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Depressive symptoms and alcohol use are genetically and environmentally correlated across adolescence

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BACKGROUND

- Symptoms of internalizing disorders, such as depressive disorder, commonly manifest during adolescence, with lifetime incidence of adolescent depression around 14%. In addition, most individuals begin experimenting with alcohol during their teens.
- Multiple epidemiological studies indicate that depressive symptoms/disorders and alcohol use are positively associated, in both adolescent and adult populations. However, the nature of this association is not clear.
- Twin studies suggest that the phenotypic association between these phenotypes could be accounted for in part by a shared genetic and/or environmental liability.
- The current study uses a genetically informative longitudinal sample of Finnish twins to assess the heritability of depressive symptoms and alcohol use across adolescence, and to assess the degree to which shared genetic and environmental factors account for the positive association between these phenotypes.

METHODS

Sample

We used same-sex twin pairs from the intensive sample of the FinnTwin12 study (N=1282). Data were available for 169 female monozygotic (MZ) twin pairs, 170 male MZ twin pairs, 138 female dizygotic (DZ) twin pairs, and 165 male DZ twin pairs. Twins were assessed at ages 12, 14, and 17.5.

Phenotypic Measures

Depressive symptoms were assessed at ages 12 and 14 using the Children's Depression Inventory (CDI, Kovacs 1991), and at age 17.5 using a subscale of the General Behavior Index (GBI, Depue 1987).

At age 12, participants were asked whether they had consumed alcohol without adults present, resulting in a binary (yes/no) variable. At age 14, they were asked the frequency with which they consumed alcohol, with options ranging from never to once per week or more. At age 17.5, participants were again asked the frequency with which they consumed alcohol, with options ranging from never to daily.

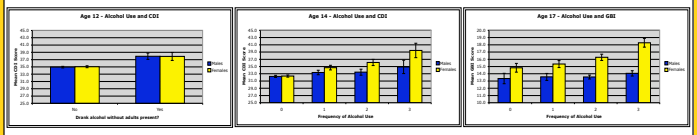
Statistical Analysis

Descriptive statistics and regression analyses were conducted in Mplus Version 5 (Muthen & Muthen 1998-2007) or SAS 9.1.3, and were corrected for twinship. Twin modeling was conducted in Mx (Neale et al. 2003) using the raw ordinal data option. Accordingly, scores on the CDI and GBI, as well as alcohol use at ages 14 and 17.5, were converted to ordinal variables.

We used a Cholesky decomposition with six variables: depressive symptoms and alcohol use at ages 12, 14, and 17.5. Model selection was conducted based on the change in -2 times the log likelihood between the full and nested model, and using the Akaike Information Criterion.

RESULTS

Phenotypic Associations



Age of Alcohol Use	Age of Depression Score	p-values	
		Males	Females
12	12	0.0047	0.0122
14	14	0.0435	<0.0001
17.5	17.5	0.3278	<0.0001
12	14	0.232	0.0075
12	17.5	0.0055	0.9325
14	17.5	0.0657	0.1392

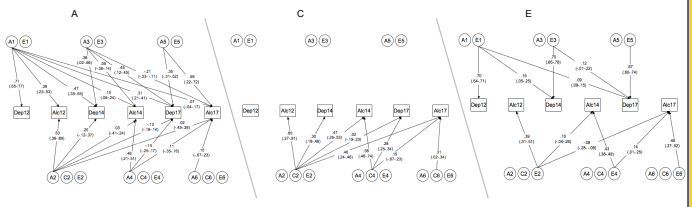
For girls, alcohol use and depressive symptoms were positively associated at each age. For boys, there was no association between phenotypes at age 17.5. In some cases, early drinking was significantly associated with later depressive symptoms or vice versa.

Twin Modeling

Variance was constrained to be equal across the sexes. Shared environmental factors C1, C3, and C5 (which load first onto depressive symptoms) could be removed. Unique environmental (E) factors were trait-specific, but not time-specific.

#	Model	Model Comparison	df	Δχ²	p value	ΔAIC
1	ACE (Full Model)		6009	10796.21		-1221.799
2	**Constrain variance across sex**	**2 vs. 1**	**63**	**72.005**	0.204	**-53.986**
3	AE Model	3 vs. 2	21	42.249	0.004	0.249
4	CE Model	4 vs. 2	21	48.016	0.001	6.016
5	**Drop factors C1, C3, and C5**	**5 vs. 2**	**12**	**9.686**	0.643	**-14.314**
6	Drop factors C1, C3, and C5, plus all C loadings onto depression	6 vs. 2	15	15.844	0.393	-14.156
7	Drop shared E cross-paths on alcohol use (across time)	7 vs. 5	3	9.215	0.027	3.215
8	Drop genetic correlation between traits	8 vs. 5	9	18.86	0.026	0.86
9	Drop genetic correlation across ages, within traits	9 vs. 5	6	51.378	0	39.378
10	Are unique environmental factors time-specific?	10 vs. 5	12	20.69	0.055	-3.31
11	**Are unique environmental factors trait-specific?**	**11 vs. 5**	**9**	**8.451**	0.489	**-9.549**
12	Are unique environmental factors time and trait specific?	12 vs. 5	15	25.023	0.05	-4.977

Best-fitting Model



Heritability, Genetic/Environmental Correlations, and Genetic Innovation/Attenuation

Variance Components

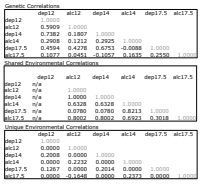
	A	C	E
Age 12 Dep.	0.51	0.00	0.49
Age 14 Dep.	0.41	0.09	0.51
Age 17.5 Dep.	0.45	0.08	0.47
Age 12 Alc. Use	0.45	0.40	0.15
Age 14 Alc. Use	0.24	0.56	0.19
Age 17.5 Alc. Use	0.44	0.33	0.23

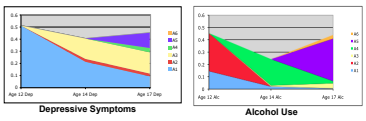
Heritability estimates were comparable to previous reports

Genetic correlations between phenotypes, within age, ranged from ~.6 to ~.25, and decreased over time.

Shared environmental correlations within age ranged from .3-1, but were derived from very low loadings onto depressive symptoms.

Unique environmental correlations within each phenotype were modest.





Genetic innovation and attenuation were observed for both depressive symptoms and alcohol use across time. The influence of genetic factors on alcohol use was especially dynamic.

DISCUSSION

- We observed a positive and statistically significant association between depressive symptoms and alcohol use across adolescence, with some variation between the sexes.
- Heritability estimates for depressive symptoms ranged from 0.41-0.51 across adolescence, with much of the remaining variance accounted for by unique environmental influences. Shared environmental influences account for <10% of the total variance at any age. Genetic effects were attenuated over time, with novel genetic influences becoming relevant at later ages.
- Heritability estimates for alcohol use varied from 0.24-0.45, with shared environmental factors accounting for a substantial portion of the remaining variance. Unique environmental factors accounted for 15-23% of the variance. Again, we observed genetic innovation and attenuation over time.
- Depressive symptoms and alcohol use were genetically correlated: within-age estimates of r_G ranged from .26-.59. The model also supported shared environmental correlations, although loadings on depressive symptoms were quite low. Unique environmental correlations could be removed from the model.
- These results indicate that the phenotypic association between depressive symptoms and alcohol use is due at least in part to a shared liability to these phenotypes. The nature of this shared liability is dynamic across adolescence, with both genetic and shared environmental correlations decreasing over time even as individual heritabilities remain relatively static.
- These results underscore the need for additional work in genetically informative adolescent samples to further our understanding of the relationship between these phenotypes and potential clinical implications.

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