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SUBJECTIVE EFFECTS FOR ALCOHOL, TOBACCO, AND MARIJUANA ASSOCIATION WITH CROSS-DRUG OUTCOMES

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Abstract

METHODS—The cross-drug relationship of subjective experiences between alcohol, tobacco, and marijuana and problem drug use behaviors were examined. Data were drawn from 3853 individuals between the ages of 11 and 30 years of age participating in the Colorado Center on Antisocial Drug Dependence [CADD]. Subjective experiences were assessed using a 13-item questionnaire that included positive and negative responses for alcohol, tobacco, and marijuana. Lifetime abuse and dependence on these three drugs was assessed using the Composite International Diagnostic Interview, Substance Abuse Module [CIDI-SAM].

RESULTS—Positive and negative subjective experience scales were similar for alcohol, tobacco, and marijuana, although the hierarchical ordering of items differed by drug. Subjective experience scales for each of the three drugs examined correlated significantly, with the strongest relationship being for alcohol and marijuana experiences. Significant associations were identified between how a person experienced a drug and abuse and dependence status for the same or different drug.

CONCLUSION—Cross-drug relationships provide evidence for a common liability or sensitivity towards responding in a similar manner to drugs of abuse within and across different pharmacological classes.

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Keywords

Subjective effects; alcohol; tobacco; marijuana

1. Introduction

A long-standing observation in clinical and epidemiological research into substance use has been that users of one drug typically do not limit their use to a single substance (Palmer et al., 2009; Rhee et al., 2003; Duhig et al., 2005). For example, alcohol and tobacco are commonly used by the same person and often in the same setting, as are tobacco and marijuana. Though the synergistic effects of these particular drugs have been suggested as a potential explanation (Martin et al., 1996; Pakula et al., 2009; Chait et al., 1994), another interesting possibility is that individuals have an underlying liability to drug use within and across different pharmacological classes. Support for this notion has been shown for both licit and illicit drugs in a variety of populations and drug use phenotypes (Kendler et al., 2003; Kendler et al., 2007; Young et al., 2006; Tsuang et al., 1998; Vanyukov et al., 2003). As poly-substance use is associated with problematic use and reduced treatment efficacy (Chung et al., 2008; Brown et al., 2001), identifying informative precursors to the onset of abuse and dependence remains a priority.

Among the variety of factors that have been examined as an early indicator of later, more problematic use patterns, how someone experiences a drug, (i.e., subjective experience), is one of the most interesting. Subjective experiences are thought to reflect individual differences in the pharmacological effects of a drug (Schuckit et al., 2004; Pomerleau et al, 2004; Rios-Bedoya et al., 2009; Lyons et al., 1997). Factor analytic studies of these experiences frequently yield two main factors: pleasant or positive and unpleasant or negative (Pomerleau et al., 2004; Green et al., 2003; Grant et al., 2005; Davidson et al., 1994; Wachtel et al., 2002; Scherrer et al., 2009). Positive subjective experiences often include euphoria, relaxation, and feeling less inhibition. Negative subjective experiences include nausea, difficulty inhaling, dizziness and sadness. Though weakly correlated (Rios-Bedoya et al., 2009; Lyons et al., 1997; Fergusson et al., 2003), users of a drug sometimes report both positive and negative experiences.

Alcohol, tobacco, and marijuana are the most commonly used licit and illicit drugs. Studies examining the subjective experiences to these drugs have generally found that how a person responds to a particular drug is predictive of more problematic use of the same drug. For example, dependent cigarette users more frequently endorse positive experiences than regular smokers and moderate-to-heavy drinkers report experiencing greater stimulant-like effects to alcohol than lighter drinkers (Holdstock et al., 2000; Pomerleau et al., 1998). A similar relationship has been demonstrated for marijuana use (Fergusson et al., 2003). Although results are mixed, negative experiences to tobacco and marijuana have also been positively associated with problematic use (Grant et al., 2005; Scherrer et al., 2009; Zeiger et al., 2010). For alcohol consumption, low levels of response, primarily measured using negative subjective effects, have been associated with an increased risk of an alcohol use disorder (AUD) as lower thresholds to the sedative effects of alcohol protected against developing abuse later in life (Schuckit et al., 2004; Schuckit et al., 1997; Chung et al., 2009).

A handful of previous studies have suggested that subjective experiences for different drugs may share a common etiology (Perkins et al., 2001; De Wit and Doty, 1994). In particular, subjective experiences to a variety of drugs are correlated and can predict levels of involvement for substances in other pharmacological classes. This observation has been

shown for pleasurable experiences of alcohol and tobacco where both drugs were predictive of current alcohol use in a college aged sample (Pomerleau et al., 2004). Further, marijuana use has been shown to increase a sense of "liking" among non-smokers whereas alcohol has no effect on the subjective experiences of cigarettes (Rhea et al., 2006). Lastly, greater rates of alcohol dependence and illicit drug use have been observed among high marijuana users as defined by greater rates of sensitivity to positive and negative subjective experiences (Scherrer et al., 2009). Though additional studies are needed, these cross-drug results indicate that how a person responds to a drug is predictive of how they will respond to other drugs.

In this report we detail findings from a study of subjective experiences to alcohol, tobacco, and marijuana in a sample of young adults participating in the Colorado Center for Antisocial Drug Dependence. Subjective experiences were collected from both clinical and community participants using a questionnaire developed by Lyons and colleagues (Lyons et al., 1997). Our analyses were designed to address three questions. First, how do positive and negative subjective experiences across alcohol, tobacco, and marijuana compare? Second, to what extent do subjective experiences to alcohol, tobacco, and marijuana overlap? Lastly, to what degree do subjective experiences to one drug associate with more problematic use behaviors for a different drug?

2. Methods

2.1 Sample

Participants were drawn from the Colorado Center on Antisocial Drug Dependence [CADD] and consisted of 3,853 participants (57% male) between the ages of 11 and 30 years old and included both community and clinical participants. Our community-based sample (n = 2881) was drawn from those participating in the Colorado Twin Registry (CTR), Colorado Adoption Project (CAP), with clinical controls drawn from the Colorado Adolescent Substance Abuse Family Study (ASA; Petrill et al., 2003; Rhea et al., 2006). Our clinical sample (n = 486) was drawn from adolescents in treatment for substance abuse and delinquency as a part of the ASA study (Stallings et al., 2003). Additional clinical participants were drawn from an adjudicated sample from the Denver metropolitan area (Hartman et al., 2008). Siblings of the clinical subjects (n= 486) were also included.

All participants in the current study met one or more of the following criteria: 1) they had consumed at least six drinks in their lifetime, 2) had used tobacco daily for at least one month, or 3) had used marijuana six or more time in their lifetime.

2.2 Measures

Patterns of alcohol, tobacco and marijuana use, abuse and dependence symptomatology were collected using the Composite International Diagnostic Interview- Substance Abuse Module (CIDISAM; Cottler et al., 1995). Abuse and dependence status as defined by the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) was determined using scoring algorithms based on whole life substance related problems.

Retrospective subjective experiences were collected using a 23-item questionnaire developed by Lyons and colleagues (Lyons et al., 1997). The original Lyons questionnaire was comprised of 23 items. As discussed in Zeiger et al., (2010), due to the CADD interview length the original Lyons questionnaire was shortened after wave 1b; a factor analysis was conducted on the Lyons questionnaire and 10 items with lower or mixed loadings were dropped. Subsequently, most subjects received the shortened 13-item questionnaire, thus these analyses were conducted on the 13-item response set from all subjects The 13-items included: *social, mellow, creative, top of the world, increased sex*

drive, energetic, dizzy, nauseous, drowsy, lazy, unable to concentrate, out of control, and guilty. Participants were asked "*in the period shortly after you used (substance name) did it make you feel*…."? Responses were scored as present (1) or absent (0) and the item scores summed to make the positive and negative scales. Responses collected during the most recent interview were used for these analyses.

2.3 Mokken Scale Analysis

To examine the dimensionality of the 13 subjective experiences examined for each substance, we conducted Mokken Scale Analysis (MSA; Mokken, 1997) using the statistical software STATA (version 10.1). Mokken scaling analysis extends traditional factor analysis by systematically hierarchically ordering items that are highly correlated. Mokken analysis provides a nonparametric, iterative scale-building technique that identifies the smallest set of internally consistent scales from a given item pool. This model assumes the presence of one or more latent traits that can be measured by subject responses to a set of items (Luinge et al., 2006; Watson et al., 2008). MSA is probabilistic and hierarchical, meaning that the items can be ordered by a degree of "difficulty"; individuals who agree with a more difficult item will tend to agree with less difficult items (Watson et al., 2008; Wismeijer et al., 2008). Scales from MSA are formed by taking pairs of items with the highest correlation and including other items until there is no further improvement (Webber and Huxley, 2007). Loevinger's H coefficients, which indicate the fit of an item to the scale, are computed for each item (H_i) within a scale and for the scale as a whole (H). H coefficients ranging between 0.3 and 0.4 indicate a weak scale, 0.4 to 0.5 a medium scale, and 0.5 to 0.9 a strong scale. In MSA, an item(s) can remain "unscaled" because it could not be added to one of the alternative scales without weakening the scale's homogeneity.

Based on our previous analyses (Zeiger et al., 2010), we used the scaling derived from the CADD sample. Positive and negative scales were standardized by age, sex, and clinical status with two groups (community subject and clinical families; Zeiger et al 2010). Pairwise correlations between the resulting two scales were then determined for alcohol, tobacco, and marijuana.

2.4 Regression Analyses

A four-step hierarchical forward stepwise regression was conducted to determine the extent of the cross-drug relationship between positive and negative subjective experience scales and DSM-IV diagnosis of abuse and dependence using a 0.05 significance level for model inclusion. This method was used to provide an initial screening of the candidate variables and to test for the unique variance of each of the variable (Skenderian et al., 2008). The regressions were performed on the subjects who used all three drugs using abuse or dependence for alcohol and marijuana and tobacco dependence (i.e., 5 separate models) as the dependent variables. In step 1, the demographic variables were added (age, sex, clinical status), in step 2 the scales for the drug being used as the dependent variable were added. In steps 3 and 4 the scales for the other drugs were added. All analyses were corrected for familiality in STATA using the cluster option that allows specification of a variable indicating to which group each observation belongs.

3. Results

3.1 Demographics

Sample demographics are presented in Table 1. The mean age at testing was 20.6 (± 3.8 years) with a range of 11–30. A total of 3746 participants (54% male) endorsed having consumed at least six alcoholic beverages while 2291 (59% male) reporting using tobacco daily for a month and marijuana at least six times in their lifetime. Approximately 44% (n =

1713) reported using all three drugs and 1122 reported using all three drugs in the past six-months. A further 13.4% (n = 517) had only used alcohol and tobacco and 12.0% (n = 451) had used both alcohol and marijuana. A total of 28.0% reported only using alcohol. Based on DSM-IV abuse criteria, marijuana was more frequently abused (27%) in this sample than alcohol (20%). Dependence on a drug was highest for tobacco (52%) and lowest for alcohol (25%).

3.2 Mokken scale analysis for alcohol, tobacco, marijuana

Two consistent subjective experience scales were revealed using MSA. The item guilty did not fit into either scale for any substance. The item out of control was dropped due to extremely low endorsement for tobacco and because this item fluctuated between the positive scale (alcohol, tobacco) and the negative scale (marijuana). For all three drugs the positive scale included: relaxed, sociable, creative, euphoric, energetic, and increased sex drive. Items included in the negative scale for all three drugs were: lazy, drowsy, unable to concentrate, dizzy, and nauseous.

Table 2 provides the H-coefficients for the positive and negative scales for each of the three drugs with the items shown in their hierarchical ordering. For the positive subjective experiences H-coefficients for alcohol, tobacco, and marijuana were 0.45, 0.52, and 0.43, respectively. For the negative scale, the H-coefficients were 0.42, 0.52, and 0.54, respectively.

Means and standard deviations for each subjective experience scale across all three drugs are shown in Table 3. Mean scores differed as a function of age, sex, and clinical status. For all but marijuana, younger subjects had significantly lower mean scores on both positive and negative scales. Males scored significantly higher for the positive scales across all drugs than females. Males also had a higher mean score for the alcohol negative scale and a lower mean score for the marijuana negative scale. Mean scores on the positive experiences to tobacco and negative experiences to marijuana scales were higher in our community sample than in our clinical sample. Mean scores were lower in our community sample than in our clinical sample for positive experiences to marijuana and negative experiences to alcohol scales.

3.3 Cross drug correlations

After correcting for age, gender, and clinical status, the highest within-drug correlation was between positive and negative experiences to alcohol (r = 0.30), as shown in Table 4. The lowest within-drug correlations were for the two marijuana scales (r = 0.05) suggesting that these two types of experiences shared little common etiology. The highest cross-drug correlations were between positive experiences (r= 0.41) and negative experiences (r = 0.46) to alcohol and marijuana and suggested that these two drugs impact similar physiological and psychological systems. There were no appreciable differences in the correlations between the full sample and those participants who used all three drugs in the past six-months.

3.4 Cross-drug associations

Results from the step-wise regression procedures are shown in Table 5. There was evidence of cross-drug associations between the MSA scales and abuse or dependence for the three drugs and especially with the negative scales. The marijuana negative scale was associated not only with marijuana abuse/dependence, but with alcohol abuse/dependence and tobacco dependence, and the alcohol negative scale was positively associated with both alcohol abuse and dependence as well as tobacco dependence and marijuana abuse and dependence.

4. Discussion

In the current report, we examined subjective experiences to three commonly used drugs of abuse among young adults from the general community and an area treatment program. In these data, we obtained results that supported previous observations indicating positive and negative subjective experiences for a particular drug were predictive of problem use of that same drug. We then extended this relationship in two ways. First, we obtained results that supported the notion that positive and negative experiences to one drug are similar to those experienced for another drug(s) and second, that subjective experiences to a drug are predictive of the risk for problem use of other drugs. We interpret these findings to suggest that subjective experiences may be a useful indicator of a common liability towards use and problem use of multiple substances.

Following on our previous work on marijuana and subjective experiences (Zeiger et al., 2010), we used Mokken scaling to simultaneously examine whether subjective experiences to three drugs are associated with drug use outcomes. From these analyses we observed that the subjective experience scales for each of the three drugs were comparable to those found in previous studies despite using a different methodology (Rios-Bedoya et al., 2009: Scherrer et al., 2009; Le Strat et al., 2009). We observed differences in item means and hierarchical ordering of the items by substance suggesting that subjects are reporting drug specific subjective experiences. This interpretation is consistent with findings from laboratory-based studies which have shown that subjects can differentiate between a placebo and a drug or between different drugs based on subjective experiences (Perkins et al., 2005; Chait et al., 1988; Lile et al., 2009).

As different combinations of alcohol, tobacco, and marijuana use are commonly reported in epidemiological studies, we investigated the relationship between subjective experiences to different drugs in poly-substance users. We observed that subjective experiences to one drug were significantly correlated with experiences to another drug, though the strength of the relationship varied for different drug combinations. The strongest relationships were between alcohol and marijuana, replicating two previous studies (Scherrer et al., 2009; Heishman et al., 1989), and between alcohol and tobacco. These particular drug combinations target similar neuronal receptor systems and are reported to enhance the overall drug experience when taken together (Wise 2008; Zeiger et al., 2008) Further, as subjective experiences are thought to reflect the underlying physiology of a drug's actions (Schuckit et al., 2004; Pomerleau et al., 2004; Rios-Bedoya et al., 2009; Lyons et al., 1997), these cross-substance relationships may provide a closer approximation of a common risk factor suitable for molecular genetic investigation.

In this sample of community and clinical subjects, subjective experiences for one drug were associated with outcomes related to a different drug. Though our results replicate findings that relate positive experiences with greater use of other drugs, we also identified that negative experiences were predictive of abuse and dependence status of a different drug. In particular, negative effects of alcohol and marijuana were associated with misuse of these same drugs as well as tobacco. Although this may appear counter-intuitive, a possible explanation could be that subjects who needed greater amounts of a drug in order to feel its effects drove the observed association. Findings from laboratory-based drug discrimination studies suggest that some subjects are unable to differentiate between drug and placebo at a standard training dose (Schuster and Johanson, 1998). Differences between the two conditions could, however, be reported as non-discriminators were exposed to greater doses of a drug. Interestingly, those who were able to discriminate between non-exposure and exposure to a drug reported stronger positive and negative subjective experiences, often simultaneously (Skendarian et al., 2008; Le Strat et al., 2009; Schuster and Johanson 1988;

Kamien et al., 1993), at greater doses. This underscores the importance of dose in determining individuals' drug sensitivity as assessed by subjective experiences.

The relationship between drug dose, the resulting subjective experiences, and problem drug use has also been examined using self-ratings to the effects of alcohol [SRE; 28]. The SRE primarily assesses negative experiences to alcohol such as dizziness and passing out as related to the dosing levels needed to feel the sedative effects of alcohol. Among adolescent and adult samples of both sexes and family-history positive studies of alcoholics (Schuckit et al., 2004; Schuckit et al., 1997; Chung et al., 2009; Schuckit et al., 1984), low levels of response, as measured by the SRE have been implicated as a risk factor for alcohol use disorders. This notion that some drinkers need to ingest greater amounts of alcohol to feel its sedative effects and that this effect is related to greater drinking quantities has been recently supported (Chung et al., 2009) and extended to include the observation that this relationship is also relevant to those reporting lower levels of stimulant effects during the first five drinks. Our finding that negative alcohol experiences were predictive of problem alcohol use is consistent with this research, despite using a different questionnaire, and extends it to include the potential prediction of other drug use problem behaviors.

4.1 Limitations

Findings from the current study should be considered in light of a number of limitations. First, subjective experiences were collected from participants who ranged between 11 and 30 years of age. Though scaling of the different experiences was consistent between younger and older subjects, the older subjects have typically had a longer use history of alcohol, tobacco, and marijuana. Second, subjective experiences were only collected from those who reported using alcohol and marijuana six or more times and daily use of tobacco for a month. Thus, we were not able to include experiences from those who had used only a few times. Third, we were not able to measure differences in dosage, quality of a drug, depth of inhalation, peer use and drug use setting (Chait et al., 1988; Block et al., 1998; Ilan et al., 2005) some of which impact self-reported subjective experiences. Fourth, we were not able to establish the reference point from which people were making their ratings. This is due to the unclear phrasing of the stem questions that asks about experiences "shortly after using." We cannot know whether subjects were reporting their initial experiences, experiences in the minutes or hours immediately following recent drug intake or the conglomeration of their drug experience, making causal inferences regarding the observed associations not possible. Lastly, the lower endorsement rates for the experiences of tobacco may be due to the dichotomous fashion of responses that limit the sensitivity to detect the milder effects. Further, there more stringent requirements for collecting subjective experiences to tobacco may have made it more difficult to detect significant relationships with subjective experiences to alcohol, tobacco, and their more problematic use behaviors.

4.2 Conclusion

Findings from the current study indicate that positive and negative subjective experiences are related to problem use behaviors, though for negative effects the relationship is less straightforward. Further we showed, for the first time, that subjective experiences to one drug were informative for how a person experiences another drug within and across different pharmacological classes. Lastly, our results indicated that subjective experiences to a particular drug can be informative of the risk towards problem use of the same and different drug. Together, our results suggest a general liability or sensitivity towards experiencing drugs of abuse and that this sensitivity may be a contributor to a generalized risk to abuse and dependence.

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Table 1

Demographic and clinical characteristics

	Alcohol (n=3746)		Tobacco (n=2291)		Marijuana (n=2232)	
Sex	***N***	**%**	***n***	**%**	***n***	**%**
Male	2136	57	1465	64	1435	64
Female	1610	43	826	36	797	36
Diagnosis						
None	2171	59	1105	48	1069	48
Abuse	812	21			606	27
Dependence	763	20	1186	52	557	25
	Mean	**SD**				
Age at testing	20.7	3.8	21.1	3.8	20.6	3.9
Age initiation	14.9	2.8	13.7	3.1	14.4	2.6
Number times used in the past 6 months	25.0	35	96.5	80.9	41.1	62.7
No use past 6 months	477	13%	449	19.6%	820	37%

Table 2

Mean endorsements (standard deviation), Mokken Scales and hierarchy of items for alcohol, tobacco and marijuana subjective effects

Alcohol (n=3746)					
Positive Scale	**Mean (SD)**	**H**	**Negative Scale**	**Mean (SD)**	**H**
Sociable	0.80 (0.40)	0.62	Drowsy	0.46 (0.50)	0.42
Mellow	0.68 (0.47)	0.38	Dizzy	0.45 (0.50)	0.42
Top of the World	0.47(0.50)	0.47	Nauseous	0.44 (0.50)	0.42
Energetic	0.43 (0.50)	0.41	Unable to concentrate	0.43 (0.49)	0.43
Increased sex drive	0.38 (0.48)	0.37	Lazy	0.32 (0.47)	0.42
Creative	0.24 (0.43)	0.51			
Scale H		**0.45**			**0.42**
Tobacco (n=2291)					
Positive Scale	**Mean (SD)**	**H**	**Negative Scale**	**Mean (SD)**	**H**
Mellow	0.60 (0.49)	0.54	Dizzy	0.28 (0.45)	0.57
Sociable	0.28 (0.45)	0.45	Nauseous	0.22 (0.42)	0.52
Energetic	0.15 (0.35)	0.44	Lazy	0.11 (0.31)	0.47
Top of the World	0.13 (0.34)	0.46	Drowsy	0.09 (0.28)	0.53
Creative	0.05 (0.22)	0.62	Unable to concentrate	0.04 (0.19)	0.50
Increased sex drive	0.01 (0.09)	0.36			
Scale H		**0.48**			**0.52**
Marijuana (n=2232)					
Positive Scale	**Mean (SD)**	**H**	**Negative Scale**	**Mean (SD)**	**H**
Mellow	0.89 (0.31)	0.65	Lazy	0.72 (0.45)	0.57
Sociable	0.57 (0.49)	0.41	Drowsy	0.59 (0.49)	0.52
Creative	0.56 (0.50)	0.42	Unable to concentrate	0.44 (0.50)	0.49
Top of the World	0.48 (0.50)	0.40	Dizzy	0.18 (0.38)	0.56
Energetic	0.27 (0.44)	0.42	Nauseous	0.07 (0.26)	0.63
Increased sex drive	0.19 (0.39)	0.37			
Scale H		**0.43**			**0.54**

Table 3

Means (standard deviation) for unstandardized Mokken scales by clinical status, age and gender1 for alcohol, tobacco and marijuana

	Alcohol		Tobacco		Marijuana	
	Positive Scale	**Negative Scale**	**Positive Scale**	**Negative Scale**	**Positive Scale**	**Negative Scale**
Whole sample	3.00 (1.74)	2.11 (1.72)	1.21 (1.19)	0.74 (1.13)	2.96 (1.61)	1.99 (1.35)
Age[2]						
<17	2.35 ** (1.76)	1.95 * (1.67	1.04 ** (1.27)	0.58 ** (1.07)	2.94 (1.72)	1.75 *** (1.30)
>/= 17	3.10 (1.72)	2.13 (1.74)	1.24 (1.17)	0.76 (1.14)	2.96 (1.59)	2.04 (1.35)
Sex[2]						
Male	3.07 ** (1.77)	2.22 *** (1.80)	1.26 ** (1.24)	0.75 (1.14)	3.16 *** (1.61)	1.93 ** (1.34)
Female	2.90 (1.70)	1.96 (1.67)	1.13 (1.10)	0.73 (1.11)	2.59 (1.55	2.10 (1.35)
Clinical status						
Community	2.99 (1.72)	1.99 *** (1.68)	1.27 *** (1.20)	0.73 (1.10)	2.83 *** (1.56)	2.06 *** (1.33)
Clinical	3.10 (1.85)	2.68 (1.87)	1.06 (1.14)	0.77 (1.22)	3.30 (1.68)	1.88 (1.37)
Type of drug use						
Used all 3	3.40 *** (1.71)	2.63 *** (1.77)				
Alcohol only	2.37 (1.64)	1.44 (1.46)				

[1] Group differences tested by independent sample t-test

[2] Within group tests:

* p<0.05,

** p<0.01;

*** p<0.001,

Table 4

Correlations between Mokken scales for alcohol, tobacco and marijuana

	Alcohol Positive	Alcohol Negative	Tobacco Positive	Tobacco Negative	Marijuana Positive	Marijuana Negative
Alcohol Positive	--	0.23* (1110)	0.32* (946)	0.24* (951)	0.41* (1014)	0.23* (1014)
Alcohol Negative	0.30* (3740)	--	0.14* (946)	0.29* (952)	0.21* (1014)	0.44* (1015)
Tobacco Positive	0.31* (2217)	0.15* (2218)	--	0.18* (948)	0.24* (896)	0.17* (896)
Tobacco Negative	0.22* (2214)	0.27* (2216)	0.17* (2264)	--	0.19* (901)	0.22* (902)
Marijuana Positive	0.41* (2159)	0.21* (2158)	0.25* (1723)	0.20* (1722)	--	0.06 (1024)
Marijuana Negative	0.23* (2161)	0.46* (2161)	0.19* (1724)	0.22* (1724)	0.05 (2226)	--

* p<0.00

Table 5

Step-wise Regression with Mokken scales and outcomes for alcohol, tobacco and marijuana abuse and dependence

Stepwise regression*	OR	95% CI
Alcohol Abuse or dependence		
Alcohol Positive	1.29	1.21–1.39
Alcohol Negative	1.16	1.08–1.24
Marijuana Negative	1.18	1.07–1.29
Tobacco Dependence		
Tobacco Positive	1.34	1.21–1.47
Alcohol Negative	1.18	1.11–1.26
Marijuana Negative	1.19	1.09–1.30
Marijuana Abuse or Dependence		
Marijuana Positive	1.25	1.16–1.34
Marijuana Negative	1.16	1.06–1.27
Alcohol Negative	1.16	1.08–1.24
Tobacco Positive	1.12	1.01–1.23

*All step-wise regression models included the 6 scales (standardized by age, clinical status and sex), clinical status, age, and sex and were adjusted for familiality. Only the significant variables are shown.