–6 scale, indicating “never,” “once or twice,” “once a month or less,” “2 or 3 days a month,” “once or twice a week,” “3 to 5 days a week,” and “nearly everyday,” in order. Any tobacco use is indicated by a value of 1to 6; heavy tobacco use is indicated by a value of 6—that is, the respondent smokes cigarettes nearly every day.

The in-school alcohol use measure is based on the question, “During the past twelve months, how often did you drink beer, wine, or liquor?” Response categories are identical to those of the tobacco use measure just described. Any alcohol use is indicated by a value of 1 to 6; heavy alcohol use is indicated by values of 4 or higher—that is, the respondent drinks alcohol at least once a week. Co-use is indicated if the respondent reports both behaviors at the threshold in question.

School measures—We calculate the school health behavior environment in two different ways: the proportion of co-users, and the excess proportion of co-users using both ‘any’ and ‘heavy’ cutoffs for tobacco and alcohol use. The proportion of students who engage in these behaviors are then calculated separately by school, and then the school excess proportion for that cutoff is then calculated using equation (1). Because substance use patterns differ greatly between high school and middle school, middle schoolers are assigned the excess proportion measure for the high school into which their school feeds.

In-home tobacco and alcohol use measures—Dependent variable measures of tobacco and alcohol use come from the in-home survey, where more detailed measures were available. We employ measures that combine information on the frequency and intensity of tobacco and alcohol use over the previous 30 days and 12 months respectively to obtain an estimate of the total cigarettes and alcoholic beverages consumed over those periods. Tobacco use frequency is measured using the question, “During the past 30 days, on how many days did you smoke cigarettes?” Tobacco use intensity is measured by the question, “During the past 30 days, on the days you smoked, how many cigarettes did you smoke each day?” Multiplying these responses yields the estimated number of cigarettes smoked over the last 30 days. For analytical purposes, two dichotomous versions of this variable are created. First, any cigarette smoking is assigned a value of 1 if this number is greater than 0,

and 0 otherwise. Second, heavy cigarette smoking is assigned a value of 1 if this number is greater than the sample-wide median, and 0 otherwise.

Alcohol use frequency is measured more coarsely, using ordinal responses to the question, “During the past 12 months, on how many days did you drink alcohol?” Responses were reverse coded so that they ranged from 0 to 6, respectively indicating “never,” “1 or 2 days,” “once a month or less,” “2 or 3 days a month,” “1 or 2 days a week,” “3 to 5 days a week,” and “every day or almost every day.” Alcohol use intensity was then measured using the question, “Think of all the times you have had a drink during the past 12 months. How many drinks did you usually have each time? (A ‘drink’ is a glass of wine, a can of beer, a wine cooler, a shot glass of liquor, or a mixed drink.)” Legitimate skips were recoded to 0. An interval-level measure of the estimated number of alcoholic drinks consumed over the past 12 months is then derived by multiplying these values. Two dichotomous versions of this variable are then created, following an identical procedure as with smoking.

Controls—We also employ two school-level and six individual-level measures as controls. Because average rates of tobacco and alcohol use are potentially related to the excess proportion of co-users, we employ these measures as key controls. At the individual level, we also control for demographic characteristics such as self-reported race (coded as white, black, Hispanic, Asian/Pacific Islander, and other/multiracial), sex, parental education (coded as the highest parental response, with less than high school, high school, some college, and bachelor's degree or higher categories), and age. Finally, because both substance use and *5HTTLPR* gene are associated with delinquent behaviors and depressive symptoms, we also control for these characteristics, measured in wave I following Wang and colleagues (Wang et al. 1999). Descriptive statistics for all variables are provided in Table 1.

Analysis

Using these data, we use multinomial logistic regression models to predict tobacco use alone, alcohol use alone, or co-use of tobacco and alcohol, compared to no substance use in waves 3 and 4, as a function of the school level measures, substance use in the previous wave, and a set of school, individual demographic, and psychological controls. By predicting substance use in wave III as a function of excess proportion while controlling for substance use in wave II (or the equivalent between waves III and IV), our analysis assesses the odds of transitioning to a substance use category net of baseline substance use. Our statistical inferences employ the sandwich standard error estimator (Rogers 1993) to account for the non-independence of observations. Additionally, we investigate the effect of high school excess proportion on the probability of persisting in co-use of tobacco and alcohol between waves 3 and 4. Finally, we estimate two gene-environment interaction models. The first pools person-wave observations in a logistic regression model of the probability of co-use as a function of the interaction of school measures and *5HTTLPR*; the second estimate a sibling conditional logit model of co-use to determine whether these findings hold with adjustment for population stratification and other forms of confounding.

Results

Transitions in Substance Use—Table 2 provides information on the cross-wave substance use transition matrix in Add Health, examining the rates at which persons with one substance use profile (tobacco use only, alcohol use only, co-use, or no use) shows different substance use profiles at the subsequent wave, for both any-use and heavy-use patterns. Several patterns are immediately apparent. First, there is a high degree of fluctuation in substance use patterns over time. Between waves II and III, for instance, any-use patterns show that only those who report alcohol-only and co-use have a probability of remaining in that status of greater than 0.50. A *majority* of non-users in wave II have adopted alcohol-only use by wave III, and a majority of tobacco-only users from wave II have transitioned into co-use by wave III. In short, alcohol use is very commonly adopted between waves II and III, as expected given the stages of the life course represented during this transition (from 13-19 to 19-25). Moreover, co-users of tobacco and alcohol in wave II are much more likely to quit using tobacco (38%) than alcohol (13%). Similar patterns are observed during the same transition period for heavy substance use. However, using this definition of substance use, the tendency to remain in the same substance use category reported in wave II is stronger, and accordingly somewhat less volatility is observed.

The transition from wave III (early adulthood) to IV (established adulthood) also shows a high degree of fluctuation in health behaviors. For instance, less than half of non-users or tobacco-only users in wave III remain in those statuses in wave IV, with the majority of changers transitioning into adding alcohol consumption. Persistence in alcohol use is high, as 72% of alcohol users in wave III continue to use alcohol only in wave IV (and only 16% cease using alcohol). Finally, less than 5% of wave III co-users cease all substance use, while 14% transition to tobacco use only, 22% transition to alcohol use only, and 60% remain co-users. Similar patterns are observed for heavy use in the wave-III-to-IV transition. However, using this definition it is much more common for non-users to remain non-users, and less common for alcohol users and co-users in wave III to remain in those statuses in wave IV.

School Health Environments and Substance Use Transitions

Wave 2 to 3 Substance Use Transitions—Table 3 shows selected multinomial logistic regression results predicting wave 3 substance use outcomes net of wave 2 substance use as a function of two indicators of the school health environment – excess proportion (EP), and proportion co-users (PC). Both indicators are associated with substance use patterns in wave 3 in all models presented. Both are positively associated with all substance use compared to none, and especially strongly associated with co-use compared to none. Introducing controls for school substance use reduces these associations somewhat. For any use, the association of both measures with tobacco-only use is no longer statistically significant in this model. However, both measures are positively associated with alcohol-only use and co-use compared to no use in this model, and they are positively associated with all three non-reference categories in the equivalent heavy use models. Finally, introducing controls for delinquency and depression does not substantively affect these conclusions.

Wave 3 to 4 Transitions—Table 4 shows equivalent results for wave 3 to 4 substance use transitions. As with the wave 2 to 3 transitions, indicators of the school health environment are associated with wave 4 substance use net of wave 3 substance use in the baseline models. Both measures are positively associated with any alcohol use or co-use compared to none. Adding controls for school substance use and individual demographic factors eliminates the association with co-use, maintains the association with alcohol (marginally for PC), and produces a statistically significant, negative association with tobacco use compared to no use. Controlling for psychological characteristics largely eliminates these associations for EP (the tobacco association is marginally significant), but the associations are maintained with PC.

Somewhat different patterns are observed for heavy use. Both EP and PC are associated with concurrent heavy use, whereas PC only is associated with tobacco and alcohol use (marginally in the latter case). All associations are eliminated by controls for demographic and school characteristics, and additional controls for psychological characteristics do not change this conclusion.

Co-Use Persistence—Table 5 shows the association of school health behavioral environmental characteristics with the odds of persisting in co-use between waves III and IV among those who co-used in wave III. These analyses show that school excess proportion is negatively associated with the odds of quitting heavy, but not any, co-use between waves III and IV, although including the controls render the association only marginally significant for heavy co-use. However, these associations are fully significant in all three models for proportion co-users. Thus, although school environmental characteristics are not associated with substance use patterns in wave IV overall, it does predict the persistence of co-use between waves III and IV.

Gene-Environment Interactions—The first column of Table 6 shows the results of a series of logistic regression models predicting any or heavy co-use. The key coefficients for present purposes are the interaction terms between *5HTTLPR* and the school environmental measures. Starting with EP models, this is marginally significant for the baseline and school and demographic controls heavy use models. However, adding controls for delinquency and depression eliminates the gene-environment interaction, suggesting that this association may be mediated by these factors. These associations are stronger and more consistent, however, when PC is used as the school environmental measure. Positive interactive effects are found for all full sample models, and these interactive effects are statistically significant for all but the psychological controls model for heavy use.

However, evidence that this relationship may be spurious is provided in the sibling conditional logit regression models, which control for population stratification and other sources of family-level confounding. The results of these models consistently reject the hypothesis that there is a positive gene-environment interaction between EP, *5HTTLPR*, and tobacco and alcohol co-use – if anything, these models conclude that this interaction is typically negative, not positive. (The exception is the PC models for any co-use.) This suggests that the positive interaction estimates obtained from the full sample data are potentially due to between-family sources of spurious variation, which could be the result of

some combination of population stratification and other family-level variables related to both *5HTTLPR* and co-use.

Discussion and Conclusions

The transition from adolescence to young adulthood crucially influences trajectories of health behaviors. As many young adults leave their parents' homes and form new households, the transition to adulthood is marked by a steep decline in the proportions who eat right, get enough sleep, and avoid smoking and heavy drinking (Frech 2012). Like other life course research on health behaviors (Crosnoe and Elder 2002, Crosnoe 2004, Elder, Johnson, and Crosnoe 2003, Frech 2012), our study shows that the influence of home, school, and neighborhood during adolescence does not end when young people reach legal adulthood. We also employ two novel indicators of the school health behavioral environment that are potent predictors of joint tobacco and alcohol use throughout the life course. Finally, we investigate whether recently-documented gene-environment interactions (Daw et al. 2013) between school substance use rates, *5HTTLPR* and smoking and drinking behaviors (measured separately) apply to tobacco and alcohol co-use and our indicators of the school health environment. Although there is some weak evidence supporting this hypothesis, we conclude that this association is likely spurious due to confounding with depression, delinquency, or family-level causes (including genetic ancestry).

Explanations of this social clustering of health behaviors tend to focus on the racial and socioeconomic composition, cumulative disadvantage, or absence of social control as the key social mechanisms responsible for the clustering of poor health behaviors (Ennett et al. 1997, Galea et al. 2007, O'Malley et al. 2006, Reboussin et al. 2010) — the same domains that are regularly highlighted in the life course research on health behaviors. However, little attention is paid to the role of social factors that shape expected co-morbid behaviors for a particular context at a particular time, and no work has considered the long-term associations of these social forces. Our work is in line with the key tenets of the life course perspective and point to the importance of behavioral expectations that are structured and maintained by social institutions such as schools. However, life course research typically does not address the potential for these social influences to have genetically-contingent effects, a limitation that this paper addresses.

Because the measures included are very similar to those used by Daw and colleagues (Daw et al. 2013) and because smoking and drinking rates are highly correlated with each other and with other school health behavior environments (not shown), it is surprising that the evidence for a gene-environment interaction for co-use is much weaker than the evidence for smoking and drinking measured separately. This suggests that these previously-documented interactions are associated with the rates of substance use themselves, and not their joint profile. Insofar as these previous findings reflected differential susceptibility to modeling peers' behaviors, the current data suggest that this emulation occurs separately for each behavior. It is also important to consider that the difference in the results between the population model and the sibling fixed effects model may be due to allele frequency differences across racial and ethnic groups. The minor (short) allele frequency for non-Hispanic whites is .43 but only .27 for non-Hispanic black respondents. As such, the positive

interaction evident in our G×E models may have simply been an indication that compared to non-Hispanic and black students, non-Hispanic and white students are more likely to have co-using health behaviors that match those of their schoolmates. This was not the case for the single behaviors shown in the Daw et al. (2013), in which the sibling fixed effects results confirmed these associations. This contrast emphasizes that gene-environment interactions that describe one outcome may not characterize other, even closely related, outcomes, even in the same dataset. As such, we encourage others to explore these potential social influences on otherwise small genetic associations using independent data sources.

Research on candidate gene-environment interactions increasingly suggests caution when interpreting novel findings. For instance, Caspi's seminal findings on stressful life events and depression (Caspi et al. 2003) has an inconsistent record of replication (Risch et al. 2009, Karg et al. 2011), and remains in scientific dispute. A recent review of candidate gene-environment interaction research finds that this body of work is consistent with substantial publication bias (Duncan and Keller 2011) suggesting that novel gene-environment interaction findings should await replication before being incorporated into the scientific corpus. Although it is possible that the null findings in the G×E analysis reflect this type of random outcome, the fact that these null results resulted from an investigation of the same variables in the same dataset, but operationalized differently, suggests that there is a substantively important distinction between the processes in question that differentiates the etiology of cigarette smoking, alcohol consumption, and alcohol and tobacco co-use.

References

Alexander C, Piazza M, Mekos D, Valente T. Peers, schools, and adolescent cigarette smoking. Journal of Adolescent Health. 2001; 29(1):22–30.10.1016/s1054-139x(01)00210-5 [PubMed: 11429302]

Aslund C, Comasco E, Nordquist N, Leppert J, Oreland L, Nilsson KW. Self-reported family socioeconomic status, the 5-HTTLPR genotype, and delinquent behavior in a community-based adolescent population. Aggress Behav. 2013; 39(1):52–63.10.1002/ab.21451 [PubMed: 22987641]

Aveyard, Paul; Markham, Wolfgang A.; Cheng, KK. A Methodological and Substantive Review of the Evidence that Schools Cause Pupils to Smoke. Social Science & Medicine. 2004; 58:2253–2265. [PubMed: 15047082]

Beasley, Lucy J.; Hackett, Allan F.; Maxwell, Sheila. The dietary and health behaviour of young people aged 18–25 years living independently or in the family home in Liverpool, UK. International Journal of Consumer Studies. 2004; 28(4):355–363.

Belsky J, Pluess M. Beyond Diathesis Stress: Differential Susceptibility to Environmental Influences. Psychological Bulletin. 2009; 135(6):885–908.10.1037/a0017376 [PubMed: 19883141]

Boardman JD, Finch BK, Ellison CG, Williams DR, Jackson JS. Neighborhood disadvantage, stress, and drug use among adults. Journal of Health and Social Behavior. 2001; 42(2):151–165.10.2307/3090175 [PubMed: 11467250]

Botticello AL. School Contextual Influences on the Risk for Adolescent Alcohol Misuse. American Journal of Community Psychology. 2009; 43(1-2):85–97.10.1007/s10464-008-9226-4 [PubMed: 19156512]

Brener ND, Collins JL. Co-occurrence of health-risk behaviors among adolescents in the United States. Journal of Adolescent Health. 1998; 22(3):209–213.10.1016/s1054-139x(97)00161-4 [PubMed: 9502008]

Brody GH, Yu T, Chen YF, Kogan SM, Evans GW, Beach SR, Windle M, Simons RL, Gerrard M, Gibbons FX, Philibert RA. Cumulative socioeconomic status risk, allostatic load, and adjustment: a prospective latent profile analysis with contextual and genetic protective factors. Dev Psychol. 2013; 49(5):913–27.10.1037/a0028847 [PubMed: 22709130]

Cardon, Lon R.; Palmer, Lyle J. Population stratification and spurious allelic association. Lancet. 2003; 361(9357):598. [PubMed: 12598158]

Caspi A, Sugden K, Moffitt TE, Taylor A, Craig IW, Harrington H, McClay J, Mill J, Martin J, Braithwaite A, Poulton R. Influence of life stress on depression: Moderation by a polymorphism in the 5-HTT gene. Science. 2003; 301(5631):386–389.10.1126/science.1083968 [PubMed: 12869766]

Castellsague X, Munoz N, De Stefani E, Victora CG, Castelletto R, Rolon PA, Quintana MJ. Independent and joint effects of tobacco smoking and alcohol drinking on the risk of esophageal cancer in men and women. International Journal of Cancer. 1999; 82(5):657–664.10.1002/(sici)1097-0215(19990827)82:5<657: :aid-ijc7>3.0.co;2-c [PubMed: 10417762]

Chassin L, Presson CC, Sherman SJ, Corty E, Olshavsky RW. Predicting the Onset of Cigarette-Smoking in Adolescents - A Longitudinal Study. Journal of Applied Social Psychology. 1984; 14(3):224–243.10.1111/j.1559-1816.1984.tb02233.x

Cleveland HH, Wiebe RP. The moderation of genetic and shared-environmental influences on adolescent drinking by levels of parental drinking. Journal of Studies on Alcohol. 2003; 64(2): 182–194. [PubMed: 12713191]

Conley D, Rauscher E, Siegal ML. Beyond Orchids and Dandelions: Testing the 5-HTT “Risky” Allele for Evidence of Phenotypic Capacitance and Frequency-Dependent Selection. Biodemography and Social Biology. 2013; 59(1):37–56.10.1080/19485565.2013.774620 [PubMed: 23701535]

Conley, Dalton; Rauscher, Emily. Genetic Interactions with Prenatal Social Environment: Effects on Academic and Behavioral Outcomes. Journal of Health and Social Behavior. 2013; 54(1):109–127. [PubMed: 23475742]

Connell, Christian M.; Gilreath, Tamika D.; Aklin, Will M.; Brex, Robert A. Social-Ecological Influences on Patterns of Substance Use Among Non-Metropolitan High School Sudents. American Journal of Community Psychology. 2010; 45:36–48. [PubMed: 20077132]

Costello, Mary Jean E.; Leatherdale, Scott T.; Ahmed, Rashid; Church, Dana L.; Cunningham, John A. Co-morbid substance use behaviors among youth: any impact of school environment? Global Health Promotion. 2012; 19(1):50–59. [PubMed: 24801315]

Crosnoe R. Social Capital and the Interplay of Families and Schools. Journal of Marriage and Family. 2004; 66(2):267–280.

Crosnoe R, Elder GH. Successful Adaptation in the Later Years: A Life Course Approach to Aging. Social Pschology Quarterly. 2002; 65(4):309–328.

Daw, Jonathan; Nowotny, Kathryn M.; Boardman, Jason D. Changing Patterns of Tobacco and Alcohol Co-Use by Gender in the United States, 1976-2010. Demographic Research. 2013

Daw, Jonathan; Shanahan, Michael; Harris, Kathleen Mullan; Smolen, Andrew; Haberstick, Brett; Boardman, Jason D. Genetic Sensitivity to Peer Behaviors: 5HTTLPR, Smoking, and Alcohol Consumption. Journal of Health and Social Behavior. 2013; 54(1):92–108. [PubMed: 23292504]

Duncan GJ, Boisjoly J, Kremer M, Levy DM, Eccles J. Peer effects in drug use and sex among college students. Journal of Abnormal Child Psychology. 2005; 33(3):375–385.10.1007/s10802-005-3576-2 [PubMed: 15957564]

Duncan, Laramie E.; Keller, Matthew C. A Critical Review of the First Ten Years of Candidate Gene-by-Environment Interaction Research in Psychiatry. American Journal of Psychiatry. 2011; 168(10):1041–1049. [PubMed: 21890791]

Eitle DJ, Eitle TM. School and county characteristics as predictors of school rates of drug, alcohol, and tobacco offenses. Journal of Health and Social Behavior. 2004; 45(4):408–421. [PubMed: 15869113]

Elder, GH.; Johnson, MK.; Crosnoe, R. The Emergence and Development of Life Course Theory. In: Mortimer, JT.; Shanahan, MJ., editors. Handbook of the Life Course. New York: Kluwer Academic; 2003. p. 10-19.

Ellickson PL, Bird CE, Orlando M, Klein DJ, McCaffrey DE. Social context and adolescent health behavior: Does school-level smoking prevalence affect students' subsequent smoking behavior? Journal of Health and Social Behavior. 2003; 44(4):525–535.10.2307/1519797 [PubMed: 15038147]

Ellis BJ, Boyce WT. Biological sensitivity to context. Current Directions in Psychological Science. 2008; 17(3):183–187.10.1111/j.1467-8721.2008.00571.x

Ennett, Susan T.; Flewelling, Robert L.; Lindrooth, Richard C.; Norton, Edward C. School and Neighborhood Characteristics Associated with School Rates of Alcohol, Cigarettte, and Marijuana Use. Journal of Health and Social Behavior. 1997; 38(1):55–71. [PubMed: 9097508]

Fowler T, Langley K, Rice F, van den Bree MBM, Ross K, Wilkinson LS, Owen MJ, O'Donovan MC, Thapar A. Psychopathy trait scores in adolescents with childhood ADHD: the contribution of genotypes affecting MAOA, 5HTT and COMT activity. Psychiatric Genetics. 2009; 19(6):312–319.10.1097/YPG.0b013e3283328df4 [PubMed: 19829167]

Frech, Adrianne. Healthy Behavior Trajectories between Adolescence and Young Adulthood. Advances in Life Course Research. 2012; 17:59–68. [PubMed: 22745923]

Galea, Sandro; Ahern, Jennifer; Tracy, Melissa; Vlahov, David. Neighborhood Income and Income Distribution and the Use of Cigarettes, Alcohol, and Marijuana. American Journal of Preventive Medicine. 2007; 32(6S):S195–S202. [PubMed: 17543711]

Gerra G, Garofano L, Santoro G, Bosari S, Pellegrini C, Zaimovic Z, Moi G, Bussandri M, Moi A, Brambilla F, Donnini C. Association between low-activity serotonin transporter genotype and heroin dependence: Behavioral and personality correlates. American Journal of Medical Genetics Part B-Neuropsychiatric Genetics. 2004; 126B(1):37–42.10.1002/ajmg.b.20111

Grant BF. Age at smoking onset and its association with alcohol consumption and DSM-IV alcohol abuse and dependence: Results from the national longitudinal alcohol epidemiologic survey. Journal of Substance Abuse. 1998; 10(1):59–73.10.1016/s0899-3289(99)80141-2 [PubMed: 9720007]

Guo G, Tong YY, Xie CW, Lange LA. Dopamine transporter, gender, and number of sexual partners among young adults. European Journal of Human Genetics. 2007; 15(3):279–287.10.1038/sj.ejhg.5201763 [PubMed: 17245411]

Harris KM, Gordon-Larsen P, Chantala K, Udry JR. Longitudinal trends in race/ethnic disparities in leading health indicators from adolescence to young adulthood. Archives of Pediatrics & Adolescent Medicine. 2006; 160(1):74–81.10.1001/archpedi.160.1.74 [PubMed: 16389215]

Harris KM, Halpern CT, Haberstick BC, Smolen A. The National Longitudinal Study of Adolescent Health (Add Health) Sibling Pairs Data. Twin Research and Human Genetics. 2013; 16(1):391–398.10.1017/thg.2012.137 [PubMed: 23231780]

Harris, Kathleen M.; Halpern, CT.; Whitsel, E.; Hussey, J.; Tabor, J.; Entzel, P.; Udry, JR. The National Longitudinal Study of Adolescent Health: Research Design. 2009. Available from http://www.cpc.unc.edu/projects/addhealth/design

Hayward MD, Gorman BK. The long arm of childhood: the influence of early-life social conditions on men's mortality. Demography. 2004; 41:87–107. [PubMed: 15074126]

Henry KL, Slater MD, Oetting ER. Alcohol use in early adolescence: The effect of changes in risk taking, perceived harm and friends' alcohol use. Journal of Studies on Alcohol. 2005; 66(2):275–283. [PubMed: 15957679]

Hoffman JH, Welte JW, Barnes GM. Co-occurrence of alcohol and cigarette use among adolescents. Addictive Behaviors. 2001; 26(1):63–78.10.1016/s0306-4603(00)00089-7 [PubMed: 11196293]

Jackson KM, Sher KJ, Cooper ML, Wood PK. Adolescent alcohol and tobacco use: onset, persistence and trajectories of use across two samples. Addiction. 2002; 97(5):517–531.10.1046/j.1360-0443.2002.00082.x [PubMed: 12033653]

Johnson PB, Boles SM, Vaughan R, Kleber HD. The co-occurrence of smoking and binge drinking in adolescence. Addictive Behaviors. 2000; 25(5):779–783.10.1016/s0306-4603(99)00066-0 [PubMed: 11023019]

Johnston, LD.; O'Malley, PM.; Bachman, JG.; Schulenberg, JE. Monitoring the future: National survey results on drug use, 1975–2007. In: National Institute on Drug Abuse. , editor. Secondary school students. Vol. 1. Bethesda, MD: 2008a.

Johnston, LD.; O'Malley, PM.; Bachman, JG.; Schulenberg, JE. Monitoring the future: National survey results on drug use, 1975–2007. In: National Institute on Drug Abuse. , editor. College students and adults ages 19–45. Vol. II. Bethesda, MD: 2008b.

Kalman D, Kim S, DiGirolamo G, Smelson D, Ziedonis D. Addressing tobacco use disorder in smokers in early remission from alcohol dependence: The case for integrating smoking cessation services in substance use disorder treatment programs. Clinical Psychology Review. 2010; 30(1): 12–24.10.1016/j.cpr.2009.08.009 [PubMed: 19748166]

Karg, Katja; Burmeister, Margit; Shedden, Kerby; Sen, Srijan. The Serotonin Transporter Promoter Variant (5-HTTLPR), Stress, and Depression Meta-Analysis Revisited. Archives of General Psychiatry. 2011; 68(5):444–454. [PubMed: 21199959]

Karriker-Jaffe, Katherine J. Areas of Disadvantage: A Systematic Review of Effects of Area-Level Socioeconomic Status on Substance Use Outcomes. Drug and Alcohol Review. 2011; 30:84–95. [PubMed: 21219502]

Koopmans JR, vanDoornen LJP, Boomsma DI. Association between alcohol use and smoking in adolescent and young adult twins: A bivariate genetic analysis. Alcoholism-Clinical and Experimental Research. 1997; 21(3):537–546.10.1097/00000374-199705000-00022

Lau R, Jacobs Quadrel M, Hartman KA. Development and Change of Young Adults' Preventive Health Beliefs and Behavior: Influence from Parents and Peers. Journal of Health and Social Behavior. 1990; 31(3):240–259. [PubMed: 2133479]

Leatherdale, Scott T.; Ahmed, Rashid. Alcohol, marijuana, and tobacco use among Canadian Youth: Do we need more multi-substance prevention programming? Journal of Primary Prevention. 2010; 31:99–108. [PubMed: 20352492]

Levine A, Huang YY, Drisaldi B, Griffin EA, Pollak DD, Xu SQ, Yin DQ, Schaffran C, Kandel DB, Kandel ER. Molecular Mechanism for a Gateway Drug: Epigenetic Changes Initiated by Nicotine Prime Gene Expression by Cocaine. Science Translational Medicine. 2011; 3(107)

Liao DL, Hong CJ, Shih HL, Tsai SJ. Possible association between serotonin transporter promoter region polymorphism and extremely violent crime in Chinese males. Neuropsychobiology. 2004; 50(4):284–287.10.1159/000080953 [PubMed: 15539857]

Lindstrom M, Moden B, Rosvall M. A life-course perspective on economic stress and tobacco smoking: a population-based study. Addiction. 2013; 108(7):1305–1314.10.1111/add.12143 [PubMed: 23432606]

Lovato C, Watts A, Brown KS, Lee D, Sabiston C, Nykiforuk C, Eyles J, Manske S, Campbell HS, Thompson M. School and Community Predictors of Smoking: A Longitudinal Study of Canadian High Schools. American Journal of Public Health. 2013; 103(2):362–368.10.2105/ajph.2012.300922 [PubMed: 23237165]

Maes, Lea; Lievens, John. Can the School Make a Difference? A Multilevel Analysis of Adolescent Risk and Health Behavior. Social Science & Medicine. 2003; 56:517–529. [PubMed: 12570971]

McDermott LJ, Dobson AJ, Owen N. From partying to parenthood: young women's perceptions of cigarette smoking across life transitions. Health Education Research. 2006; 21(3):428–439.10.1093/her/cyl041 [PubMed: 16740675]

Munafo MR, Clark TG, Johnstone EC, Murphy MFG, Walton RT. The genetic basis for smoking behavior: A systematic review and meta-analysis. Nicotine & Tobacco Research. 2004; 6(4):583–597.10.1080/14622200410001734030 [PubMed: 15370155]

Nelson, David E.; Jarman, Dwayne W.; Rehm, Jurgen; Greenfield, Thomas K.; Rey, Gregoire; Kerr, William C.; Miller, Paige; Shield, Kevin D.; Ye, Yu; Naimi, Timothy S. Alcohol-Attributable Cancer Deaths and Years of Potential Life Lost in the United States. American Journal of Public Health. 2013; 103(4):641–648. [PubMed: 23409916]

O'Malley, Patrick M.; Johnston, Lloyd D.; Bachman, Jerald G.; Schulenberg, John E.; Kumar, Revathy. How Substance Use Differs Among American Secondary Schools. Prevention Science. 2006; 7:409–420. [PubMed: 16900406]

Organization, World Health. Tobacco. Fact Sheet. 2012:339.

Orlando M, Tucker JS, Ellickson PL, Klein DJ. Concurrent use of alcohol and cigarettes from adolescence to young adulthood: An examination of developmental trajectories and outcomes. Substance Use & Misuse. 2005; 40(8):1051–1069.10.1081/ja-200030789 [PubMed: 16040368]

Pampel, Fred C.; Mollborn, Stefanie; Lawrence, Elizabeth M. Life Course Transitions in Early Adulthood and SES Disparities in Tobacco Use. Social Science Research. 2014; 43:45–59. [PubMed: 24267752]

Poulton R, Caspi A, Milne BJ, Thomson WM, Taylor A, Sears MR, Moffitt TE. Association between children's experience of socioeconomic disadvantage and adult health: a life-course study. Lancet. 2002; 360(9346):1640–1645.10.1016/s0140-6736(02)11602-3 [PubMed: 12457787]

Price, Alkes L.; Patterson, Nick J.; Plenge, Robert M.; Weinblatt, Michael E.; Shadick, Nancy A.; Reich, David. Principal components analysis corrects for stratification in genome-wide association studies. Nature Genetics. 2006; 38:904–909. [PubMed: 16862161]

Pritchard JK, Stephens M, Rosenberg NA, Donnelly P. Association mapping in structured populations. American Journal of Human Genetics. 2000; 67(1):170–181. [PubMed: 10827107]

Ramachandran S, Deshpande O, Roseman CC, Rosenberg NA, Feldman MW, Cavalli-Sforza LL. Support from the relationship of genetic and geographic distance in human populations for a serial founder effect originating in Africa. Proceedings of the National Academy of Sciences of the United States of America. 2005; 102(44):15942–15947.10.1073/pnas.0507611102 [PubMed: 16243969]

Reboussin, Beth A.; Preisser, John S.; Song, EunYoung; Wolfson, Mark. Geographic Clustering of Underage Drinking and the Influence of Community Characteristics. Drug and Alcohol Dependence. 2010; 106:38–47. [PubMed: 19740611]

Retz W, Retz-Junginger P, Supprian T, Thome J, Rosler M. Association of serotonin transporter promoter gene polymorphism with violence: Relation with personality disorders, impulsivity, and childhood ADHD psychopathology. Behavioral Sciences & the Law. 2004; 22(3):415–425.10.1002/bsl.589 [PubMed: 15211560]

Risch, Neil; Herrell, Richard; Lehner, Thomas; Liang, KungYee; Eaves, Lindon; Hoh, Josephine; Griem, Andrea; Kovacs, Maria; Ott, Jurg; Merkangas, Kathleen Ries. Interaction Between the Serotonin Transporter Gene (5-HTTLPR), Stressful Life Events, and Risk of Depression: A Meta-analysis. Journal of the American Medical Association. 2009; 301(23):2462–2471. [PubMed: 19531786]

Rogers, William H. sg17: Regression standard errors in clustered samples. Stata Technical Bulletin. 1993; 13:19–23.

Rose RJ, Viken RJ, Dick DM, Bates JE, Pulkkinen L, Kaprio J. It does take a village: Nonfamilial environments and children's behavior. Psychological Science. 2003; 14(3):273–277.10.1111/1529-1006.03434 [PubMed: 12741753]

Sabiston CM, Lovato CY, Ahmed R, Pullman AW, Hadd V, Campbell HS, Nykiforuk C, Brown KS. School Smoking Policy Characteristics and Individual Perceptions of the School Tobacco Context: Are They Linked to Students' Smoking Status? Journal of Youth and Adolescence. 2009; 38(10):1374–1387.10.1007/s10964-009-9422-z [PubMed: 19779813]

Sellstrom E, Bremberg S. “Is there a school effect” on pupil outcomes? A review of multilevel studies. Journal of Epidemiology and Community Health. 2006; 60(2):149–155.10.1136/jech.2005.036707 [PubMed: 16415266]

Simons, Ronald L.; Lei, Man Kit; Beach, Steven RH.; Brody, Gene H.; Philibert, Robert A.; Gibbons, Frederic X. Social Environment, Genes, and Aggression: Evidence Supporting the Differential Susceptibility Perspective. American Sociological Review. 2011; 76(6):883–912.

Snedker, Karen A.; Herting, Jereald R.; Walton, Emily. Contextual Effects and Adolescent Substance Use: Exploring the Role of Neighbohoods. Social Science Quarterly. 2009; 90(5):1272–1297.

Sumter SR, Bokhorst CL, Steinberg L, Westenberg PM. The developmental pattern of resistance to peer influence in adolescence: Will the teenager ever be able to resist? Journal of Adolescence. 2009; 32(4):1009–1021.10.1016/j.adolescence.2008.08.010 [PubMed: 18992936]

Telama R, Yang X, Laakso L, Viikari J. Physical Activity in Childhood and Adolescence as Predictor of Physical Activity in Young Adulthood. American Journal of Preventive Medicine. 1997; 13(4):317–323. [PubMed: 9236971]

Topolski TD, Patrick DL, Edwards TC, Huebner CE, Connell FA, Mount KK. Quality of life and health-risk behaviors among adolescents. Journal of Adolescent Health. 2001; 29(6):426–435.10.1016/s1054-139x(01)00305-6 [PubMed: 11728892]

Umberson, Debra; Crosnoe, Robert; Reczek, Corinne. Social relationships and health behaviors across the life course. Annual Review of Sociology. 2010; 36:139–157.

Van Ryzin MJ, Fosco GM, Dishion TJ. Family and peer predictors of substance use from early adolescence to early adulthood: An 11-year prospective analysis. Addictive Behaviors. 2012; 37(12):1314–1324.10.1016/j.addbeh.2012.06.020 [PubMed: 22958864]

Vaughn MG, DeLisi M, Beaver KM, Wright JP. DAT1 and 5HTT Are Associated With Pathological Criminal Behavior in a Nationally Representative Sample of Youth. Criminal Justice and Behavior. 2009; 36(11):1113–1124.10.1177/0093854809342839

Wang, Min Qi; Fitzhugh, Eugene C.; Green, Bernard Lee; Turner, Lori W.; Eddy, James M.; Westerfield, R Carl. Prospective Social-Psychological Factors of Adolescent Smoking Progression. Journal of Adolescent Health. 1999; 24:2–9. [PubMed: 9890358]

Weitzman ER, Chen YY. The co-occurrence of smoking and drinking among young adults in college: National survey results from the United States. Drug and Alcohol Dependence. 2005; 80(3):377–386.10.1016/j.drugalcdep.2005.05.008 [PubMed: 16009507]

White HR, McMorris BJ, Catalano RF, Fleming CB, Haggerty KP, Abbott RD. Increases in alcohol and marijuana use during the transition out of high school into emerging adulthood: The effects of leaving home, going to college, and high school protective factors. Journal of Studies on Alcohol. 2006; 67(6):810–822. [PubMed: 17060997]

Wu CY, Wu YS, Lee JF, Huang SY, Yu L, Ko HC, Lu RB. The association between DRD2/ANKK1, 5-HTTLPR gene, and specific personality trait on antisocial alcoholism among Han Chinese in Taiwan. American Journal of Medical Genetics Part B-Neuropsychiatric Genetics. 2008; 147B(4): 447–453.10.1002/ajmg.b.30626

Yang SM, Lynch JW, Raghunathan TE, Kauhanen J, Salonen JT, Kaplan GA. Socioeconomic and psychosocial exposures across the life course and binge drinking in adulthood: Population-based study. American Journal of Epidemiology. 2007; 165(2):184–193.10.1093/aje/kwj357 [PubMed: 17074968]

Young-Wolff KC, Enoch MA, Prescott CA. The influence of gene-environment interactions on alcohol consumption and alcohol use disorders: A comprehensive review. Clinical Psychology Review. 2011; 31(5):800–816.10.1016/j.cpr.2011.03.005 [PubMed: 21530476]

Table 1

Proportion Using Substances by Wave and School-Level Descriptive Statistics

Individual Characteristics	N	Mean	SD	Min.	Max.
Gender	55,084				
Male		0.480	--	0	1
Female		0.520	--	0	1
Race	55,044				
White		0.530	--	0	1
Black		0.219	--	0	1
Hispanic		0.160	--	0	1
Asian		0.075	--	0	1
Other		0.015	--	0	1
Parental Education	47,316				
<HS		0.113	--	0	1
HS		0.244	--	0	1
Some College		0.306	--	0	1
BA+		0.337	--	0	1
CES-D	55,016	10.9	7.45	0	56
Delinquency Scale	54,820	4.12	5.03	0	45
Age by Wave					
Wave 1	13,765	15.2	1.65	13	20
Wave 2	9,702	16.2	1.57	13	21
Wave 3	10,239	21.9	1.70	18	27
Wave 4	10,600	28.4	1.70	24	31
5HTTLPR	44,941				
L′/L′		0.237	--	0	1
S′/L′		0.482	--	0	1
S′/S′		0.280	--	0	1
School Variables	**N**	**Mean**	**SD**	**Min.**	**Max.**
School Mean Tobacco Use	133				

Individual Characteristics	N	Mean	SD	Min.	Max.
Any Use		35.4	8.2	5.6	53.6
Heavy Use		10.4	4.9	0.0	25.7
School Mean Alcohol Use	133				
Any Use		53.9	9.5	12.0	72.9
Heavy Use		10.8	3.9	0.0	22.9
School Excess Proportion (EP)	133				
Any Use		9.08	2.5	1.2	15.6
Heavy Use		2.75	1.2	-0.2	8.3
School Proportion Co-Users (PC)	129				
Any Use		29.0	7.5	5.6	49.9
Heavy Use		4.02	1.9	0.0	14.2

Note: All school variable values are multiplied by 100, here and in regression models. The analytical sample includes 13,773 individuals, observed across four in-home waves of the Add Health dataset. Sample sizes for individual characteristics reflect pooled person*wave observations (with the exception of age by wave). Sample sizes for schools are the number of discrete schools, and descriptive statistics are calculated at the school level.

Table 2

Tobacco and Alcohol Use Behavior Transitions

Any Use						Heavy Use					
	Wave 3						Wave 3				
Wave 2	None	Tobacco	Alcohol	Concurrent	N	Wave 2	None	Tobacco	Alcohol	Concurrent	N
None	0.338	0.033	0.501	0.128	3,742	None	0.562	0.052	0.299	0.088	5,511
Tobacco	0.157	0.128	0.192	0.523	578	Tobacco	0.144	0.332	0.147	0.377	313
Alcohol	0.123	0.018	0.680	0.180	1,663	Alcohol	0.269	0.054	0.514	0.164	1,252
Co-Use	0.073	0.060	0.305	0.561	1,546	Co-Use	0.104	0.197	0.181	0.519	453
	Wave 4						Wave 4				
Wave 3	None	Tobacco	Alcohol	Concurrent	N	Wave 3	None	Tobacco	Alcohol	Concurrent	N
None	0.473	0.060	0.390	0.078	1,856	None	0.721	0.037	0.215	0.028	4,069
Tobacco	0.099	0.379	0.099	0.423	362	Tobacco	0.211	0.436	0.080	0.273	653
Alcohol	0.138	0.024	0.717	0.121	4,172	Alcohol	0.355	0.026	0.562	0.058	2,783
Co-Use	0.045	0.135	0.217	0.603	2,261	Co-Use	0.120	0.223	0.213	0.444	1,146

Note: All proportions are row-normalized.

Biodemography Soc Biol. Author manuscript; available in PMC 2016 April 25.

Table 3

Multinomial Logistic Regressions, Wave 2 to 3 Transitions in Tobacco and Alcohol Use Behaviors

Any Use	**Baseline**			**+ School & Demographic Controls**			**+Psychological Controls**		
	Tobacco vs. None	**Alcohol vs. None**	**Co-Use vs. None**	**Tobacco vs. None**	**Alcohol vs. None**	**Co-Use vs. None**	**Tobacco vs. None**	**Alcohol vs. None**	**Co-Use vs. None**
Excess Proportion	1.122*	1.139*	1.212*	0.989	1.092*	1.074*	0.985	1.090*	1.073*
Proportion Co-Users	1.046*	1.048*	1.068*	0.945	1.088*	1.060*	0.943	1.088*	1.061*
	Baseline			**+ School & Demographic Controls**			**+Psychological Controls**		
Heavy Use	Tobacco vs. None	Alcohol vs. None	Co-Use vs. None	Tobacco vs. None	Alcohol vs. None	Co-Use vs. None	Tobacco vs. None	Alcohol vs. None	Co-Use vs. None
Excess Proportion	1.419*	1.292*	1.439*	1.264*	1.176*	1.200*	1.264*	1.173*	1.199*
Proportion Co-Users	1.252*	1.170*	1.259*	1.210*	1.127*	1.154+	1.211*	1.124*	1.153+

NOTE:

+ <.10;

* : p<.05.

All models include controls for previous wave health behavior. School and demographic controls include controls for race, gender, age, and school proportion smoking and drinking. Psychological controls include an index of delinquent behaviors and CES-D score.

Biodemography Soc Biol. Author manuscript; available in PMC 2016 April 25.

Table 4

Multinomial Logistic Regressions, Wave 3 to 4 Transitions in Tobacco and Alcohol Use Behaviors

Any Use	Baseline			+ School & Demographic Controls			+Psychological Controls		
	Tobacco vs. None	Alcohol vs. None	Co-Use vs. None	Tobacco vs. None	Alcohol vs. None	Co-Use vs. None	Tobacco vs. None	Alcohol vs. None	Co-Use vs. None
Excess Proportion	1.000	1.077*	1.069*	0.938*	1.075*	1.026	0.943+	1.031	0.999
Proportion Co-Users	1.012	1.027*	1.029*	0.914*	1.046+	1.011	0.911*	1.044+	1.008
Heavy Use	**Baseline**			**+ School & Demographic Controls**			**+Psychological Controls**		
	Tobacco vs. None	Alcohol vs. None	Co-Use vs. None	Tobacco vs. None	Alcohol vs. None	Co-Use vs. None	Tobacco vs. None	Alcohol vs. None	Co-Use vs. None
Excess Proportion	1.059	1.045	1.153*	0.874	0.977	1.010	0.883	0.992	1.021
Proportion Co-Users	1.071*	1.032+	1.119*	0.868	0.966	0.999	0.882	0.982	1.013

NOTE:

+ :<.10;

* : p<.05.

All models include controls for previous wave health behavior. School and demographic controls include controls for race, gender, age, and school proportion smoking and drinking. Psychological controls include an index of delinquent behaviors and CES-D score.

Table 5
Co-Use Persistence Between Waves 3 & 4

Any Use	**Baseline**	**+ School & Demographic Controls**	**+Psychological Controls**
Excess Proportion	0.977	1.010	1.008
Proportion Co-Users	0.990	0.992	0.991
Heavy Use	**Baseline**	**+ School & Demographic Controls**	**+Psychological Controls**
Excess Proportion	0.865*	0.833+	0.832+
Proportion Co-Users	0.913*	0.796*	0.795*

Note: N=2,599 for the any use models (2,595 for the psychological control model); N= 1,345 for the heavy use models (1,342 for the psychological control model).

Table 6

Gene-Environment Interaction Models of Tobacco and Alcohol Co-use

Any Co-Use	**Baseline**		**+ School & Demographic Controls**		**+ Psychological Controls**	
	All	**Sibling FE**	**All**	**Sibling FE**	**All**	**Sibling FE**
EP	1.096*	--	0.998	--	1.011	--
5HTTLPR*S′	0.936	2.039	0.915	2.039	1.017	1.994
EP × 5HTTLPR*S′	1.007	0.931	1.010	0.931	0.999	0.931
Prop Co-Use (PC)	1.038*	--	0.988	--	0.994	--
5HTTLPR*S′	0.774*	0.663	0.748*	0.664	0.807*	0.612
PC × 5HTTLPR*S′	1.009*	1.013	1.010*	1.013	1.008*	1.015
Heavy Co-Use	**Baseline**		**+ School & Demographic Controls**		**+ Psychological Controls**	
	All	Sibling FE	All	Sibling FE	All	Sibling FE
EP	1.306*	--	1.033	--	1.056	--
5HTTLPR*S′	0.813*	1.907	0.829+	1.875	0.878	1.997
EP × 5HTTLPR*S′	1.050+	0.802	1.051+	0.795	1.034	0.786
Prop Co-Use (PC)	1.182*	--	1.019	--	1.057	--
5HTTLPR*S′	0.773*	1.588	0.784*	1.529	0.878	1.493
PC × 5HTTLPR*S′	1.047*	0.901	1.048*	0.900	1.034	0.910

Note:

*: p<.05;

+: p<0.10.

Two-tailed tests are used for all coefficients except interactions, which are one-tailed tests.