Published in final edited form as:
Nicotine Tob Res. 2008 June ; 10(6): 1009–1020. doi:10.1080/14622200802097563.

Assessing dimensions of nicotine dependence:

An evaluation of the Nicotine Dependence Syndrome Scale (NDSS) and the Wisconsin Inventory of Smoking Dependence Motives (WISDM)

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Abstract

Considerable research, ranging from survey to clinical to genetic, has utilized traditional measures of tobacco dependence, such as the Fagerstrom Test of Nicotine Dependence (FTND) and the Diagnostic and Statistical Manual (DSM-IV) criteria, that focus on endpoint definitions of tobacco dependence such as heavy smoking, time to first cigarette in the morning, and smoking despite consequences. In an effort to better understand possible theories and mechanisms underlying tobacco dependence, which could be used to improve treatment and research, two multidimensional measures of tobacco dependence have been developed: the Nicotine Dependence Syndrome Scale (NDSS) and the Wisconsin Inventory of Smoking Dependence Motives (WISDM). This research used data from three randomized smoking cessation trials to examine the internal consistency and validity (convergent, concurrent and predictive) of these scales, relative to each other and the traditional measures. Results reveal that NDSS and WISDM subscales are related to important dependence

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This research was conducted at the University of Wisconsin, Madison and at the University of Pennsylvania, Pittsburg.

criteria, but in a heterogeneous fashion. The data suggest that there are important underlying mechanisms or motives that are significantly related to different important outcomes, such as withdrawal and cessation. The FTND was most strongly related to abstinence at 1 week and 6 months post-quit, whereas the WISDM Tolerance subscale was most strongly related to abstinence at the end of treatment. The NDSS Priority subscale was consistently predictive of outcome at all three follow-up time points. There is also evidence that WISDM subscales are related to a biomarker of the rate of nicotine metabolism.

Introduction

Scientists have developed numerous theories to account for the compulsive use of drugs and alcohol despite serious consequences. These theories implicate different mechanisms of addictive motivation, such as negative reinforcement (Baker, Piper, McCarthy, Majeskie & Fiore 2004; Lindesmith, 1947; Wikler, 1948); tolerance (DiChiara, 2000; Jellinek, 1960; Kalant, 1987; Perkins, 2002; Pratt, 1991); positive reinforcement (Stewart, de Wit, & Eikelboom, 1984; Stewart & Wise, 1992); opponent-processes (Solomon, 1977; Solomon & Corbit, 1974); incentive effects (Robinson & Berridge, 1993, 2003); and social learning (Abrams & Niaura, 1987; Marlatt & Gordon, 1985). Recently, two new measures of dependence have been developed to assess such relatively discrete dependence facets: the Nicotine Dependence Syndrome Scale (NDSS; Shiffman, Waters & Hickcox, 2004) and the Wisconsin Inventory of Smoking Dependence Motives (WISDM; Piper et al., 2004). These multidimensional measures reflect a long history of research that focuses on dependence and smoking motivations and reflect the prior work on multidimensional instruments that have assessed such motives as habitual/automatic, positive affect/indulgent, negative affect/tension reduction/sedative, addictive, stimulation, psychosocial, and sensorimotor manipulation (e.g., Best and Hakstian, 1978; Edwards, 1976, 1986; Ikard, Green, and Horn, 1969; McKennell, 1970; Russell, Peto, & Patel, 1974; Tate, Pomerleau, and Pomerleau, 1994; Tomkins, 1966). Research done using these earlier instruments suggested that dependence and tobacco motivation were multifactorial and that the various factors possessed meaningful discriminative validity (Best and Hakstian, 1978; Coan, 1973; Ikard et al., 1969; Russell et al., 1974; Tate et al., 1994).

Use of nicotine dependence measures that target specific mechanisms or dimensions of dependence are important for many reasons. For instance, scientists have become increasingly interested in characterizing relatively specific intermediate phenotypes that may be related to particular genetic variants (i.e., alleles, haplotypes). An example of this is the relation of a taste sensitivity haplotype with a dependence measure that focuses on a taste motive (vs. on a general feature of smoking such as number of cigarettes smoked per day: Cannon et al., 2005). In addition, dimensional, explanatory measures might result in better characterization of smokers into discrete “types” or latent classes (Muthén & Asparouhov, 2006; Xian et al., 2007).

While these new multifactorial measures of dependence were designed for research purposes, it is also possible that such measures might have clinical utility. Such measures might provide accurate prognostications of withdrawal severity or relapse likelihood. Indeed, such measures might provide predictions that are superior to those of traditional, global (measures intended to assess dependence per se rather than any subcomponents or types) measures of dependence such as the Fagerström Test of Nicotine Dependence (FTND; Heatherton, Kozlowski, Frecker, & Fagerström, 1991). This could occur to the extent that the new measures are more reliable than the traditional measures, or to the extent that the discrete dimensions of dependence assessed by these measures have additive predictive validities.

Traditional measures of dependence tend to assess the end-products of dependence (e.g., heavy smoking, smoking despite consequences), rather than putative mechanisms of dependence. The two main tobacco dependence assessments that are used both clinically and in research are the FTND (Heatherton et al., 1991) and the Diagnostic and Statistical Manual, 4th Edition (DSM-IV; APA, 1994) criteria. The items from the FTND were originally designed to measure the construct of *physical* dependence (Schuster & Johanson, 1974) whereas the DSM-IV definition includes: "...a cluster of cognitive, behavioral, and physiological symptoms indicating that the individual continues use of the substance despite significant substance-related problems," and "...a pattern of repeated self-administration that usually results in tolerance, withdrawal, and compulsive drug-taking behavior." (APA, 1994, p. 176).

While these traditional measures provide relatively little insight into the nature or mechanisms of dependence, they have been shown to predict clinically important dependence criteria such as smoking heaviness and relapse (Alterman, Gariti, Cook, & Cnann, 1999; Breslau & Johnson, 2000; Campbell, Prescott, & Tjeder-Burton, 1996; Fagerström & Schneider, 1989; Kawakami, Takatsuka, Inaba & Shimizu, 1999; Patten, Martin, Calfas, Lento, & Wolter, 2001; Westman, Behm, Simel, & Rose, 1997). Therefore, they provide a meaningful benchmark with which to compare the new multidimensional measures in terms of the prediction of clinically important outcomes.

The goal of this article is to evaluate the NDSS and the WISDM in terms of their ability to predict such clinically useful dependence criteria as relapse likelihood and withdrawal severity. The NDSS (Shiffman, Waters & Hickcox, 2004) is a 19-item self-report measure that was developed as a multidimensional scale to assess nicotine dependence using Edwards' theory of the dependence syndrome (Edwards, 1986). The WISDM (Piper et al., 2004) comprises 68 items designed to assess 13 different theoretically-derived motivational domains. See Table 1 for subscale descriptions. Each measure will be evaluated based on its internal consistency and its relations with other tobacco dependence measures such as: the FTND and DSM-IV, tobacco dependence criteria such as cigarettes smoked per day, and clinically important tobacco dependence criteria such as withdrawal, cessation outcome, and the rate of nicotine metabolism (which might be related to such factors as optimal nicotine replacement dosage).

Methods

Data were collected from three randomized placebo-controlled smoking cessation trials. In Study 1 (N = 608: Piper et al., in press), participants were randomly assigned to one of the three treatment groups: active bupropion + active 4-mg nicotine gum (AA, n = 228); active bupropion SR + placebo nicotine gum (AP, n = 224); or placebo bupropion SR + placebo gum (PP, n = 156). All participants also received three 10-minute counseling sessions (one week pre-quit, on the Quit Day, and one week post-quit). In Study 2 (N = 463: McCarthy et al., 2007) participants were randomly assigned to receive active bupropion + counseling (AC, n = 113), active bupropion + no counseling (ANc, n = 116), placebo + counseling (PC, n = 121) or placebo + no counseling (PNc, n = 113) in a 2 (active bupropion SR vs. placebo) × 2 (counseling vs. no counseling) factorial design. Counseling consisted of eight sessions of brief (10-minute) individual cessation counseling. In Study 3 (N = 481: Lerman et al., 2006) participants who provided plasma samples were randomly assigned to either a nicotine patch (n = 241) or nicotine nasal spray (n = 240) condition. All participants also received seven counseling sessions.

Participants

Participants were recruited through mass media in Milwaukee, WI (Study 1), Madison, WI (Study 2), Washington D.C. (Study 3) or Philadelphia, PA (Study 3) to participate in large-scale smoking cessation trials. Participants were eligible for each study if they reported

smoking 10 or more cigarettes per day, were motivated to quit smoking, did not have any serious physical or mental health issues that would prevent them from participating in or completing the study, and were not pregnant or breast-feeding and took steps to prevent pregnancy during treatment. In Study 3, participants were also excluded it they had uncontrolled hypertension, unstable angina, heart attack or stroke in the last 6 months, current treatment or recent diagnosis for cancer, drug or alcohol dependence, any use of bupropion or other nicotine-containing products other than cigarettes.

Measures

Cotinine and 3-hydroxycotinine—Nicotine is metabolized to cotinine and then to trans-3′-hydroxycotinine (3-HC) by the liver enzyme cytochrome P450 (CYP) 2A6 (Nakajima et al., 1996). The ratio of 3-HC to cotinine is an index of the rate of nicotine metabolism which provides a phenotypic measure of CYP 2A6 activity and, in some studies, correlated with number of cigarettes smoked per day (Benowitz, Pomerleau, Pomerleau & Jacob, 2003; Dempsey et al., 2004; Malaiyandi et al., 2006). This ratio has also been shown to predict smoking cessation following nicotine patch therapy (Lerman et al., 2006). Assays of cotinine and 3-HC were performed on blood samples collected at baseline in Study 3 only.

Demographics and Smoking History—These questionnaires (the same for Studies 1 and 2 and different for Study 3) assessed characteristics such as gender, ethnicity, age, marital status, education level, and employment. The smoking history questionnaire included items such as the number of cigarettes smoked per day, age of smoking initiation, smoking status (e.g., daily smoker, occasional smoker, etc.), number of quit attempts, longest time abstinent, and other smokers in the household.

Fagerström Test of Nicotine Dependence **(FTND; Heatherton, et al., 1991)—**The FTND is a 6-item scale designed to measure tobacco dependence. Each item has its own individual response scale and previous research indicates that it has fair internal consistency (α = .61; Heatherton, et al., 1991).

Nicotine Dependence Syndrome Scale **(NDSS; Shiffman et al., 2004)—**The NDSS is a 19-item self-report measure, comprising five theoretically derived subscales (see Table 1). Each item is rated on a 5-point Likert scale from 1 = “Not at all true” to 5 = “Extremely true”. This measure is scored using factor loadings. To calculate an individuals’ score on each subscale and on the total NDSS, the researcher must multiply the participant’s answer on each question by the specific factor loading provided by Shiffman et al. (2004) and then sum each factor-adjusted answer relevant to the subscale being calculated. Some items are reversed scored and have negative factor loadings. In addition, a number of items load on multiple subscales but they may have positive loadings on some subscales and negative loadings on other subscales. The total NDSS does not include all 19 items used in the subscales. The NDSS was not administered in Study 3.

Tobacco Dependence Screener **(TDS; Kawakami, et al., 1999)—**The TDS is a self-report measure designed to assess 10 DSM-IV tobacco dependence criteria, with 0 indicating lack of the symptom and 1 indicating endorsement of the criterion. Research shows the TDS has good internal consistency (α ranging from .76 to .81 across three studies). The TDS was not administered in Study 3.

Wisconsin Inventory of Smoking Dependence Motives **(WISDM; Piper et al., 2004)—**The WISDM comprises 68 items designed to assess 13 different theoretically-derived motivational domains (see Table 1) on a 7-point Likert scale ranging from 1 - “Not true of me at all” to 7 - “Extremely true of me.” Subscales are scored by taking the average of all of the

answers relevant to that subscale. Only Craving, Cue Exposure/Associative Processes, Negative Reinforcement, Positive Reinforcement, and Tolerance were administered in Study 3, to a subset of participants, because the WISDM scales were added after the study had already begun.

Procedure

In all three studies, eligible participants were invited to an Orientation Session at which they were told about the study and provided written informed consent along with demographic and smoking history information, including a carbon monoxide breath test (excluded if CO < 10 parts per million). Participants also completed the multiple tobacco dependence measures described above. Participants were contacted at 6-months post-quit. At this time, all participants who reported abstinence for the previous seven days were scheduled to return to the clinic and provide a breath sample for CO analysis.

Participants in Studies 1 and 2 also provided ecological momentary assessment (EMA) data about their smoking, stressors, withdrawal symptoms (e.g., desire to smoke, difficulty concentrating, sadness, irritability), and other life events. In Study 1, participants carried cellular phones for two weeks, centered around the quit day, and responded to four calls: one after waking, one before going to bed and two other prompts that occurred randomly during the day. Eleven items from the Wisconsin Smokers Withdrawal Scale (WSWS; Welsch et al., 1999), answered on a 1-5 Likert scale (1 = “disagree” and 5 = “agree”), were used in Study 1 to assess craving, hunger, negative affect, and difficulty concentrating within the last 30 minutes. Data from all four calls were aggregated to summarize withdrawal during each day. In Study 2, participants carried electronic diaries for 2 weeks pre-quit and 4 weeks post-quit and responded to at least six alarms per day (one upon waking, one prior to going to bed and four or more random prompts). In Study 2, 20 items from the WSWS (Welsch et al., 1999), answered on a 1-11 Likert scale (1 = “low” and 11 = “high”) were used to assess craving, hunger, negative affect, and difficulty concentrating. From Study 2, only the evening report data (collected before going to bed) was used in the withdrawal calculations because the time frames for the morning and evening reports were different from the time frames for the random prompts and use of the evening report data provided to the only comprehensive assessment of withdrawal across the entire day.

Analytic Methods

Data for all analyses are based on data pooled across Study 1 and Study 2, unless otherwise noted. The same pattern of results was found for both individual studies unless otherwise noted. Data from Study 3 were used solely to examine the relation of the scales with the log of the ratio of 3-HC to cotinine. The log of the ratio was taken to create a normally distributed independent variable and has been shown to be the optimal measure for estimating clearance (Levi et al., 2006). All analyses were conducted using SPSS 14.0 for Windows (SPSS, Inc., 2006) unless otherwise noted. Both Bonferroni corrected and uncorrected p-values are supplied for the multiple validation analyses. Hierarchical Linear Modeling (HLM; Scientific Software International, 2001) software was used to analyze increase in withdrawal on the quit day and over the first week post-quit. Data from all participants were included in the analyses, regardless of smoking status, because previous research suggests that eliminating lapsers from analyses inappropriately constrains withdrawal relations (Piasecki, Jorenby, Smith, Fiore & Baker, 2003a). Best-fitting models to predict cessation outcome were created using Hosmer & Lemeshow’s (2000) model-building criteria.

Results

Participant Characteristics

The combined sample from Study 1 and Study 2 comprised 1,071 smokers (54.6% women; see Table 2 for demographic information). While the two study samples were comparable, there were statistically significant differences in the proportion of women (χ^2 (1, N=1071) = 6.08, $p < .01$), racial composition (χ^2 (1, N= 1047) = 59.90, $p < .01$), education (χ^2 (1, N= 1066) = 25.89, $p < .01$), age (t (1069) = -4.19, $p < .01$), baseline CO (t (1068) = -3.59, $p < .01$), although some of these differences were relatively modest (e.g., mean age difference is 3.02 years, mean CO difference is 2.6 ppm). Thus, the combined sample comprised a more diverse population than did the individual samples. Participants in Study 3 were 54.7 % women and 28.3% African-American (see Table 2).

Dependence Scores and General Psychometrics

Means and standard deviations were calculated for all of the dependence scales for the total sample, men, women, White smokers and African-American smokers (Table 3). Only 29 individuals (2.8%) identified themselves as neither White nor African-American and were not included in analyses of race. Results indicated that men and women differed on several subscales, as did White and African-American smokers (Table 3). However, analyses showed that neither gender nor race interacted significantly with nicotine dependence scale and subscale scores in the prediction of dependence criteria.

Psychometric analyses revealed that the NDSS subscales had rather poor internal consistencies (using the factor-scaled scores for all items; α = .30-.59)[1], but the overall measure had acceptable internal consistency (α = .79). The WISDM subscales all demonstrated acceptable to good internal consistency (α = .74-.94), as did the total WISDM (α = .96). See Table 1 for results. These internal consistency estimates were consistent for men, women, White and African-American participants (data not shown).

Convergent and concurrent validity

To assess the validity of the NDSS and WISDM, their relations with established tobacco dependence measures (i.e., FTND and TDS) and with specific tobacco dependence criteria (i.e., cigarettes smoked per day, CO, and cessation outcome) were examined both at the subscale and total score levels. Correlation analyses revealed that almost all of the NDSS and WISDM subscales were statistically significantly related to both the FTND and TDS, with the size of the correlations ranging from modest to moderate, with $p < .002$ indicating a significant correlation Bonferroni-corrected for the 22 comparisons conducted for each dependent variable (Table 1). The WISDM Tolerance subscale had the strongest correlations with the FTND (r = .71, $p < .002$) and the NDSS Total and WISDM Total had the highest correlations with the TDS (r = .37 and .39, $p < .002$, respectively). The Total WISDM and Total NDSS were moderately correlated with one another (r = .61, p < .01).

With respect to concurrent validity, the number of cigarettes smoked per day was statistically significantly related to all scales, with the exception of WISDM Weight Control. Again, the magnitude of the correlations ranged from modest to moderate (see Table 1). In terms of the multifactorial measures, the NDSS Total and WISDM Tolerance scales had the strongest correlation with cigarettes smoked per day (r = .35 and .43, p's $\leq .002$, respectively). The strongest correlation across all scales with daily cigarette consumption was obtained for the

[1]When only the three highest loading items on each factor were used in the internal consistency analysis (Shiffman et al., 2004), results revealed α = .26-.65. These relatively low internal consistency estimates may be attributed in part to the fact that the sample comprised treatment seekers and this may have restricted the range of NDSS scores.

FTND (r = .54), which reflects the fact that the FTND directly assesses number of cigarettes smoked each day. There were fewer statistically significant relationships between the dependence measures and CO (see Table 1). Among the NDSS and WISDM subscales, the WISDM Tolerance subscale provided the strongest prediction of CO, but even this was modest (r = .28) and the FTND had the strongest relation (r = .34).

Finally, correlation analyses revealed that the log of the 3-HC to cotinine ratio was modestly related to number of cigarettes smoked per day (n = 476, r = .12, p = .01), the WISDM Craving subscale (n = 354, r = .13, p = .02) and the WISDM Cue Exposure/Associative Processes subscale (n = 354, r = .11, p = .05). Thus, the data suggest that individuals with faster metabolism tended to smoke more and reported that they were more likely to smoke due to cravings and smoking cues. However, these effects are quite modest and the p-values do not exceed the Bonferroni alpha correction which results in $p < .007$ for the seven correlations computed in Study 3. The other candidate predictors tested, WISDM Negative Reinforcement, WISDM Positive Reinforcement, WISDM Tolerance and FTND shared even weaker relations with nicotine metabolism. Study 3 did not administer the NDSS.

Predictive validity - withdrawal

Next, we examined the ability of the NDSS and WISDM subscales to predict two different aspects of withdrawal: the change in withdrawal symptoms on the quit day and the post-quit slope, or change in withdrawal over the first week post-quit. For this purpose, we fit two-level hierarchical linear models in which a random intercept (interpretable as change in withdrawal symptoms on the quit day) and slope (interpretable as average daily change in withdrawal symptoms post-quit) were determined for each individual using Empirical Bayes' estimates (see Piper et al., in press, for details). Models allowed for random error and did not use cigarette smoking as a time-varying covariate since previous analyses with these data revealed that withdrawal symptoms are very modestly related to such smoking (e.g., Piper et al., in press). Data from Study 1 and Study 2 were analyzed separately due to their different metrics for measuring withdrawal. Results revealed that, after controlling for treatment, the NDSS Drive and WISDM Negative Reinforcement scales showed the strongest relations with the empirical Bayes' estimates of change in withdrawal on the quit day in both studies (see Table 1). Neither of these effects was statistically significant following Bonferroni correction. In general, the magnitude of predicted relations was modest, with NDSS Drive accounting for approximately 1.4-4.2% of the variance and WISDM Negative Reinforcement accounting for approximately 1.0-1.3% of the variance in change in withdrawal on the quit day, relative to treatment, which accounted for approximately 0.5-3.6% of the variance in change in withdrawal on the quit day, across the two studies. It is important to note that the relative magnitude of HLM coefficients across the two studies is also influenced by the different units of measurement in the withdrawal assessment. No subscales were significant predictors of the change in withdrawal symptoms over time and there were no consistent predictors of change in craving on the quit day or post-quit slope in craving across the two studies. The FTND was not related to either withdrawal or craving dimensions.

Predictive validity - cessation outcome

Logistic regression analyses suggested that few dependence scales or subscales were related to smoking at the three time points assessed (1-week post-quit, end of treatment/8 weeks post-quit, and 6-months post-quit; Table 1), after controlling for treatment and study. Treatment was coded as 1 for individuals who received active bupropion and 0 for those who did not. We did not code for use of nicotine gum in Study 1, given that it did not have a statistically significant effect on outcome (see Piper et al., in press) nor did we code for counseling effects in Study 2, for similar reasons (see McCarthy et al, in press). Study was used as a control variable because participants in Study 1 were significantly more likely to be abstinent at 1-

week and end of treatment than were participants in Study 2 (data not shown). The NDSS Total and the NDSS Priority subscale significantly predicted abstinence across all three time points, with odds ratios ranging from 1.21-1.28 for Priority and 1.17 to 1.23 for NDSS Total. Only two WISDM subscales predicted abstinence at all three time points: Automaticity and Tolerance, with odds ratios ranging from 1.10-1.15 and 1.15-1.24, respectively.

Best-fitting models were created for the NDSS, the WISDM and for a combined NDSS/WISDM model for each follow-up time point, controlling for treatment and study (Table 4). Results revealed that WISDM Tolerance predicted abstinence at each time point but that its prediction of early abstinence (at 1-week post-quit and end of treatment) was augmented by Social/Environmental Goads (Table 4). Amongst NDSS subscales, Priority was the only consistent predictor of outcome at each time point and was augmented by the Stereotypy subscale in predicting outcome at 1-week post-quit. Results also showed that when the WISDM and NDSS subscales were entered simultaneously, only the WISDM Tolerance and Social/Environmental Goads subscales were retained in the best-fitting model of smoking at 1-week post-quit. The best-fitting model predicting smoking at the end of treatment contained the NDSS Priority and the WISDM Social/Environmental Goads subscales and the best-fitting model predicting smoking at 6-months post-quit contained the NDSS Priority and WISDM Tolerance subscales.

To determine whether the FTND could improve on prediction of outcome for the NDSS, WISDM and combined models, we entered FTND score as a third step in a hierarchical regression analysis, after controlling for treatment and study. Results revealed that for models predicting outcome at 1 week and the end of treatment, adding the FTND resulted in a significant improvement in model fit, based on the step chi-square (χ^2 = 6.28 to 25.82, p = .01 to < .001). However, at 6-months post-quit, adding the FTND improved prediction of the NDSS model (χ^2 = 10.20, p = .001), but did not improve prediction of the WISDM or the combined NDSS/WISDM models. We also examined whether the NDSS and WISDM subscales could improve on the ability of the FTND to predict of cessation outcome. Results revealed that adding the best NDSS/WISDM model as a second step in a hierarchical regression analysis improved prediction, based on the step chi-square, at the end of treatment (χ^2 = 14.50, p < .01) but the NDSS/WISDM model did not significantly improve prediction at 1-week (χ^2 = 3.58, p = .17) or 6-months (χ^2 = 5.17, p = .08) post-quit.

Data were also analyzed to examine the performance of these best-fitting models in men and women and White and African-American smokers (there was insufficient power to analyze any other racial/ethnic group). There were no statistically significant differences in the performance of these models in predicting outcome for either gender or either racial/ethnic group when gender/ethnicity and scale by gender/ethnicity interactions were included in the model. However, it should be noted that there were only 155 African-American smokers in this sample, so power may not have been sufficient to detect a significant effect.

Discussion

The present research describes the ability of current tobacco dependence measures to assess such clinically important outcomes as withdrawal and cessation outcome. The data suggest that in order to achieve optimal prediction of these important outcomes, one needs to use different scales to achieve the best overall prediction. Thus, this research extends to the newer multifactorial instruments a conclusion drawn from research on the traditional dependence instruments: viz. none of the dependence instruments predicts outcomes well across all major dependence criteria (abstinence, self-administration heaviness, and withdrawal severity: Piper et al., 2006).

It is clear from the examination of the results that the FTND tends to yield better prediction of cessation outcomes than any other single scale or subscale. Adding the FTND to the WISDM and NDSS models improved model fit at 1-week and end of treatment. However, the FTND did not improve prediction over the WISDM and the combined NDSS/WISDM models at 6-months post-quit. Conversely, adding the best NDSS/WISDM scales to the FTND resulted in improved prediction only at the end of treatment. While the FTND may be the best predictor of cessation outcome, the use of the multidimensional scales may provide some insight into the motivations that influence relapse, such as the density of smoking cues in the environment predicting early cessation success.

The chief value of the NDSS and WISDM may be that they permit assessment of particular motivational influences on smoking and may be more sensitive to particular smoking motives or in subpopulations. The different patterns of relations of scales with criteria may suggest different causal influences on smoking features or outcomes, a notion that has been studied for more than 40 years among researchers of smoking motivations (e.g., Best and Hakstian, 1978; Ikard et al., 1969; McKennell, 1970; Russell et al., 1974; Tate et al., 1994; Tomkins, 1966). In the present research, the scales that had the highest relations with withdrawal (NDSS Drive and WISDM Negative Reinforcement) were different from those that were most highly predictive of cessation outcome (NDSS Priority, WISDM Automaticity and Tolerance). In addition, the WISDM Craving and Cue Exposure subscales were relatively highly related to individual rate of nicotine metabolism, although the relations observed were still of small magnitude and did not meet our conservative criterion for statistical significance. Thus, the increase in withdrawal symptoms on the quit day was related to self-reported need for cigarettes to control cravings and influence affect while smoking at follow-up was related to a pattern of self-reported heavy and constant smoking that occurred outside of conscious control (automatically: see TTURC Nicotine Dependence Phenotype Working Group, 2007). The fact that the different subscales had varying patterns of relations with validation measures suggests that a single facet of tobacco dependence cannot optimally predict outcomes across all of the dependence criteria (e.g., heaviness of smoking, withdrawal, relapse risk; Pomerleau et al., 2005). Furthermore, scales that are intended to assess the same construct (i.e., the WISDM and NDSS Tolerance scales) may have different predictive relations if they approach the construct in different ways. For instance, the WISDM Tolerance items focus on being a “heavy” smoker and needing to smoke after periods of abstinence (e.g., overnight) whereas the NDSS focuses more on assessing the effects of smoking, including both the need to smoke more to achieve the same subjective effects and the ability to smoke more without experiencing the negative effects. The different foci of these two assessments of the Tolerance construct might suggest which elements are more implicated in dependence. In other words, it appears that self-reported heavy smoking and the need to smoke after deprivation are more strongly related to cessation outcome than is the self-report of the positive and negative drug effects.

An example of how multidimensional measures might shed light on differences across subpopulations of smokers comes from analyses contrasting the performance of men and women on the different scales. While traditional measures of nicotine dependence end-states, such as the FTND and TDS, do show significant gender differences, they do not implicate particular dependence features in these differences. The NDSS and WISDM, however, are informative because of the pattern of gender differences across the various subscales (Table 3). Specifically, results suggest that women tend to score higher on scales that reflect the impact of environmental cues and smoking to control negative moods and weight. These findings are consistent with prior data that indicate that smoking may be more cue-dependent among women than men, and that control of negative affect may be a more salient goal for women (e.g., Perkins, Donny, & Caggiula,1999;Perkins et al., 2001;Wetter et al., 1994). In comparison, men earned higher scores on the NDSS Continuity and NDSS Stereotypy subscales indicating that men report a greater tendency to smoke continuously or regularly across time and place. In

theory, such findings might allow researchers to develop treatments that are better tailored to each sex. Although absolute levels of abstinence outcomes might be the same, it is possible that different dependence subtypes or motives might reflect different vulnerabilities or sensitivities that might ultimately end in a return to smoking. However, it is important to note that despite these differences in dependence motivations, there were no gender by scale interactions in the prediction of cessation outcome.

Another insight offered by this research is the possible link between cigarettes smoked per day, the WISDM Craving and WISDM Cue Exposure subscales and the rate of nicotine metabolism, suggesting that individuals who quickly metabolize nicotine are more likely to be heavier smokers, may smoke more in response to cravings and may be more influenced by smoking-related cues (see also Lerman et al., 2006; Malaiyandi et al., 2006). This tentative observation, combined with the finding that individuals with high WISDM Craving scores were more likely to have more severe withdrawal, suggests that individuals who are faster metabolizers of nicotine need to smoke more to maintain sufficient central nervous system levels of nicotine in their systems and may be more sensitive to both interoceptive and exteroceptive cues to maintain high nicotine levels in the body (Baker et al., 2004). Furthermore, more rapid metabolism means that nicotine levels in the blood and brain decline more quickly after smoking a cigarette, which could explain more severe withdrawal symptoms, including more craving. However, as noted earlier, such findings were of modest size and require replication. There are limitations, both with respect to the new multidimensional measures, and with the research in general. First, some subscales have modest internal consistencies (e.g., the NDSS Tolerance and Continuity subscales) and this may explain why these subscales were not more highly related to other measures. Second, although these multidimensional measures may shed light on the nature of nicotine dependence, neither the NDSS nor the WISDM measures do as good a job of predicting cessation outcome as does the FTND. However, there was evidence that optimal combination of subscales have the potential to yield abstinence outcome predictions that are superior to those yielded by the FTND. Further research is needed to extend and replicate these findings.

Acknowledgements

This research was supported, in part by NIH grants CA/DA #P50-84178, #P50-CA84724-05 and #P50-DA0197-06.

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Table 1

Dependence constructs, internal consistency and validity results

			Correlations[a]				Linear regression, controlling for treatment and study (B, SE)[b,‡]	Logistic regression, controlling for treatment and study (Wald, OR)[c]		
Subscale (Number of items)	**Target construct**	**α**	**FTND**	**TDS**	**Cig/day**	**CO**	**Increase in withdrawal symptoms on the quit day**	**1-week abstinence**	**End of treatment (8-week) abstinence**	**6-month abstinence**
NDSS Drive (8)	Characterized by craving, withdrawal and smoking compulsions	.59	.28†	.41†	.12†	.08**	.05, .02** *.19, 05***	.22, .97	.02, .99	.55, 1.06
NDSS Priority (8)	Characterized by preference for smoking over other reinforcers	.43	.27†	.24†	.18†	.04	.004, .02 *.04, .04*	8.86, 1.21**	11.90, 1.28**	7.78, 1.28**
NDSS Tolerance (8)	Characterized by reduced sensitivity to the effects of smoking	.30	.29†	.11†	.29†	.14†	.00, .02 *-.03, .04*	2.35, 1.10	.58, 1.05	.13, 1.03
NDSS Continuity (8)	Characterized by the regularity of smoking rate	.46	.19†	-.06	.13†	.14†	.02, .02 *-.02, .05*	.02, 1.01	.16, .97	.05, .98
NDSS Stereotypy (8)	Characterized by the invariance of smoking across situations	.47	.28†	-.04	.26†	.10†	-.01, .02 *-.07, .04*	7.67, 1.20**	1.22, 1.08	1.92, 1.12
NDSS Total (14)		.79	.50†	.37†	.35†	.15†	.03, .02 *.11, .05**	6.27, 1.20**	4.43, 1.17*	5.31, 1.23*
WISDM Affiliative Attachment (5)	Characterized by a strong emotional attachment to smoking and cigarettes	.88	.31†	.28†	.19†	.06	.01, .01 *.04, .03*	.91, 1.04	.04, .99	.36, 1.03
WISDM Automaticity (5)	Characterized by smoking without awareness or intention	.90	.46†	.24†	.37†	.22†	.01, .01 *.01, .03*	7.41, 1.11**	5.33, 1.10*	8.89, 1.15**
WISDM Control (4)	Based on the notion that once dependence becomes ingrained, the dependent person believes that he or she has lost volitional control over drug use	.78	.40†	.33†	.29†	.19†	.01, .01 *.04, .03*	.67, 1.04	1.30, 1.06	1.18, 1.06
WISDM Behavioral Choice/Melioration (7)	Characterized by smoking despite constraints on smoking or negative consequences and/or the lack of other options or reinforcers	.84	.36†	.33†	.21†	.07*	.01, .01 *.05, .03*	.67, 1.04	.38, .97	.32, .97
WISDM Cognitive Enhancement (5)	Characterized by smoking to improve cognitive functioning (e.g., attention)	.92	.23†	.27†	.16†	.04	.02, .01 *.09, .03***	.02, 1.01	.16, .98	.02, .99
WISDM Cravings (4)	Characterized by smoking in response to craving or experiencing intense and/or frequent urges to smoke	.80	.41†	.35†	.25†	.11†	.02, .01 *.07, .04*	4.66, 1.11*	.08, 1.02	1.02, 1.06
WISDM Cue Exposure/ Associative Processes (7)	Characterized by frequent encounters with nonsocial smoking cues or a strong	.80	.20†	.32†	.10†	.03	.02, .01 *.10, .04**	.03, .99	.00, 1.00	.05, 1.01

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			Correlations[a]				Linear regression, controlling for treatment and study (B, SE)[b,‡]	Logistic regression, controlling for treatment and study (Wald, OR)[c]		
Subscale (Number of items)	**Target construct**	**α**	**FTND**	**TDS**	**Cig/day**	**CO**	**Increase in withdrawal symptoms on the quit day**	**1-week abstinence**	**End of treatment (8-week) abstinence**	**6-month abstinence**
	perceived link between cue exposure and the desire or tendency to smoke									
WISDM Negative Reinforcement (6)	Characterized by the tendency or desire to smoke in order to ameliorate negative internal states	.86	.22†	.34†	.10†	.04	.03, .01* *.08, .03***.	.19, 1.02	.13, 1.02	.27, 1.03
WISDM Positive Reinforcement (5)	Characterized by the desire to smoke in order to experience a "buzz" or a "high," or to enhance an already positive feeling or experience	.86	.20†	.23†	.12†	.03	.02, .01* *.06, .03*	.05, 1.01	.14, .98	.03, 1.01
WISDM Social/ Environmental Goads (4)	Characterized by social stimuli or contexts that either model or invite smoking	.94	.09**	.04	.10†	-.04	-.01, .01 *-.04, .02*	6.66, 1.09**	9.12, 1.12**	2.19, 1.07
WISDM Taste/Sensory Properties (6)	Characterized by the desire or tendency to smoke in order to experience the orosensory/ gustatory effects of smoking	.88	.17†	.16†	.12†	.04	.01, .01 *.04, .03*	.72, .96	.11, 1.02	.47, 1.04
WISDM Tolerance (5)	Characterized by the need to smoke increasing amounts over time and the tendency to smoke large amounts	.74	.71†	.25†	.43†	.28†	-.002, .01 *.002, .03*	20.72, 1.24†	7.65, 1.15**	11.04, 1.21†
WISDM Weight Control (5)	Characterized by the use of cigarettes to control body weight or appetite	.90	.05	.19†	.04	.01	.02, .01 *.000, .03*	.04, .99	.41, .98	.38, .97
WISDM Total (68)		.96	.44†	.39†	.29†	.13†	.002, .001 *.01, .004*	3.08, 1.01	1.11, 1.01	1.72, 1.01
FTND (6)	Physical dependence	.64	----	.26†	.54†	.34†	.003, .01 *.02, .02*	37.23, 1.20†	14.21, 1.13**	12.93, 1.14†
TDS (10)	DSM-IV dependence criteria	.64	.26†	----	.12†	.07*	.02, .01 *.04, .03*	3.31, 1.06	1.95, 1.05	4.73, 1.09*

α = Cronbach's alpha

*p < .05, the Bonferroni corrected alpha for the 22 comparisons for each dependent variable

**p ≤ .01, the Bonferroni corrected alpha for the 22 comparisons for each dependent variable

†p ≤ .002, the Bonferroni corrected alpha for the 22 comparisons for each dependent variable

‡Data from Study 1 and Study 2 were analyzed separately due to separate withdrawal metrics. Study 1 results are in standard font and Study 2 results are in *italics*.

[a]N's range from 1,026-1,070.

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[b] N's range from 594-603 for Study 1 and 378-296 for Study 2.

[c] N's range from1,038-1,070.

Table 2

Demographics

	Combination of Study 1 + Study 2 (N=1071)	Study 1 (N=608)	Study 2 (N=463)	Study 3 (N = 481)
% Women*	54.6	57.9	50.3	54.7
% White*	82.4	76.0	90.8	65.2
% African-American*	14.8	22.0	5.5	28.3
% high school or greater education*	92.9	90.7	95.7	95.9
% Married	45.0	46.5	43.0	44.7
Age (SD)*	40.48 (11.79)	41.78 (11.34)	38.76 (12.16)	45.49 (10.35)
Mean cigarettes per day (SD)	22.22 (10.11)	22.44 (9.87)	21.93 (10.44)	21.76 (9.84)
Baseline CO in ppm (SD)*	25.98 (11.80)	27.11 (11.69)	24.51 (11.80)	24.40 (12.59)

*Statistically significant differences between the Study 1 and Study 2. Study 3 was not compared as it was not combined with any other data set.

Table 3

Means (standard deviations) by gender and ethnicity

Subscale	Total (N = 1071)	Men (n = 486)	Women (n = 585)	White (n = 863)	African-American (n = 155)
NDSS Drive*	-.08 (1.00)	-.17 (.95)*	.01 (1.03)*	-.06 (.98)	-.16 (1.09)
NDSS Priority*	.28 (1.05)	.20 (1.01)*	.35 (1.07)*	.21 (.99)	.23 (.94)
NDSS Tolerance	-.16 (1.07)	-.14 (1.06)	-.18 (1.07)	-.15 (1.07)	-.31 (1.07)
NDSS Continuity**	-.13 (.97)	-.01 (.92)**	-.22 (1.00)**	-.10 (.97)	-.18 (.94)
NDSS Stereotypy**	.20 (.98)	.36 (.93)**	.07 (1.00)**	.21 (.99)	.23 (.97)
NDSS Total	-.09 (.93)	-.10 (.92)	-.08 (.94)	-.07 (.91)	-.18 (1.02)
WISDM Affiliative Attachment**	2.98 (1.58)	2.79 (1.46)**	3.13 (1.66)**	3.02 (1.59)	2.83 (1.55)
WISDM Automaticity	4.56 (1.70)	4.47 (1.72)	4.63 (1.67)	4.56 (1.68)	4.49 (1.78)
WISDM Control‡	5.12 (1.40)	5.08 (1.40)	5.15 (1.39)	5.18 (1.36)‡	4.75 (1.58)‡
WISDM Behavioral Choice/Melioration†	3.19 (1.34)	3.10 (1.30)	3.26 (1.37)	3.23 (1.35)†	2.93 (1.30)†
WISDM Cognitive Enhancement‡	3.25 (1.61)	3.18 (1.58)	3.30 (1.62)	3.28 (1.61)‡	2.83 (1.42)‡
WISDM Cravings	4.94 (1.30)	4.92 (1.26)	4.95 (1.32)	4.95 (1.24)	4.79 (1.60)
WISDM Cue Exposure/Associative Processes**‡	4.69 (1.25)	4.52 (1.25)**	4.83 (1.24)**	4.76 (1.20)‡	4.21 (1.48)‡
WISDM Negative Reinforcement**†	4.16 (1.36)	3.93 (1.32)**	4.35 (1.38)**	4.19 (1.35)†	3.87 (1.40)†
WISDM Positive Reinforcement†	3.67 (1.44)	3.60 (1.37)	3.74 (1.49)	3.71 (1.43)†	3.41 (1.50)†
WISDM Social/Environmental Goads	3.79 (1.91)	3.68 (1.89)	3.88 (2.00)	3.82 (1.89)	3.52 (1.96)
WISDM Taste/Sensory Properties	4.18 (1.41)	4.20 (1.36)	4.17 (1.46)	4.20 (1.37)	4.06 (1.63)
WISDM Tolerance†	4.90 (1.41)	4.86 (1.40)	4.94 (1.42)	4.85 (1.42)†	5.16 (1.38)†
WISDM Weight Control**†	2.86 (1.71)	2.29 (1.38)**	3.33 (1.81)**	2.93 (1.71)†	2.58 (1.68)†
WISDM Total**†	52.28 (12.46)	50.63 (12.08)**	53.67 (12.62)**	52.69 (12.21)†	49.43 (13.92)†
FTND*	5.41 (2.25)	5.62 (2.31)*	5.24 (2.18)*	5.42 (2.30)	5.40 (2.01)
TDS*†	6.45 (1.94)	6.30 (1.95)*	6.58 (1.92)*	6.51 (1.90)†	6.09 (2.13)†

Independent samples t-tests between genders:

Independent samples t-tests between ethnic groups:

* $p < .05$, the Bonferroni corrected alpha for the 22 comparisons for each dependent variable

** $p \leq .002$, the Bonferroni corrected alpha for the 22 comparisons for each dependent variable

† $p < .05$, the Bonferroni corrected alpha for the 22 comparisons for each dependent variable

‡ $p \leq .002$, the Bonferroni corrected alpha for the 22 comparisons for each dependent variable

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Table 4

Best fitting models for predicting smoking after controlling for treatment and study

		Wald	OR	p
1-week				
WISDM model: $\chi^2 = 127.19$, $p < .001$	WISDM Tolerance	18.23	1.23	< .01
	WISDM Social/Environmental Goads	4.11	1.07	.04
NDSS model: $\chi^2 = 118.16$, $p < .001$	NDSS Priority	11.14	1.24	< .01
	NDSS Stereotypy	8.85	1.23	< .01
NDSS/WISDM model: $\chi^2 = 127.19$, $p < .001$	WISDM Tolerance	18.23	1.23	< .01
	WISDM Social/Environmental Goads	4.11	1.07	.04
FTND model: $\chi^2 = 141.57$, $p < .001$	FTND	45.57	1.22	< .01
End of treatment				
WISDM model: $\chi^2 = 47.48$, $p < .001$	WISDM Tolerance	5.90	1.13	.02
	WISDM Social/Environmental Goads	7.41	1.11	< .01
NDSS model: $\chi^2 = 42.16$, $p < .001$	NDSS Priority	11.90	1.28	< .01
NDSS/WISDM model: $\chi^2 = 49.73$, $p < .001$	NDSS Priority	9.71	1.26	<.01
	WISDM Social/Environmental Goads	7.49	1.11	<.01
FTND model: $\chi^2 = 45.99$, $p < .001$	FTND	14.21	1.13	< .01
6-months				
WISDM model: $\chi^2 = 29.66$, $p < .001$	WISDM Tolerance	11.04	1.21	< .01
NDSS model: $\chi^2 = 25.20$, $p < .001$	NDSS Priority	7.78	1.28	.01
NDSS/WISDM model: $\chi^2 = 32.60$, $p < .001$	NDSS Priority	4.96	1.23	.03
	WISDM Tolerance	7.45	1.18	.01
FTND model: $\chi^2 = 32.32$, $p < .001$	FTND	22.93	1.14	< .01