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Examining the internalizing pathway to substance use frequency in 10 cultural groups

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HIGHLIGHTS

- Mother- and self-reported age 13–14 substance use frequency varied over 10 cultures.
- Cultures with greater use opportunities at age 12 had higher rates of use.
- A pathway marked by behavioral inhibition and depression led to substance use.
- A pathway marked by depression, externalizing behavior and peer support led to use.
- Early depressive and externalizing symptoms work in tandem and lead to later use.

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ABSTRACT

Use of alcohol, tobacco, and drugs (i.e., substance use) is a leading cause of global health burden for 10-to-24-year-olds, according to the World Health Organization's index of number of years of life lost, leading international health organizations to prioritize the prevention of substance use before it escalates in adolescence. Pathways defined by childhood externalizing symptoms and internalizing symptoms identify precursors to frequent substance use toward which interventions can be directed. However, these pathways are rarely examined beyond the United States and Europe. We investigated these pathways in our sample of 1083 children from 10 cultural groups followed from ages 8–14. We found that age-10 externalizing symptoms predicted more frequent mother-reported age-13 and self-reported age-14 substance use. We also found that a depressive pathway, marked by behavioral inhibition at age 8 and subsequent elevation in depressive symptoms across ages 8–12 predicted more frequent substance use at age 13 and 14. Additionally, we found a combined externalizing and internalizing pathway, wherein elevated age-9 depressive symptoms predicted elevated externalizing symptoms at age-10 which predicted greater peer support for use at age-12, which led to more frequent

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substance use at age-13 and -14. These pathways remained significant within the cultural groups we studied, even after controlling for differences in substance use frequency across groups. Additionally, cultures with greater opportunities for substance use at age-12 had more frequent adolescent substance use at age-13. These findings highlight the importance of disaggregating between- and within-culture effects in identifying the etiology of early adolescent substance use.

1. Introduction

Frequent illicit substance use, along with mental disorders, account for the largest percentage of global health burden for 10–24-year-olds, according to the World Health Organization (Degenhardt, Stockings, Patton, Hall, & Lynskey, 2016). Therefore, international health organizations have prioritized adolescent substance use prevention (Degenhardt et al., 2016) by identifying and ameliorating preadolescent pathways to frequent adolescent substance use (Hussong, Jones, Stein, Baucom, & Boeding, 2011).

Currently, two such risk pathways have been hypothesized: the externalizing and internalizing pathways to substance use (Hussong, Rothenberg, Smith, & Haroon, 2018). The externalizing pathway is more widely studied and marked in childhood by the emergence of externalizing behaviors that persist into adolescence and predict substance use escalation (Zucker, Heitzeg, & Nigg, 2011). Strong evidence for this pathway emerges in longitudinal studies (Hussong et al., 2018).

The internalizing pathway to substance use is less studied, and hypothesized to be marked in infancy and childhood by behavioral inhibition (i.e., dispositional cautiousness/shyness/avoidance), which leads to the development of internalizing symptoms (i.e., anxiety, depression; Hussong et al., 2011). These symptoms persist throughout childhood and lead to interpersonal skill deficits. In adolescence, internalizing symptoms and interpersonal skill deficits predict the escalation of substance use, as adolescents turn to substance use to cope with these problems (Hussong et al., 2018). Questions remain about how the internalizing pathway operates.

One question is whether the entire internalizing pathway can be found in one sample over time. Specifically, behavioral inhibition in childhood predicts greater alcohol-related problems at age-21 (Caspi, Moffitt, Newman, & Silva, 1996). Additionally, child internalizing symptoms prospectively predict frequent substance use (Hussong, Ennett, Cox, & Haroon, 2017), and a lack of social ties exacerbates frequent substance use in adolescents experiencing depressive symptoms (Cole et al., 2019; Hussong et al., 2018). Yet, to our knowledge, no investigation has ever simultaneously investigated all of these primary predictor and outcome variables in a single sample. The present study does so, providing a strong test of the internalizing pathway's validity.

A second question considers how the internalizing pathway functions alongside the externalizing pathway. Systematic reviews find that only symptoms of depression (not anxiety) predict frequent adolescent substance use after controlling for externalizing symptoms (Hussong et al., 2017). Therefore we only investigate depressive symptoms presently. Additionally, externalizing symptoms can be integrated into

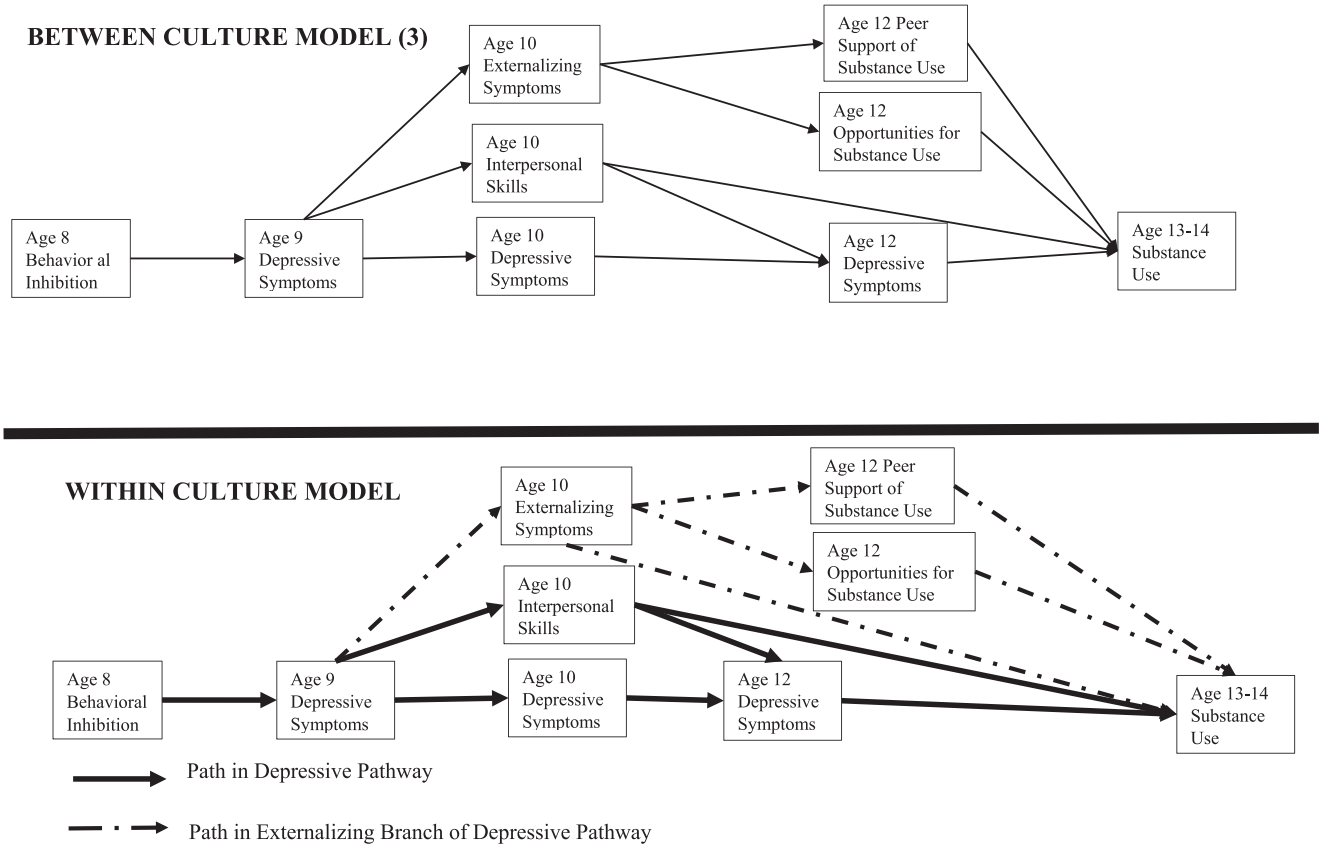

Fig. 1. Conceptual model depicting study hypotheses. Each path design corresponds to each study objective. Solid paths evaluate the first study objective: to evaluate the existence of the internalizing pathway after taking into account between-culture variations in substance use. Dashed paths evaluate the second study objective: to test how externalizing symptoms and subsequent peer support and opportunities for use influence adolescent substance use. The title labeled 3 evaluates the third study objective: to investigate whether the internalizing pathway is associated with variability in substance use both between and within cultures.

internalizing pathway conceptualizations (Eiden et al., 2016). Childhood internalizing symptoms might subsequently lead to the emergence of adolescent externalizing symptoms as youth high in internalizing symptoms turn to deviance to avoid rejection/loneliness and "fit in" with peers (Hussong et al., 2011). Elevated externalizing symptoms are then posited to lead to affiliations with deviant peers who support substance use, and greater substance use opportunities (Hussong et al., 2011).

Eiden and colleagues have evaluated aspects of this "externalizing branch" of the internalizing pathway longitudinally, demonstrating that early adolescent behavioral inhibition predicts mid-adolescent internalizing symptoms (Rhodes et al., 2013), and that mid-adolescent externalizing symptoms subsequently predict affiliation with peers who support substance use and eventual increased substance use (Eiden et al., 2016). However, the prospective link between internalizing and externalizing symptoms along this pathway has not been evaluated, nor has this "externalizing branch" been investigated alongside the typical internalizing pathway. We fill both gaps presently.

A third question is whether the internalizing pathway is cross-culturally generalizable. This pathway has only been studied in American/European samples due to a paucity of data worldwide (Degenhardt et al., 2016). Yet, scholars have identified markers of this pathway, including internalizing behaviors, peer support of use, and substance use availability as risk factors for frequent adolescent substance use that might be applicable in cultures worldwide (Degenhardt et al., 2016). Therefore, studies that investigate this pathway across cultures are needed (Degenhardt et al., 2016).

An important cross-cultural starting point is to determine the extent to which adolescent substance use frequency is explained by differences between cultures, versus differences within cultures (Deater-Deckard et al., 2018). This knowledge would be beneficial for two reasons. First, it would be useful to know whether the internalizing pathway predicts substance use frequency *within cultures even after accounting for variations in adolescent substance use frequency across cultures.* Answering this question evaluates the cross-cultural generalizability of the internalizing pathway. Second, it would be useful to know whether between-culture differences in internalizing pathway variables predict between-culture variation in adolescent substance use frequency. Answering this question identifies prospective risk factors in countries at highest risk for frequent adolescent substance use (Degenhardt et al., 2016).

We answer both questions by investigating the internalizing pathway in a sample of children followed from ages 8–14 in 10 cultural groups from countries ranging from 8th to 145th in the 2015 Human Development Index (United Nations Development Programme, 2015).

1.1. Study objectives

We have three objectives. First, we examine each of the links in the internalizing pathway across childhood and adolescence (Fig. 1 solid paths). We expect the internalizing pathway to emerge even after accounting for between-culture variations in substance use frequency, and the powerful direct effects of earlier externalizing symptoms on later substance use frequency. Second, we seek to understand how externalizing symptoms inform internalizing pathway development by testing Hussong's "externalizing branch" of the internalizing pathway (Fig. 1 dashed paths). Third, we investigate whether the internalizing pathway is associated with variability in substance use frequency both between- and within-cultures (Fig. 1; part of the model labeled 3).

Importantly, we employ the recommended multi-reporter, multi-method longitudinal design to study adolescent substance use frequency (Eiden et al., 2016). Specifically, we evaluate objectives with two models: one using adolescent self-reports of depressive and externalizing symptoms, and age-14 substance use frequency, and a second where depressive and externalizing symptoms combine all available reports (mother/father/adolescent), and age-13 substance use frequency is mother-reported.

2. Materials & Methods

2.1. Participants

Participants included 1,083 children (M = 8.29 years, SD = 0.66, 51% girls) followed from ages 8–14, their mothers (M = 36.93 years, SD = 6.27), and their fathers (M = 39.96 years, SD = 6.52). Families were recruited from 10 ethnic/cultural groups including: Shanghai, China (n = 121); Medellín, Colombia (n = 108); Naples (n = 100) and Rome (n = 103), Italy; Kisumu, Kenya (n = 100); Manila, Philippines (n = 120); Chiang Mai, Thailand (n = 120); and Durham, NC, USA (n = 111 White, n = 103 Black, n = 97 Latino)[1]. Participants were recruited through letters sent from schools. Most parents (82%) were married and biological parents (97%); nonresidential/non-biological parents also provided data. Samples were ethnically and socioeconomically representative of their cities. At age-13, 93% of the original sample continued to provide data, and attriters did not differ on any demographic variables.

2.2. Procedure

Measures were administered in each country's predominant language, following forward- and back-translation and methodological validation to ensure conceptual equivalence of the instruments (Erkut, 2010; Peña, 2007). Two-hour interviews were conducted after parent consent and child assent in participant-chosen locations. At first assessment for parents, and until age-10 for children, interviews were conducted orally. Subsequently, participants chose to complete written or oral measures.

2.3. Measures

All measures are cross-culturally validated and used in cross-cultural research in this and other samples (Table 1; Bornstein et al., 2017; Lansford et al., 2018).

2.3.1. Mother educational attainment and child gender

Number of years of mother education and child gender were included as covariates predicting adolescent substance use frequency (both mother education and child gender) and other substantive variables (just child gender; Table 3). Given that depression, interpersonal skills, and temperamental characteristics may vary by gender, and that substance use frequency may vary by gender and educational attainment (Patrick, Wightman, Schoeni, & Schulenberg, 2012), we wanted to ensure other effects persisted after controlling for these covariates.

2.3.2. Age-8 child behavioral inhibition

Past six-month behavioral inhibition was measured using mother, father, and child reports on 7 items (0 = *not true* to 2 = *very/often true*; "shy," "withdrawn") from the Withdrawn/Depressed subscale of the Achenbach System of Empirically-Based Assessment (ASEBA; Achenbach & Rescorla, 2001). In the child-reported model, child self-reports were used. In the multi-reporter model, mother and father reports were averaged into one score (Withdrawn/Depressed subscale αs = 0.81–0.88 across reporters).[2]

[1] The larger study from which this sample was drawn also included participants from Jordan and Sweden, but institutional review boards (IRBs) in those nations prohibited questions about adolescent substance use, and are therefore not included here.

[2] Several converging lines of evidence indicate that this scale appears to appropriately measure behavioral inhibition. First, the scale shows strong stability from one year to the next (r = 0.56, p < .01) as is to be expected of measures of temperamental behavioral inhibition (Hussong et al., 2011). Second, the scale is significantly but not completely correlated with concurrent (r = 0.27, p < .01) and next year (r = 0.41, p < .01) depressive symptoms, and is a

Table 1
Means and Standard Deviations of Study Variables by Cultural Group.

Variable	China *M(SD)*	Colombia *M(SD)*	Italy-Naples *M (SD)*	Italy-Rome *M (SD)*	Kenya *M(SD)*	Philippines *M (SD)*	Thailand *M(SD)*	US-Black *M(SD)*	US-Latino *M (SD)*	US-White *M(SD)*
Mother Education Age 8	13.55(2.88)	10.64(5.60)	10.14(4.35)	14.14(4.07)	10.69(3.65)	13.61(4.07)	12.30(4.76)	13.65(2.36)	9.83(4.08)	16.95(2.84)
Behavioral Inhibition Age 8	2.85(1.50)	3.88(1.80)	2.88(1.73)	2.73(1.58)	3.03(1.59)	3.38(1.79)	2.70(1.49)	2.77(1.77)	3.45(1.73)	2.65(1.47)
Externalizing Symptoms Age 10	6.43(4.29)	10.44(5.21)	10.56(4.63)	9.97(5.07)	8.71(3.98)	12.06(6.03)	8.75(4.83)	8.33(6.13)	7.55(5.91)	7.99(5.55)
Interpersonal Skills Age 10	3.34(0.74)	4.05(0.61)	3.56(0.63)	3.41(0.58)	3.72(0.71)	3.57(0.67)	3.54(0.51)	3.86(0.77)	3.88(0.66)	3.74(0.71)
Depressive Symptoms Age 9	0.29(0.22)	0.34(0.22)	0.33(0.24)	0.33(0.23)	0.14(0.14)	0.41(0.23)	0.31(0.18)	0.22(0.21)	0.27(0.23)	0.28(0.22)
Depressive Symptoms Age 10	0.25(0.22)	0.26(0.16)	0.30(0.22)	0.26(0.23)	0.10(0.11)	0.38(0.21)	0.28(0.19)	0.19(0.17)	0.22(0.21)	0.24(0.21)
Depressive Symptoms Age 12	0.23(0.22)	0.29(0.21)	0.30(0.27)	0.30(0.23)	0.23(0.19)	0.41(0.24)	0.28(0.20)	0.20(0.23)	0.19(0.20)	0.31(0.27)
Peer Support of Substance Use Age 12	0.04(0.13)	0.44(0.51)	0.40(0.54)	0.49(0.46)	0.29(0.45)	0.13(0.28)	0.18(0.31)	0.28(0.51)	0.27(0.44)	0.26(0.41)
Opportunities for Substance Use Age 12	0.04(0.11)	0.16(0.28)	0.16(0.28)	0.31(0.43)	0.12(0.35)	0.06(0.16)	0.10(0.21)	0.04(0.13)	0.03(0.14)	0.13(0.28)
Mother-Reported Adolescent Substance Use Age 13	0.06(0.11)	0.12(0.21)	0.09(0.18)	0.14(0.28)	0.00(0.03)	0.03(0.11)	0.04(0.13)	0.05(0.25)	0.00(0.03)	0.03(0.10)
Percentage of Sample Endorsing Use of At Least 1 Substance at Age 13	23.64%	34.57%	26.09%	33.00%	1.16%	6.85%	11.49%	4.82%	1.59%	8.99%
Self-Reported Adolescent Substance Use Age 14	0.07(0.33)	0.21(0.47)	0.18(0.42)	0.35(0.57)	0.0(0.0)	0.06(0.23)	0.14(0.38)	0.08(0.35)	0.0(0.0)	0.16(0.40)
Percentage of Sample Endorsing Substance Use at Age 14	4.54%	17.95%	17.24%	30.10%	0.00%	5.56%	12.94%	5.77%	0.00%	14.77%

Note. To preserve space and parsimony, only the measures of behavioral inhibition, externalizing, depressive symptoms that average mother, father, and child report are reported here. However, reports on each of these separate measures can be obtained from the first author upon request.

2.3.3. *Age-9, 10, 12 child depressive symptoms*

Past six-month depressive symptoms were measured by averaging mother, father, and child reports (for the multi-reporter model) or child-self reports (for the self-reported model) on 6 items (0 = *not true* to 2 = *very/often true*; αs = 0.78–0.82 across reporters; "unhappy, sad, or depressed") from the Depressive Problems subscale of the ASEBA.

2.3.4. *Age-10 child externalizing symptoms*

Past six-month externalizing symptoms were measured by averaging mother, father, and child reported sum scores (for the multi-reporter model) or child-reported sum scores (for the self-reported model) on 33 items (0 = *not true* to 2 = *very/often true*; αs = 0.84–0.88 across reporters; "bullying," "disobedience") from the ASEBA.

2.3.5. *Age-10 child interpersonal skills*

Mothers completed a 7-item scale indicating how skilled their child was in several kinds of interpersonal interactions (e.g., "generating good solutions to interpersonal problems"; Pettit, Harris, Bates, & Dodge, 1991). Items were rated from 1 = *very poor* to 5 = *very good* (α = 0.89) and averaged to create a single score.

2.3.6. *Age-10 peer support of substance use*

Children rated the extent to which their peers supported their past-year involvement in 4 substance-use activities (drinking beer/wine, drinking liquor, smoking cigarettes, using drugs) on a 0 = *same-age peers discourage the behavior* to 2 = *same age peers support the behavior* scale (α = 0.80).

2.3.7. *Age-12 child opportunities to use substances*

Children rated the extent to which they had past-year opportunities to engage in the same 4 substance-use activities on a 0 = *no/few opportunities* to 2 = *many opportunities* scale (α = 0.75).

2.3.8. *Age-13 child substance use frequency*

Mothers were asked to rate their adolescent's past-year engagement in the same 4 substance-use activities on a 0 = *never* to 2 = *often* scale (α = 0.99).

For peer support of use, child opportunities to use, and age-13 substance use frequency, items were averaged to create overall scores.

2.3.9. *Age-14 child substance use frequency*

Using an ASEBA item, adolescents rated how often they had "used alcohol or drugs other than for medical conditions" (0 = *not true* to 2 = *very/often true*) during the last 6 months.

(*footnote continued*)
significant predictor of next year depressive symptoms even when past year depressive symptoms are controlled ($B = 0.06$, $p = .01$). Additionally, the Withdrawn/Depressed measure does not overlap in its item content with the measure of depressive symptoms used in the current study because we ensured that any items that overlapped with the Depressive Symptoms subscale (e.g., "enjoys little, lacks energy, sad") were not included in our scoring of the Withdrawn/Depressed subscale. Therefore, this measure demonstrates both convergent and incremental validity, and demonstrates that it is measuring something other than adolescent depressive symptoms. Third, the measure's items (e.g., "shy," "withdrawn," "would rather be alone") align with Hussong et al. (2011) description of behavioral inhibition as a cautious, avoidant, and shy interaction style. Fourth, past studies have found significant associations between these withdrawn/depressed items measured at age 8, and infant inhibited temperament (measured via activity level; Colder, Mott, & Berman, 2002). Therefore, taken together these lines of evidence seem to indicate that this measure adequately captures late childhood manifestations of behavioral inhibition, or at the very least serves as an appropriate proxy variable for such inhibition.

Table 2
Zero-Order Correlations Between Study Variables.

Variable	1	2	3	4	5	6	7	8	9	10	11
1. Mother Education Age 8	1.00										
2. Behavioral Inhibition Age 8	−0.21*	1.00									
3. Externalizing Symptoms Age 10	−0.11*	0.29*	1.00								
4. Interpersonal Skills Age 10	0.05	−0.18*	−0.31*	1.00							
5. Depressive Symptoms Age 9	−0.10*	0.38*	0.43*	−0.21*	1.00						
6. Depressive Symptoms Age 10	−0.04	0.36*	0.54*	−0.25*	0.63*	1.00					
7. Depressive Symptoms Age 12	0.01	0.29*	0.32*	−0.17*	0.46*	0.50*	1.00				
8. Peer Support of Substance Use Age 12	0.03	0.03	0.13*	0.04	0.06	0.06	0.16*	1.00			
9. Opportunities for Substance Use Age 12	0.08*	0.00	0.10*	−0.04	0.08*	0.10*	0.16*	0.46*	1.00		
10. Substance Use Age 13	−0.02	−0.01	0.12*	0.01	0.07*	0.04	0.12*	0.22*	0.29*	1.00	
11. Substance Use Age 14	0.04	0.07	0.12*	-0.0.03	0.11*	0.11*	0.18*	0.25*	0.28*	0.37*	1.00

Note. As in Table 1, to preserve space and parsimony, only the measures of behavioral inhibition, externalizing, depressive symptoms that average mother, father, and child report are reported here. However, correlations between each of these separate measures can be obtained from the first author upon request. *$p < .05$.

3. Results

Descriptive statistics (Table 1; Table 2) revealed that 15.7% of mothers reported their 13-year-olds had used at least one substance in the past year, and 12.0% of 14-year-olds self-reported use of substances in the past 6 months.

Significant Intraclass Correlations revealed that 93% of age-13 and 99% of variance in age-14 adolescent substance use frequency in each respective model was attributable to within-culture differences. Therefore, we grand-mean centered predictor variables to capture between-culture effects, and group-mean centered them to capture within-culture effects (Curran & Bauer, 2011). We conducted multilevel path analysis in Mplus to evaluate study objectives and used full-information-maximum-likelihood estimation with robust standard errors (MLR) to account for missing data and significant skew in adolescent substance use frequency measures (Muthén & Muthén, 1998, 2017). To investigate study questions we estimated two separate models; a multi-reporter model that predicted mother-reported age-13 substance use frequency, and a self-reported model that predicted adolescent self-reported age-14 substance use frequency (Figs. 2 and 3)[3].

3.1. Evaluating the internalizing pathway

Our hypothesis that the internalizing pathway would significantly predict adolescent substance use frequency within cultures was partially supported (Figs. 2 and 3). One subpath of the internalizing pathways was supported across both models (Table 4). Children with higher behavioral inhibition than average in their culture at age-8 also had higher depressive symptoms than average in their culture at age-9, which were associated with higher depressive symptoms at age 10, which were associated with higher depressive symptoms at age 12, which subsequently predicted higher mother-reported age-13 (*Indirect Effect* $B = 0.006$, $p < .05$; Table 4) and self-reported age-14 (*Indirect Effect* $B = 0.002$, $p < .05$) substance use frequency. Notably, this depressive pathway remained significant in both models after controlling for externalizing symptoms and other predictors (Table 3). However, no part of the pathway including age-10 interpersonal skills significantly predicted substance use frequency in either model.

3.2. Integrating externalizing symptoms into the internalizing pathway

Our results support Hussong's "externalizing branch" to the internalizing pathway. Specifically we found two significant externalizing branch mediational subpaths (Table 3). In both models, higher age-9 depressive symptoms than average for one's culture predicted higher-than-average-age-10 externalizing symptoms, which predicted greater-than-average age-12 peer support of substance use, which was associated with higher age-13 mother-reported (*Indirect Effect* $B = 0.003$, $p < .05$; Table 4)[4] and age-14 self-reported (*Indirect Effect* $B = 0.004$, $p < .05$) substance use frequency. Additionally, higher age-9 depressive symptoms than average for one's culture predicted higher-than-average-age-10 externalizing symptoms which predicted higher age-13 substance use frequency (*Indirect Effect* $B = 0.049$, $p < .05$).

Two additional predictors also had direct effects on substance use frequency. Adolescents with higher-than-average age-10 externalizing symptoms had more-frequent-than average age-13 and age-14 substance use (Table 3). Additionally, age-12 opportunities for use were significant predictors of both age-13 and age-14 substance use frequency (Table 3).

3.3. The internalizing pathway at the Between-Culture level

We initially attempted to model the entire internalizing pathway between cultures. However, model fit was poor due to empirical underidentification. Therefore, we simplified the between-culture model to include only the end points of the internalizing pathway (i.e., age-12 depressive symptoms, substance use opportunities, and peer support of use) as predictors of age-13 and age-14 substance use frequency differences between cultures. Importantly, between- and within-culture effects were estimated simultaneously in a single model (Figs. 2 and 3). At the between-culture level, cultures with higher-than-average age-12 opportunities for substance use, but not depression or peer support, also had higher-than-average adolescent self-reported substance use frequency at age-14 ($B = 0.70$, $p < .01$).

[3] Notably, both models included a number of paths (e.g., age 10 depressive symptoms predicting age 12 peer support of substance use) that were not hypothesized *a priori* but included in study analyses to ensure that our hypothesized pathways (depicted in Fig. 1) emerged even after accounting for these other paths. All predictive paths are reported in Table 3, but the results section focuses on describing tests of *a priori* hypothesized paths.

[4] This entire mediating pathway was significant despite the fact that the direct effect of age-12 peer support of substance use on age-13 mother-reported substance use was barely non-significant ($\beta = 0.07$, SE = 0.04, $p = .08$). Despite not being statistically significant, it appears the direct association between age-12 peer support of substance use and age-13 mother-reported substance use was large enough in magnitude to convey the indirect effects of age-10 externalizing behavior on age-13 mother-reported substance use.

Table 3
Multilevel Structural Equation Models Predicting Adolescent Substance Use Frequency at Age 13 and 14 Between and Within Cultural Groups.

	Mother-Reported Adolescent Substance Use Model		Self-Reported Adolescent Substance Use Model	
Within-Culture Level				
Predictors of Adolescent Substance Use Frequency at Age 13 (Mother-Reported Model) and Age 14 (Self-Reported Model)				
	β	SE	β	SE
Age 12 Depressive Symptoms	**0.11****	0.04	**0.10***	0.05
Age 12 Peer Support of Substance Use	0.07	0.04	**0.12****	0.04
Age 12 Opportunities for Substance Use	**0.20****	0.05	**0.16****	0.03
Age 10 Depressive Symptoms	−0.10	0.06	−0.02	0.05
Age 10 Externalizing Symptoms	**0.13****	0.02	**0.08***	0.04
Age 10 Interpersonal Skills	0.06	0.05	0.03	0.03
Age 9 Depressive Symptoms	−0.01	0.07	−0.02	0.03
Age 8 Behavioral Inhibition	−0.05	0.03	0.03	0.04
Age 8 Mother Education	−0.06	0.02	−0.02	0.04
Child Gender	0.02	0.03	0.00	0.04
Predictors of Depressive Symptoms at Age 12				
Age 10 Depressive Symptoms	**0.34****	0.06	**0.25****	0.03
Age 10 Externalizing Symptoms	0.00	0.04	−0.01	0.03
Age 10 Interpersonal Skills	**−0.07****	0.02	−0.03	0.02
Child Gender	**−0.15****	0.04	**−0.16****	0.05
Predictors of Peer Support of Substance Use at Age 12				
Age 10 Depressive Symptoms	0.04	0.02	0.03	0.03
Age 10 Externalizing Symptoms	**0.11****	**0.04**	**0.11****	**0.04**
Age 10 Interpersonal Skills	0.05	0.05	0.03	0.04
Child Gender	−0.03	0.04	−0.03	0.04
Predictors of Opportunities for Substance Use at Age 12				
Age 10 Depressive Symptoms	0.07	0.06	0.03	0.06
Age 10 Externalizing Symptoms	0.05	0.04	0.08	0.04
Age 10 Interpersonal Skills	0.01	0.03	0.00	0.03
Child Gender	0.02	0.04	0.01	0.04
Predictors of Depressive Symptoms at Age 10				
Age 9 Depressive Symptoms	**0.55****	0.03	**0.43****	0.05
Child Gender	−0.02	0.03	−0.02	0.03
Predictors of Externalizing Symptoms at Age 10				
Age 9 Depressive Symptoms	**0.39****	0.04	**0.30****	0.05
Age 8 Behavioral Inhibition	**0.09****	0.03	**0.09****	0.04
Child Gender	0.08	0.05	0.06	0.03
Predictors of Interpersonal Skills at Age 10				
Age 9 Depressive Symptoms	**−0.16****	0.03	**−0.20****	0.05
Child Gender	**−0.12****	0.03	**−0.14****	0.04
Predictors of Depressive Symptoms at Age 9				
Age 8 Behavioral Inhibition	**0.30****	0.03	**0.21****	0.03
Child Gender	−0.06	0.02	0.01	0.02
Predictors of Age 8 Behavioral Inhibition				
Child Gender	**0.06***	0.03	**−0.08****	0.02
Between-Culture Level				
Predictors of Adolescent Substance Use Frequency at Age 13 (Mother-Reported Model) and Age 14 (Self-Reported Model)				
Age 12 Depressive Symptoms	0.03	0.21	0.07	0.11
Age 12 Peer Support of Substance Use	0.23	0.49	0.29	0.20
Age 12 Opportunities for Substance Use	0.64	0.44	**0.70****	0.25
Age 8 Mother Education	−0.03	0.25	0.22	0.13

Note. *$p \leq .05$, **$p \leq .01$. Bold indicates parameters significant at $p \leq .05$. All reported parameter estimates are standardized. All contemporaneous predictors were correlated (e.g., all age 9 predictors were correlated with one another), but correlations are not reported here due to space limitations. Correlations can be obtained from the first author.

4. Discussion

4.1. Finding an internalizing pathway

This study contributes to existing literature by providing evidence that a depressive pathway to adolescent substance use frequency persists from ages 8–14 in a variety of cultural groups, even after controlling for between-culture differences. Perhaps as impressively, this within-culture depressive pathway prospectively predicts adolescent substance use frequency above-and-beyond adolescent opportunities for substance use, and earlier externalizing symptoms (two powerful use predictors; Degenhardt et al., 2016). Therefore, middle childhood behavioral inhibition, and middle childhood and early adolescent depressive symptoms could serve as intervention targets to prevent frequent substance use across cultures.

4.2. Integrating externalizing symptoms

Our results suggest a "both/and" approach wherein *both* depressive symptoms *and* externalizing symptoms are modeled simultaneously to further understand the development of adolescent substance use frequency. Doing so allows integration of previously disparate etiological conclusions. For instance, results support a decades-long body of work demonstrating that externalizing symptoms are powerful prospective

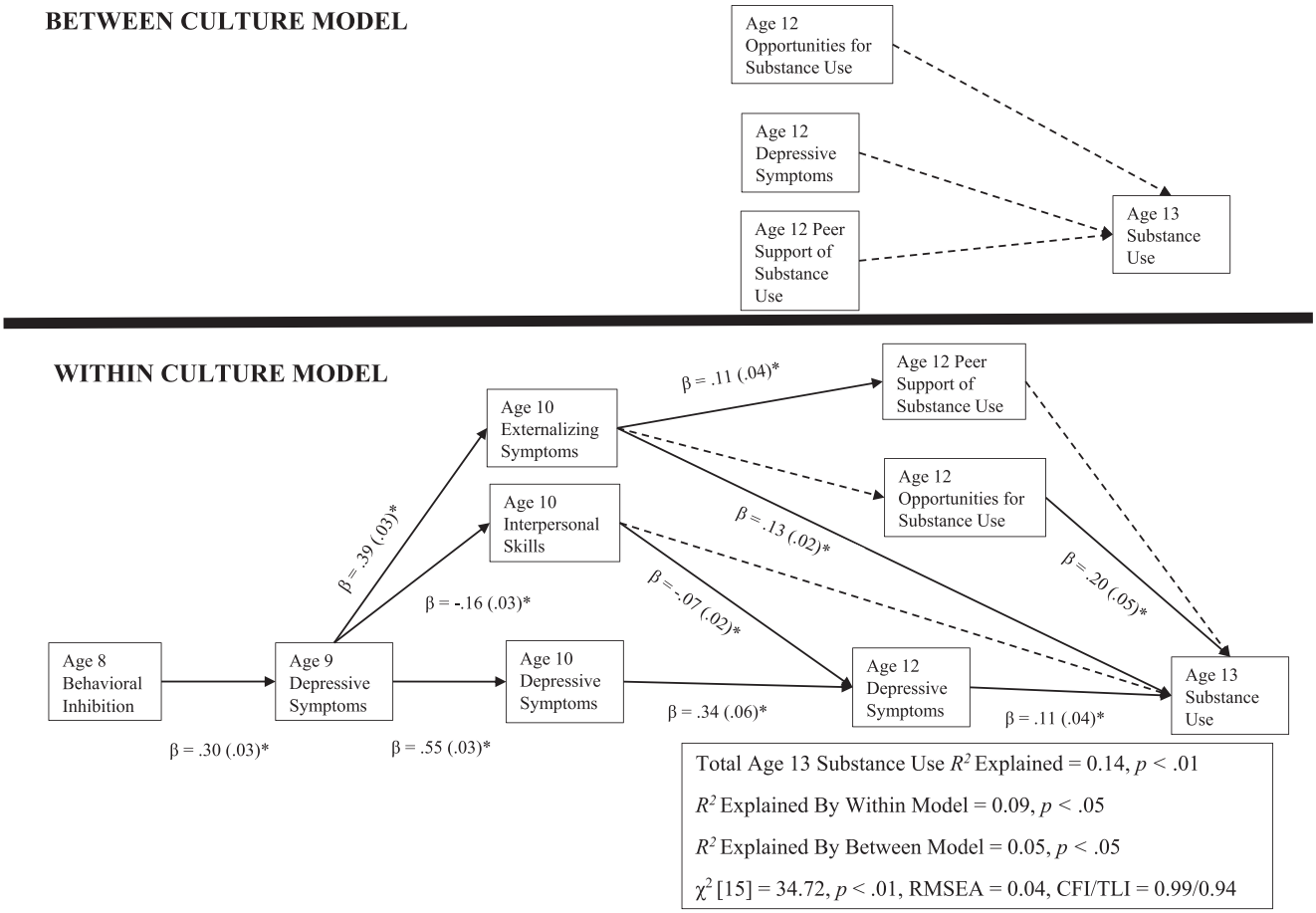

Fig. 2. Mother reports of age 13 adolescent substance use model. Model results depicted at the within- and between-culture level. Significant paths are represented by solid lines; non-significant paths are represented by dashed lines. *$p < .05$. Standardized parameter estimates reported; first number indicates parameter estimate, second number indicates standard error. For simplicity of presentation, this figure presents results for paths involved in *a priori* conceptual model that is depicted in Fig. 1. Other paths were explored in this model but not depicted. See Table 3 for full report of all parameters estimated in the model. Additionally, contemporaneous measures (e.g., age 10 externalizing symptoms, interpersonal skills, and depressive symptoms) were correlated, but correlational paths are excluded from the present model for simplicity of presentation. Correlational paths are available from the first author upon request.

predictors of adolescent substance use frequency (Zucker et al., 2011). However, results also suggest that depressive symptoms could inform escalations in these externalizing symptoms (age 9 depressive symptoms predict higher age 10 externalizing symptoms).

Moreover, our current results build upon theoretical conceptualizations and empirical investigations of an "externalizing branch" of the internalizing pathway (Rhodes et al., 2013). Results support that depressive symptoms in late childhood predict the emergence of externalizing symptoms in early adolescence, and that these externalizing behaviors are associated with subsequent affiliations with substance-using peers that lead to frequent substance use within a variety of cultural groups. Perhaps youth experiencing depressive symptoms turn to externalizing/deviant behaviors to "fit in" and avoid peer rejection, but this move to deviance leads to association with peers who support substance use and encourages adolescents to use (Eiden et al., 2016).

Additionally, age-12 opportunities for substance use emerged as the strongest predictor of both mother-reported age-13 and adolescent-reported-age-14 substance use frequency. Therefore, identifying contexts providing opportunities for adolescent substance use appears critical to preventing frequent adolescent substance use across a variety of cultural contexts.

4.3. Between-Culture variability

Results demonstrate that disaggregating between- and within-culture effects is beneficial to understanding cross-cultural substance use frequency (Deater-Deckard et al., 2018). Disaggregation allows for the identification of risk factors that prospectively predict which cultures are at greatest risk for more frequent adolescent substance use, and therefore need higher investment in preventive substance use interventions (Degenhardt et al., 2016). We identified opportunities to use substances at age-12 as one of these key, between-culture risk factors. Country-specific efforts to reduce substance use opportunities should be sensitive to the ways in which poverty, discrimination, and stigma might affect both substance use frequency and opportunities for intervention, because these factors can be barriers to receiving treatment in some cultural contexts (AlMarri & Oei, 2009). Additionally, it is interesting that at the between-culture level, only age-12 substance use opportunities were predictors of subsequent adolescent substance use. This finding is especially intriguing because zero-order correlations between substance use and peer support of use/depressive symptoms were significant. This pattern of results may have emerged because opportunities for substance use systematically vary between cultures in ways that peer support of use and depressive symptoms do not. For instance, the three cultures in our sample with the highest opportunities for substance use at age 12 (Colombia, Italy, and Kenya), all legalize drinking between ages 16–18, whereas the legal drinking age is 20–21

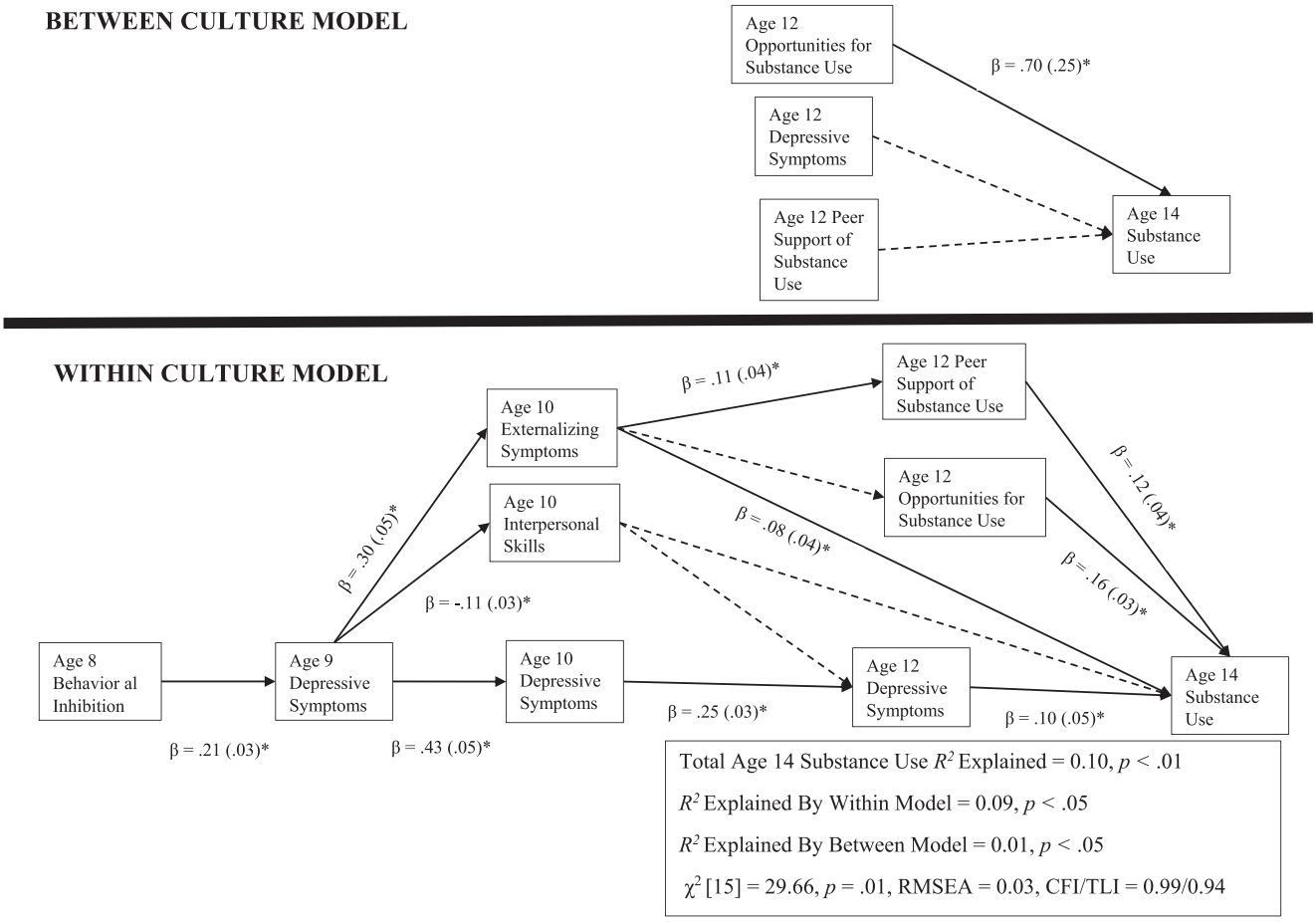

Fig. 3. Adolescent self-reported of age 14 substance use model. Model results depicted at the within- and between-culture level. Significant paths are represented by solid lines; non-significant paths are represented by dashed lines. *$p < .05$. Standardized parameter estimates reported; first number indicates parameter estimate, second number indicates standard error. For simplicity of presentation, this figure presents results for paths involved in *a priori* conceptual model that is depicted in Fig. 1. Other paths were explored in this model but not depicted. See Table 3 for full report of all parameters estimated in the model. Additionally, contemporaneous measures (e.g., age 10 externalizing symptoms, interpersonal skills, and depressive symptoms) were correlated, but correlational paths are excluded from the present model for simplicity of presentation. Correlational paths are available from the first author upon request.

in many of our cultures with the lowest opportunities for use (e.g., the United States and Thailand). More liberal cultural norms around substance use are easily manifest in culture-wide legislative and economic efforts to increase opportunities for substance use (e.g., lower drinking age, greater availability of substances in stores). In contrast, depressive symptoms and peer support of substance use are more heterogeneous within cultures, and therefore more likely to manifest as differences between individuals within cultures (as seen in our results).

Additionally, disaggregating between- and within-culture effects can also lead to the discovery of pan-cultural etiological pathways to frequent substance use that emerge even after controlling for differences between cultures. In our sample, both the aforementioned depressive and externalizing-branch pathways are examples of such etiological pathways. Characterizing pancultural pathways facilitates identification of interventions that have effects across cultures. For instance, behavioral parent training programs (BPTs) have demonstrated efficacy in ameliorating externalizing and depressive symptoms through age 10 (Gardner et al., 2019) and require minimal adaptation across culture (Gardner, Montgomery, & Knerr, 2016). Implementing BPTs might reduce frequent adolescent substance use within the cultural groups we studied by ameliorating middle childhood externalizing and depressive symptoms that precede frequent use. Our between-culture results reveal that, in countries with greater opportunities for substance use, BPTs could be coupled with country-specific efforts to reduce opportunities for adolescent substance use. Such specific recommendations are possible when between- and within-cultural effects are simultaneously evaluated.

4.4. Limitations

The current study has several limitations. First, we could not test the full internalizing pathway at the between-culture level, and we lacked the power to compare differences between specific cultures in our models. Second, the model does not include several other well-known predictors of substance use (e.g., parenting behaviors, parental substance use), nor does it control for probable cultural variability in social desirability of responses. Third, we acknowledge that though adolescent substance use often predicts abuse/dependence, it does not inevitably lead to problematic outcomes (Huynh et al., 2019). Fourth, a true measure of child inhibited temperament was not included in the current study. We utilized the Withdrawn/Depressed subscale as a proxy for child temperament, and therefore acknowledge that its associations with depressive symptoms may be greater than if a temperament measure was included.

5. Conclusion

Results indicate depressive and externalizing symptoms each uniquely predicted more frequent adolescent substance use. Results also indicate that mediating depressive and externalizing branch pathways

Table 4
Reporting Indirect Effects Tests of A Priori Hypothesized Pathways to Adolescent Substance Use at the Within-Culture Level.

	Mother-Reported Adolescent Substance Use at Age 13 Model		Self-Reported Adolescent Substance Use at Age 14 Model	
	Indirect Effect	SE	Indirect Effect	SE
Depressive Pathway to Adolescent Substance Use				
BI8 → DEP9 → DEP10 → DEP12 → SU	**0.006***	0.003	**0.002***	0.001
BI8 → DEP9 → INT10 → SU	−0.003	0.003	−0.001	0.001
BI8 → DEP9 → INT10 → DEP12 → SU	0.000	0.000	0.000	0.000
"Externalizing Branch" of Depressive Pathway to Substance Use				
DEP9 → EXT10 → SU	**0.049****	0.007	0.026^{+}	0.014
DEP9 → EXT10 → OPP12 → SU	0.004	0.003	0.004	0.003
DEP9 → EXT10 → PSU12 → SU	**0.003***	0.002	**0.004***	0.002

Note. *$p \leq .05$, **$p \leq .01$, $^{+}p = .065$. Bold indicates parameters significant at $p \leq .05$. All reported indirect effects are standardized. BI = Age 8 Behavioral Inhibition; DEP9 = Age 9 Depressive Symptoms; DEP10 = Age 10 Depressive Symptoms; DEP12 = Age 12 Depressive Symptoms; INT10 = Age 10 Interpersonal Skills, OPP12 = Age 12 Opportunities for Substance Use; PSU12 = Age 12 Peer Support of Substance Use; SU = Adolescent Substance Use Frequency at either Age 13 (in the Mother-Reported Substance Use at Age 13 Model) or Age 14 (in the Self-Reported Adolescent Substance Use at Age 14 Model).

predicted frequent substance use within many cultures. Additionally, cultures with greater age-12 substance use opportunities had more frequent age-14 adolescent substance use. Findings suggest that frequent adolescent substance use could be prevented at multiple developmental stages through the targeting of multiple cross-cultural risk factors.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.addbeh.2019.106214.

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