Published in final edited form as:
Drug Alcohol Depend. 2007 June 15; 89(1): 42–51.

The Nicotine Dependence Syndrome Scale in Finnish Smokers

Ulla Broms, MSc[1], **Pamela A.F. Madden, PhD**[2], **Andrew C. Heath, D.Phil**[2], **Michele L. Pergadia, PhD**[2], **Saul Shiffman, PhD**[3], and **Jaakko Kaprio, MD, PhD**[1,4]

[1]*Department of Public Health, University of Helsinki, Finland* [2]*Washington University School of Medicine, St. Louis, USA* [3]*Department of Psychology, University of Pittsburgh, USA* [4]*Department of Mental Health and Alcohol Research, National Public Health Institute, Helsinki, Finland*

Abstract

The Nicotine Dependence Syndrome Scale (NDSS) is a new multidimensional measure of nicotine dependence. The study aim was to examine the structure and heritability of the NDSS and its associations with nicotine dependence defined by FTND and DSM-IV criteria among Finnish smokers participating in an ongoing twin-family study. Adult twin pairs concordant for smoking from the Finnish Twin Cohort Study, and their siblings and parents were interviewed. Among 1370 smokers, the NDSS sum score (a summary measure of dependence) correlated moderately high with FTND score (r=0.62). Subjects in the highest NDSS sum score groups were more likely to be nicotine dependent according to DSM-IV criteria compared with those in the lowest quintile (odds ratio = 36.7, 95% Confidence interval 13.0–103). In exploratory factor analysis we derived three factors, named drive/priority, stereotypy/continuity and tolerance. The drive/priority factor correlated best with FTND (r=0.54). Genetic modelling showed no differences in the genetic architecture of NDSS or FTND by gender; the overall heritability estimate for NDSS was 0.30 (95% CI 0.06–0.47), and for FTND 0.40 (95% CI 0.23–0.55)

The NDSS sum score is moderately high associated with DSM-IV nicotine dependence as well as FTND. These analyses indicate that the NDSS functions well in a Finnish family-based sample and provide additional validation of a new scale developed to capture complex behavioral features of nicotine dependence.

Keywords

Tobacco use disorders; Nicotine dependence; DSM-IV; Validity and reliability; Twin study

Corresponding author: Ulla Broms, Department of Public Health, Mannerheimintie 172, P.O.Box 41, 00014 University of Helsinki, Finland, Phone: +358-9-19127572, Fax: +358-9-19127570, E-mail: ulla.broms@helsinki.fi
Co-author and their contact information: Madden, Pamela A.F., Department of Psychiatry and Missouri Alcoholism Research Center, Washington University School of Medicine, Campus Box 8134, 660 S. Euclid Avenue, St. Louis, MO 63110 USA, Tel. +1-314-286 2286, Fax. +1-314-286 2213, Email: pam@matlock.wustl.edu
Heath, Andrew C., Department of Psychiatry and Missouri Alcoholism Research Center, Washington University School of Medicine, Campus Box 8134, 660 S. Euclid Avenue, St. Louis, MO 63110 USA, Tel. +1-314-286 2203, Fax. +1-314-286 2213, Email: andrew@matlock.wustl.edu
Michele L. Pergadia, Department of Psychiatry and Missouri Alcoholism Research Center, Washington University School of Medicine, Campus Box 8134, 660 S. Euclid Avenue, St. Louis, MO 63110 USA, Tel. +1-314-286 2270, Fax. +1-314-286 2213, Email: michelep@matlock.wustl.edu
Saul Shiffman, Department of Psychology, University of Pittsburgh, 130 N. Bellefield Avenue, Suite 510, University of Pittsburgh, Pittsburgh, PA 15260 shiffman@pinneyassociates.com
Jaakko Kaprio, Department of Public Health, P.O.Box 41, Mannerheimintie 172, 00014 University of Helsinki, Finland, Phone: +358-9-19127595, Fax: +358-9-19127600, E-mail: jaakko.kaprio@hels inki.fi

1. Introduction

Nicotine dependence is associated with heavy consumption of tobacco products, compulsive use, tolerance, regulation of intake, and withdrawal (DSM-IV, APA, 1994;Shadel et al., 2000). The cognitive-affective consequences of smoking, such as pleasure, better concentration, and better tolerance of acute stress, are thought to be rewarding and in this way reinforce the smoking habit (Balfour, 2004;Walton et al., 2001). Smoking is also thought to be conditioned to external stimuli such as environment and social context, and to internal stimuli such as stress, tiredness and hunger (Perkins, 1999;Haustein, 2003). The reward associated with nicotine use and withdrawal symptoms caused by lack of nicotine have an evident neurobiological background (Balfour, 2002), as amply confirmed in animal studies (Markou et al., 1993;Watkins et al., 2000).

In the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV, APA, 1994) dependence is determined as follows: “Diagnosis of dependence requires presence of at least three of the following during a 12-month period: tolerance, manifested by decreased effect of a given dose or increased dosing to produce the same effect, withdrawal following a period of abstinence, smoking a greater amount or a more extended period than intended, a persistent desire to smoke and unsuccessful efforts to cut down, spending considerable time obtaining or using tobacco, giving up or curtailing important social, occupational, or recreational activities because of smoking, and continued smoking despite knowledge of health risks.”

Nicotine dependence has typically been assessed either by the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV, APA, 1994) criteria or the Fagerström Test for Nicotine Dependence (FTND) (Heatherton et al., 1991). These two are widely used measures of nicotine dependence. These measurements do not comprehensively cover all aspects of nicotine dependence, in part, because DSM-IV substance dependence criteria, which are loosely based on Edward and Gross’ (1976) model of the dependence syndrome are broadly applied to all substances with the exception of substance-specific withdrawal criteria. There is a need for self-report measures that capture the different dimensions specific to nicotine dependence more extensively. Shiffman and his colleagues developed and recently published (Shiffman et al., 2004) a new multidimensional measure specifically targeted for nicotine dependence, the Nicotine Dependence Syndrome Scale (NDSS). The NDSS questionnaire items were generated based on the concepts in the Edwards and Gross (1976) model of the alcohol dependence syndrome, but applied to cigarette smoking. The NDSS assesses five separate aspects of nicotine dependence: drive, priority, tolerance, continuity, and stereotypy, in addition providing a total item score of nicotine dependence; Shiffman (2004) found that 19 items formed a concise scale with five subscales. Fourteen items out of these 19 were selected as the best overall predictors of nicotine dependence and Shiffman (2004) provided scoring weights to enable computation of the NDSS T-score, a global measure of nicotine dependence.

Earlier studies on the NDSS have found 5 subscales among adult heavy smokers recruited from a smoking cessation clinic (n=317) (Shiffman et al., 2004); but, only four subscales among a sample of adolescent cigarette smokers recruited from the community and from alcohol use disorder and hospital psychiatric treatment programs (n=301) (Clark et al., 2005). In a study of young adult light (chippers, n=123, five or fewer cigarettes per day) and heavy smokers (n=130, smoking more than 20 cigarettes per day), Shiffman and Sayette (2005) found that each of the five factors derived in the original study (Shiffman et al., 2004) clearly discriminated the groups. These three studies to date suggest that the composition and smoking behaviour of the study samples may affect the factor structure of NDSS; moreover, the factor structure and functioning of NDSS has not been tested outside the U.S.A.

Genetic influences on nicotine dependence are documented in many twin studies using DSM-IV and III-R criteria (APA, 1994) and Fagerström's questionnaires (FTQ and FTND). In studies on nicotine dependence measured by DSM-III-R, the heritability estimate in US boys and girls was 0.44 (McGue et al., 2000) and among US male veterans 0.60 (True et al., 1999). Using a measure of DSM-IV nicotine dependence in a population of Australian men and women, heritability was estimated to be 0.56 (Lessov et al., 2004). Using FTQ, heritability was estimated at 0.62 among US men and women (Maes et al., 2004) and at 0.72 in a separate sample of US women (Kendler et al., 1999). In a recent study of FTND, heritability was estimated at 0.75 among Dutch men and women (Vink et al., 2005).

The aim of this study was to examine the performance of the NDSS among smokers in Finland as well as to examine how it correlates with the FTND and DSM-IV nicotine dependence among regular smokers. Furthermore we aimed to examine the effect of genetic and environmental factors on nicotine dependence measured by NDSS.

2. Methods

2.1. Participants

The data comes from the "Genetics of Vulnerability to Nicotine Addiction", an ongoing twin-family study of cigarette smoking and nicotine addiction. The study has been approved by the Ethics committee for research in epidemiology and public health of the Hospital District of Helsinki and Uusimaa on February 28th, 2001 (136/E3/2001) and followed the rules and principles of the Helsinki Declaration.

Twin pairs concordant for cigarette smoking, in which at least one twin smoked 10 or more cigarettes daily in at least one survey, were identified based on earlier questionnaires in 1975, 1981 and 1990 (for same sex pairs) and during 1996–1997 (for opposite sex pairs) of the Finnish Twin Cohort Study (Kaprio and Koskenvuo, 2002). Siblings and parents of the adult twins were also recruited and interviewed by telephone using a structured interview including the FTND and assessment of DSM-IV criteria. The diagnostic interview was based on the SSAGA (Semi-Structured Assessment for the Genetics of Alcoholism) (Bucholtz et al., 1994) with the section on nicotine use and dependence on the CIDI (The Composite International Diagnostic Interview) (Cottler et al. 1991). Subjects filled out a questionnaire with the NDSS scale (31 items) some weeks after the interview. Data were collected between October 2001 and January 2005. Ninety per cent of interviewed persons returned the questionnaire. At the time of analysis there were 1385 current (47%) or former (53%) cigarette smokers who returned the NDSS questionnaire. We carried out analyses on 1370 ever smokers who were interviewed and responded to questions on the nicotine dependence scales (NDSS, FTND and DSM-IV). Sixty nine per cent (n=942) of them were twins and the rest of them were siblings and parents of the twins coming from 601 families. Respondents' mean age was 55 years (SD 6.7, 10^{th} percentile was 47 years and 90^{th} percentile 62 years) and there were more men (63%) than women. Nicotine dependence of participants measured by FTND was 3.8 (SD 2.3) and number of DSM-IV symptoms was 3.0 (SD 1.7). Participants smoked on average 20.0 cigarettes per day (SD 10.2), among current smokers average number of cigarettes per day was 21 (SD 9.8). The mean of maximum number of cigarettes smoked in a 24 hour period was 30.2 (SD 14.7). Participants replied well to the questionnaire with low rates of missing values in individual items so that 85% (n=1160) replied to all NDSS items. Persons who had never smoked more than 100 cigarettes during their lifetime were skipped out of NDSS. In quantitative genetic modeling there were 65 monozygotic (MZ), 129 dizygotic (DZ) and 97 opposite-sex pairs where both twins had replied to the NDSS questionnaire and their NDSS score could be computed.

2.2. Interview and Questionnaire

Twins, their siblings and parents were interviewed by telephone using a structured interview including the FTND and DSM-IV. The questionnaire was sent to those participants who were interviewed and/or had given their blood samples and returned the consent form. The questionnaire included a 31 item version of NDSS. Each item/statement is answered on a 5-point likert scale ranging from 1 (Not at all true) to 5 (Extremely true). After two to three months at the most, a reminder, including a new questionnaire, was mailed to those who hadn't returned the questionnaire.

We translated the English version of the NDSS to Finnish and then an official translator back-translated it in English. We checked the translation and correspondence between the English back-translation and the original version. The translations were similar. Prior to going into the field, minor linguistic corrections were done to the Finnish version to make it more readable to subjects.

In Shiffman et al. (2004) there were five items which were not used for the NDSS T-score computation (see below). These were items 7, 9, 14 in the scale we used (Table 1) plus two other items. The questionnaire we used had three additional items included that did not survive in more recent versions of the NDSS (Shiffman et al. 2004) (items 7, 29 and 30, Table 1 of the present study).

2.3. Statistical analyses

We carried out an exploratory factor analyses using maximum likelihood to examine the factor structure. Both oblique and varimax rotation was used, the latter to obtain uncorrelated factors, following Shiffman et al. (2004). We also used confirmatory factor analysis (CFA) based on the five-factor solution from Shiffman et al. (2004) to test for the factorial stability of the NDSS in our sample.

We scored the NDSS T-score of dependence based on 14 items using the regression-based scoring procedure in the appendix of Shiffman et al. (2004). Shiffman and his colleagues (2004) created NDSS-T because in their study, a principal component analysis indicated a strong first component; this became an omnibus summary measure and was named NDSS-T (for total). NDSS-T estimates based on weights derived from Shiffman et al's (2004) sample and from the present sample correlated almost perfectly, at 0.99. Accordingly, for consistency, we used the scoring algorithm described by Shiffman et al (2004). Those participants who had missed more than two items out of the 14 items belonging to the NDSS-T (5 %, n= 68) were excluded from the analysis. For those with one or two missing values were replaced by the mean value of the subject's other items, before the final score was calculated. We used Cronbach's alpha to examine internal consistency of the items belonging to the NDSS-T.

To increase the interpretability of the NDSS responses of individual subjects and future comparability of studies based on the NDSS, we also created a sum score of the item responses to the 14 key items from NDSS. The theoretical range of scores was from 14 to 70.

We also examined the test-retest reliability of the full NDSS by mailing the instrument to two hundred randomly selected recent respondents (both smokers and ex-smokers) without any other selection criteria, and who had replied consecutively (i.e. those last 200 who had returned the first questionnaire they completed) during the spring of 2005. The retest mailing was done in the summer of 2005 with an average time difference in response of 4.7 months (SD 1.6 months). There were 159 respondents and the response rate was 79.5%. The NDSS T-score was computed for the 128 subjects who completed at least 12 out of 14 items. Of those 128, 125 also had NDSS-T in the original (i.e. first) questionnaire.

The FTND was developed as a self-administered paper and pen questionnaire (points from 0, no dependence, to 10, high dependence). In the present study FTND was assessed by the telephone interview alongside other smoking related questions. DSM-IV criteria were also assessed in the interview, and the number of positive symptoms (0 to 7), were used as a measure of degree of nicotine dependence. Those with three symptoms during the same twelve month period fulfill the diagnosis of nicotine dependence in DSM-IV.

We also used other measures of cigarette smoking including (1) number of cigarettes smoked per day during heaviest period of smoking, and (2) maximum amount of cigarettes smoked in a 24-hour period when we examined the correlations of factors and the sum score.

In the analysis of linear and logistic regression we computed robust estimators of variance and used the clustering option in Stata (Williams, 2000) to control for possible lack of independence of observations of subjects who came from the same family. Linear and logistic regression modeling was used to analyze how NDSS subscales predicted FTND and DSM-IV nicotine dependence.

The heritability of nicotine dependence measured by the NDSS was analyzed by using quantitative genetic methods based on linear structural modeling. Twin modeling is based on the assumption that MZ twins are genetically identical whereas DZ twins share on average 50% of their segregating genes. Thus, a greater similarity for MZ twins compared with DZ twins gives support to the hypothesis that genetic transmission is a component of importance, under the assumption that MZ and DZ share to the same extent their trait-relevant environmental experiences (Boomsma et al., 2002). Environmental factors are divided into those shared by a twin pair (shared environment) and factors unique to each twin individual (unique environmental effects), which also includes measurement error. The correlations for the shared environmental factors are one and for unique environmental factors 0 within both MZ and DZ twin pairs. Heritability refers to the total part of the phenotypic variance attributable to genetic influences, and comprises both additive effects of individual alleles at loci influencing a particular phenotype, and non-additive effects, reflecting interactions between alleles at the same locus (dominance) or between alleles across loci (epistasis). We estimated the proportions of trait variance accounted for by additive genetic factors (A), by shared environmental factors (C) and by factors not shared (unique) with the co-twins (E), so called ACE-model. ADE-model which includes the non-additive genetic component (D) is fit only when the ratio of MZ to DZ correlation exceeds 2.0 (Plomin et al., 1992).

Because we had information on both male and female like-sexed MZ and DZ pairs as well as male-female (opposite-sex) DZ pairs, we could test whether the genetic effects on NDSS and FTND were of the same magnitude in men and women, and whether the genetic effects in men were the same as in women (even if of different magnitude) using sex-limitation models (Neale and Cardon, 1992).

The ACE sex-limitation model was selected as a starting point of the modeling based on twin correlations. Full model was fitted including ACE effects for nicotine dependence and the correlations between the genetic and environmental components affecting that phenotype. We used Stata statistical software, version 9.0 and the Mx-statistical package (Neale MC et al., 2003) for statistical analyses and genetic modeling.

3. Results

3.1. Factor structure

We used factor analysis with varimax rotation to explore multifactor solutions (Table 1). A three-factor solution produced interpretable factors with eigenvalues greater than one, and the common variance among the items was 93%.. Loadings over 0.3 are shown in Table 1.

The first factor was named ‘drive/priority’. It had sixteen items with loading values 0.40 or above, eigenvalue was 10.4, and the common variance among the items was 74%. Highest loadings were items which described smoking drive i.e. urge to smoke as follow: “After not smoking for a while, I need to smoke to relieve feelings of restless and irritability” (item loading= 0.68) and to keep away from uncomfortable symptoms: “After not smoking for a while, I need to smoke in order to keep myself from experiencing any discomfort” (0.72). Priority means that smoking is valued over other competing reinforces as follows: “I tend to avoid restaurants that don’t allow smoking, even if I would otherwise enjoy the food” (0.50). The Cronbach’s alpha for the sum scale based on the 16 items was 0.92.

The second factor was named ‘continuity/stereotypy’. The factor had eight items with loading values 0.40 or above, eigenvalue was 1.5, and the common variance among the items was 11%. Items included continuously smoking with little interruption and a fixed pattern of smoking. The following items had highest loading values: “My cigarette smoking is fairly regular throughout the day” (item loading= 0.74) and “I smoke about the same amount on weekends as on weekdays” (0.66). The Cronbach’s alpha for the sum scale based on the seven items was 0.88.

The third factor was named ‘tolerance’. The third factor had six items with factor loadings of 0.40 or above, eigenvalue was 1.1, and the common variance among the items was 8%. This factor described smoking an increasing amount of cigarettes per day compared when he/she started to smoke. For example: “Compared to when I first started smoking, I can smoke much, much more now before I start to feel nauseated or ill” (item loading= 0.68) and “Compared to when I first started smoking I need to smoke a lot more now in order to get what I really want out of it” (0.63). The Cronbach’s alpha for this scale based on the six items was 0.83.

The factor structure was derived from using all observations. To test for the possibility that the interdependence of family members may be affecting the factor structure, we ran the factor analysis so that there was only one person per family. The factor structure and sum scale alpha values were virtually the same as in the original analysis. Also, the factor structure and sum scale alpha values in the sample consisting of current smokers only (i.e., omitting ex-smokers) were virtually the same as in the original analysis. We also carried out an oblique rotation and it gave similar result than the varimax rotation. The varimax and the oblique factors correlated also highly with each other (correlations of factors were 0.92, 0.97 and 0.91, respectively).

We also tested the five factor solution presented by Shiffman et al. (2004) by CFA. Using data including only one person in the family (n=559), we found that the five factor model had comparative fit index of 0.89 and a root mean square error of approximation of 0.08. These results are somewhat below commonly-accepted standards for a well fitting model. (Byrne, 2001).

In our sample the NDSS-T was normally distributed. The overall mean was −0.85 with standard deviation of 1.19. The NDSS sum score had a mean of 35.2, standard deviation of 10.9, with an observed range from 14 to 70. For some analyses we categorized the sum score into five categories (14–24, 25–32, 33–41, 42–54, 55–70 sum score values).

3.2. Test-retest reliability

In the retest sample the mean age of ever smoked responders was 55 years (SD 6.3, range 37–75) and 78% of them were men. The mean age, sex distribution and the initial NDSS-T of responders and non-responders did not differ. No significant mean differences emerged when the NDSS-T of the initial and the repeated questionnaires were tested by paired t-test, either overall or stratified by sex or a median split on age. The test-retest correlation for NDSS-T was 0.76 (95% CI 0.69–0.82).

3.3. Correlation with other measures of dependence

We examined the strength of the association of the five NDSS sum score categories with a diagnosis of DSM-IV nicotine dependence using logistic regression. The age-sex adjusted odds ratios of DSM-IV dependence increased linearly up to 36.7 (95% CI 13.0–103) for the fifth group of the sum score (Table 2) compared to a reference risk of 1.0 for the first group (sum score under 25); the fifth group (sum score 55–70) contained however less than 5 percent of smokers. Age was a significant predictor of dependence such that older participants were not as dependent as younger ones. However, sex was not a significant predictor of dependence. The interaction of sex and the sum score on DSM-IV nicotine dependence was non-significant ($p= 0.075$) in the logistic model.

Table 3 shows the correlations of different measurements with the sum score and three factors. The FTND correlated moderately high ($r=0.62$) with the sum score and the first factor, drive/priority ($r=0.54$) as did also the DSM-IV symptom score. Also the other measurements correlated moderately with sum score and the first factor ($r=0.73$). The other two factors of the NDSS (stereotypy/continuity and tolerance) showed only weak correlations with the other measures. In all cases, as expected, the highest correlations were seen for the sum score. The correlation was also high between FTND and number of DSM-IV symptoms ($r=0.59$), between "Quantity of cigarettes smoked per day during period of heaviest smoking" and FTND ($r=0.71$) and DSM-IV ($r=0.55$) and also between "Maximum cigarettes smoked in a 24 hour period" and FTND ($r=0.59$) and DSM-IV ($r=0.54$).

We entered the three factors both singly (unadjusted) and jointly (adjusted) into regression models for FTND nicotine dependence and DSM-IV nicotine dependence. Linear regression analyses of FTND (Table 4) showed that the first factor (drive/priority, β 1.41, 95% CI 1.28–1.53, R^2=33%) had the highest association with FTND nicotine dependence, while the second factor (stereotypy/continuity, β 0.92, 95% CI 0.78–1.06, R^2=16%) and the third factor (tolerance, β 0.79, 95% CI 0.63–0.95, R^2=13%) were less strongly associated. When modelled jointly the three factors accounted for 46 % of FTND nicotine dependence variance and β-values were about the same as in single model (β 1.25, 0.76, 0.60, respectively), as would be expected from orthogonal factor scores. Logistic regression analyses (Table 5) showed that all three factors were strongly associated with DSM-IV nicotine dependence. The ORs for the factors when entered jointly were only slightly less than when entered individually. In models predicting both the FTND and DSM-IV scores, all three NDSS factors demonstrated significant associations, indicating that each contributes unique variance to the association with other measures of dependence.

3.4. Genetic modeling of NDSS

We identified 291 pairs of smokers with the NDSS sum score. Among the 65 monozygotic (MZ), 129 same-sex dizygotic (SSDZ) and 97 opposite-sex pairs (OSDZ), the correlation for the sum score was 0.41 in MZ male pairs, 0.22 in same sex DZ male pairs, 0.34 in MZ female pairs, −0.09 in DZ female pairs and −0.08 in opposite sex pairs (Table 6). The greater correlations in MZ compared to DZ pairs is evidence for genetic influences. Genetic sex-limitation modeling showed no differences in the genetic architecture of the NDSS between

men and women (p=0.64). After starting with an ACE-model, the common environment (C) effect could be dropped from the model and thus an AE-model fit the data best. Additive genetic variance was 0.30 (95% CI 0.06–0.47) and non-shared environmental variance 0.70 (95% CI 0.53–0.89) for NDSS sum score. Due to a different pattern of correlations (Table 6) among women we also tested an ADE-model and dropped dominance (D) effect from the model. The AE-model was again the best fitting model.

Genetic sex-limitation modeling showed no differences in the genetic architecture of the second and third factors (sub-scores) between regularly smoking men and women (no evidence for sex-specific genetic effects). The best model for second stereotypy/continuity (heritability [h^2]=0.44, 95% CI 0.21, 0.61) and for third tolerance factor (h^2=0.39, 95% CI 0.18, 0.56) was an AE-model. For the first drive/priority factor the best fitting model for men was a CE-model (common environment was 0.22, 95% CI 0.05–0.37) and for women an E-model. Thus, for the first drive/priority factor no significant genetic effects were detected.

For FTND, the pairwise correlations are given in Table 6. A genetic model with additive genetic effects and unshared environmental effects fitted the best, with a heritability estimate of h^2=0.40, 95% CI 0.23, 0.55) with no evidence for sex-specific genetic effects. The correlations for DSM symptom count were small and did not differ between MZ and DZ pairs (male MZ 0.16, male DZ 0.27, female MZ −0.02, female DZ −0.15, opposite-sex pairs 0.08), and genetic modeling was not possible.

4. Discussion

These results show that sum score is moderately high associated with nicotine dependence as defined by the FTND and DSM-IV measures and the NDSS functions well among Finnish adult smokers. The NDSS was developed to assess multiple dimensions derived from a contemporary conceptualization of nicotine dependence constructs (Shiffman et al., 2004;Clark et al., 2005). The factor analysis of the present study indicates that a three-factor structure was optimal for these data, while a confirmatory factor analysis indicated relatively poor fit of our data to the five factor solution from Shiffman's original 2004 paper.

Whereas Shiffman's (Shiffman et al., 2004) data on heavy treatment-seeking smokers indicated that drive and priority were separate factors, in the present study, with a larger and more representative sample of Finnish smokers, these items and constructs comprised a single factor. Similarly, our factor analysis found the stereotypy and continuity factors to emerge as a single factor, while they were distinct in Shiffman et al's (2004) analysis. The latter could have been due, in part, to the absence in our questionnaire of two items that loaded heavily on continuity subscale in Shiffman et al's 2004 scale. The third subscale, tolerance, was seen consistently in both our study and Shiffman's (2004) original study of the NDSS. An earlier study that also attempted to factor analyze a 27-item NDSS (Clark et al., 2005) among young smokers also reported some merger of factors, but in this instance it was drive and tolerance that merged into a single first factor. This suggests that the composition and smoking behaviour of the study samples may give different factor structures of the NDSS. Differences in the number of subscales might be due to different sample sizes, population heterogeneity, different degrees of nicotine dependence of participants and differences in age distribution. In the present study participants were older than Clark's (Clark et al., 2005) and Shiffman's (Shiffman et al, 2004;Shiffman and Sayette, 2005) studies and likely to have more extensive smoking histories.

Our recently collected data is based on earlier collected (years 1975years 1981years 1990 or 1996–1997) population-based data, including twin pairs which both co-twins were current or former smokers. We selected twin pairs based on earlier self-reports of smoking in questionnaires ten to thirty years earlier than the current interview/questionnaire assessment

of NDSS nicotine dependence. Earlier studies on NDSS are mostly clinical samples, and our sample size is larger than in earlier NDSS studies. For these and other reasons, it is not surprising that we do not observe a similar factor structure as in other studies. It is also possible that despite careful translation and back-translation of the NDSS items, linguistic and cultural differences may also play a role. In any case, the analysis suggest that the factor structure reported by Shiffman et al. (2004) on US adult sample of heavy smokers seeking treatment may not be applicable across populations. Further studies in randomly selected population samples of smokers are needed.

Overall, the instrument worked quite similarly in Finland as in the U.S.A. Thus, NDSS-T reliability (Cronbach's alpha) for 14 items was 0.89 in the Finnish data compared with 0.86 in U.S.A. as reported by Shiffman (2004), indicating a good internal reliability of Finnish scale. Also scoring weights were similar even though the data were different; correlation between the NDSS-T using Shiffman's (2004) scoring weights and using scoring weights based on the factor analysis of the present data was 0.99. The sum scale based on 14 items provides an easily computable score of overall nicotine dependence, which differentiated well persons with low and high risk of nicotine dependence when assessed against DSM-IV criteria.

The NDSS sum score correlated highly with two established measures of nicotine dependence, FTND and DSM-IV. The subscale drive/priority correlated higher with FTND and DSM-IV than the other two subscales (stereotypy/continuity and tolerance) do. DSM-IV nicotine dependence is based on Edwards and Gross's (1976) construct of an alcohol dependence syndrome including persistence in the face of harm, salience and so on. DSM diagnoses have been shown to be associated with heavier smoking and to predict persistence of smoking (Breslau et al., 2001) as well as co-morbidity with depression (Breslau and Johnson, 2000). The problem is that DSM criteria are not specifically tailored to nicotine dependence. Studies comparing the Fagerström scales with DSM diagnoses have reported that DSM (III-R) defined nicotine dependence and the FTND show relatively little overlap. These measures assess different aspects of nicotine dependence (Breslau and Johnson, 2000;Moolchan et al., 2002) and suggest that dependence may be multidimensional.

FTND incorporates smoking rate into itself, whereas NDSS does not. This might be a crucial distinction between FTND and NDSS as well as between FTND and DSM-IV, though many other differences in component items exist. FTND, DSM-IV and the NDSS in part measure different aspects of dependence, and FTND and DSM-IV have generally been viewed as unidimensional compared to NDSS which has several, up to five dimensions; but this might be due to the limited number of items/symptoms in FTND and DSM-IV.

Earlier family and adoption studies support the finding of genetic influence on smoking behavior (Osler et al., 2001;Goode et al., 2003). While the heritability of dependence can only be assessed among persons who have smoked, heritability of initiation of smoking can be assessed among all persons in the population. This is generally the case in recent studies (Kendler et al., 1999;Lessov et al., 2004;Maes et al., 2004;Vink et al., 2005). Genetic two stage modeling permits inclusion of information from never smokers to the analysis (Heath et al., 2002;Broms et al., 2006) and to assess to what degree genetic influences on smoking initiation are the same as those on dependence. Earlier genetic studies on nicotine dependence have shown fairly high heritability estimates by different measurements varying from 0.44 to 0.75 (Kendler et al., 1999;True et al., 1999;McGue et al., 2000;Lessov et al., 2004;Maes et al., 2004;Vink et al., 2005). Heritability of NDSS sum score was 0.30 in our sample of twins, being higher in the second (stereotypy/continuity, h2=0.44) and third (tolerance, h2=0.39) subscale factors. In genetic modelling, the AE-model fit the data best for overall score, and the second and third factors. Somewhat unexpectedly, we were unable to detect genetic effects on the first (drive/priority) factor, for which the CE-model for men and E-model for women fitted best;

the correlations for MZ and DZ pairs were almost identical. This is quite surprising, and suggests that the core dependence symptoms of craving, withdrawal, and excess priority given to use may be less heritable than more peripheral factors such as escalation in use and continuity of use. This surprising finding seems at odds with the estimated heritability of the FTQ (Kendler at al., 1999;Maes et al, 2004) and our finding of FTND with 40% heritability, and would need to be replicated before being accepted. Interestingly the Lessov and her colleagues (2004) study did find genetic effects on many DSM items that are similar to the drive/priority factor. We could not analyse DSM-IV based nicotine dependence due to the limited number of twin pairs; the power of the twin study for binary traits is much lower than for continuous traits (Neale and Miller, 1997).

Given the relatively modest sample size of twins, and in particular the small number of female pairs, the power to detect either common environmental effects or non-additive effects was not very large. Our data include opposite sex twin pairs, and thus we were able to examine sex limitation effects in the heritability of smoking behavior. We did not find evidence for sex differences, but the power to detect sex-specific effects was limited. Hence, it is possible that in larger samples, such effects will be detected in future studies of NDSS. However, other twin studies of nicotine dependence generally have not shown such effects, and the AE model has been the optimal model also in those (Kendler et al., 1999;True et al., 1999;Lessov et al., 2004;Vink et al., 2005). The variation of heritability is not surprising taking into account that the role of genetic factors varies with population, time and place (Kendler et al., 1999).

The present study used a population based sample of smoking families and is generalizable to the Finnish smoking population. The measures examined in the study were self-report assessments using standardized instruments, not clinical tests. However, the internal consistency and test-retest reliability of NDSS were good. While the relationship between NDSS and FTND nicotine dependence has been previously examined (Shiffman et al., 2004;Shiffman et al., 2004; Clark et al., 2004), the association between the NDSS and DSM-IV nicotine dependence was not investigated in earlier reports.

The subjects in the study were mostly middle aged and older, so they have long history of smoking and their smoking behavior might be relatively well established. Only 10 percent of subjects are aged 47 or less, and only 25% under 51 years of age. Smokers in the present study are also the survivors as in this age range, smokers are starting to die off differentially. Furthermore they come from a cohort that started smoking when smoking was more normative and also when cigarettes were “stronger”. Age was significant predictor of dependence such that older participants were not as dependent as younger ones. However, sex was not significant predictor of dependence. It was shown that genetic factors influence individual differences in NDSS-defined nicotine dependence and these genes are probably the same among men and women.

Acknowledgements

The study has been funded by Doctoral Programs of Public Health, University of Helsinki, Finland (to U.B.) and the GenomEUtwin project (European Union Contract No. QLG2-CT-2002-01254). Data collection was supported by a NIH grant DA12854 to P.A.F. Madden and by Academy of Finland grants to J. Kaprio and M. Koskenvuo. This study forms part of the Academy of Finland Centre of Excellence in Complex Disease Genetics. M.L. Pergadia has been supported by NIH grant DA019951. We would like to thank the participating families for their patience and contribution. We acknowledge the contribution of the study interviewers A. Häppölä, A-M. Iivonen, K. Karhu, H-M. Kuha, U. Kulmala-Gråhn, M. Mantere, K. Saanakorpi, M. Saarinen, R. Sipilä, L. Viljanen, and E. Voipio. We thank K. Heikkilä and M. Siivola for data management.

References

American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders. 4. Washington DC: 1994.

Balfour DJK. The Neurobiology of tobacco dependence: a commentary. Respiration 2002;6:7–11. [PubMed: 11844955]

Balfour DJK. The neurobiology of tobacco dependence: A preclinical perspective on the role of the dopamine projections to the nucleus. Nicotine Tob Res 2004;6:899–912. [PubMed: 15801566]

Boomsma D, Busjahn A, Peltonen L. Classical twin studies and beyond. Nat Rev Genet 2002;3:872–882. [PubMed: 12415317]

Breslau N, Johnson EO. Predicting smoking cessation and major depression in nicotine-dependent smokers. Am J Public Health 2000;90:1122–1127. [PubMed: 10897192]

Breslau N, Johnson EO, Hiripi E, Kessler R. Nicotine dependence in the United States – Prevalence, trends, and smoking persistence. Arch Gen Psych 2001;58:810–816.

Broms U, Silventoinen K, Madden PA, Heath AC, Kaprio J. Genetic architecture of smoking behavior: a study of Finnish adult twins. Twin Res Hum Genet 2006;9:64–72. [PubMed: 16611469]

Bucholtz KK, Cadoret R, Cloninger CR, Dinwiddie SH, Hesselbrock VM, Nurnberger JI Jr, Reich T, Schmidt I, Schuckit MA. A new, semi-structured psychiatric interview for use in genetic linkage studies: A report on the reliability of the SSAGA. J Studies Alcohol 1994;55:149–158.

Byrne, BM. Basic Concepts, Applications, and Programming, Multivariate Applications series. Lawrence Erlbaum Associates; Mahwah, New Jersey: 2001. Structural Equation Modeling with AMOS.

Clark DB, Wood DS, Martin CS, Cornelius JR, Lynch KG, Shiffman S. Multidimensional assessment of nicotine dependence in adolescents. Drug Alcohol Depend 2005;77:235–242. [PubMed: 15734223]

Cottler LB, Robins LN, Grant BF, Blaine J, Towle LH, Wittchen HU, Sartorius N. The CIDI-core substance abuse and dependence questions: cross-cultural and nosological issues. The WHO/ADAMHA field trial Br J Psychiatry 1991;159:653–658.

Edwards G, Gross MM. Alcohol dependence: Provisional description of a clinical syndrome. BMJ 1976;1:1058–1061. [PubMed: 773501]

Goode EL, Badzioch MD, Kim H, Gagnon F, Rozek LS, Edwards KL, Jarvik GP. Framingham Heart Study. Multiple genome-wide analyses of smoking behavior in the Framingham Heart Study. BMC Genet 2003;31(Suppl 1):S102. [PubMed: 14975170]

Haustein, K-O. Tobacco or health: physiological and social damages caused by tobacco smoking. Berlin: Springer-Verlag; 2003.

Heath AC, Martin NG, Lynskey MT, Todorov AA, Madden PAF. Estimating Two-Stage Models for Genetic Influences on Alcohol, Tobacco or Drug Use Initiation and Dependence Vulnerability in Twin and Family Data. Twin Res 2002;5:113–124. [PubMed: 11931689]

Heatherton TF, Kozlowski LT, Frecker RC, Fagerström KO. The Fagerström Test for Nicotine Dependence: A revision of the Fagerström Tolerance Questionnaire. Br J Addict 1991;86:1119–1127. [PubMed: 1932883]

Heatherton TF, Kozlowski LT, Frecker RC, Rickert WS, Robinson J. Measuring the heaviness of smoking using self-reported time to the first cigarette of the day and number of cigarettes smoked per day. Br J Addict 1989;84:791–800. [PubMed: 2758152]

ICD-10 Classification of Mental and Behavioural Disorders. World Health Organization; Geneva: 1992.

Kaprio J, Koskenvuo M. Genetic and environmental factors in complex diseases. Twin Res 2002;5:358–365. [PubMed: 12537859]

Kendler KS, Neale MC, Sullivan P, Corey LA, Gardner CO, Prescott CA. A population-based twin study in women of smoking initiation and nicotine dependence. Psychol Med 1999;29:299–308. [PubMed: 10218922]

Lessov CN, Martin NG, Statham DJ, Todorov AA, Slutske WS, Bucholz KK, Heath AC, Madden PA. Defining nicotine dependence for genetic research: evidence from Australian twins. Psychol Med 2004;34:865–879. [PubMed: 15500307]

Maes HH, Sullivan PF, Bulik CM, Neale MC, Prescott CA, Eaves LJ, Kendler KS. A twin study of genetic and environmental influences on tobacco initiation, regular tobacco use and nicotine dependence. Psychol Med 2004;34:1251–1261. [PubMed: 15697051]

Markou A, Weiss F, Gold LH, Caine SB, Schulteis G, Koob GF. Animal models of drug craving. Psychopharmacology (Berlin) 1993;122:163–182. [PubMed: 7871016]

McGue M, Elkins I, Iacono WG. Genetic and environmental influences on adolescent substance use and abuse. Am J Med Genet 2000;96:671–677. [PubMed: 11054776]

Moolchan ET, Radzius A, Epstein DH, Uhl G, Gorelick DA, Cadet JL, Henningfield JE. The Fagerström Test for Nicotine Dependence and the Diagnostic Interview Schedule – Do they diagnose the same smokers? Addict Behav 2002;27:101–113. [PubMed: 11800217]

Neale, MC.; Boker, SM.; Xie, G.; Maes, HH. Virginia Institute for Psychiatric and Behavioral Genetics. 6. Virginia Commonwealth University, Deparment of Psychiatry; Richmond, VA: 2003. Mx: Statistical modelling.

Neale, MC.; Cardon, LR. NATO ASI Series. Series D: Behavioral and Social Sciences. 67. Kluwer Academic Publichers; Dordrecht: 1992. Methodology for Genetic Studies of Twin and Families.

Neale MC, Miller MB. The use of likelihood-based confidence intervals in genetic models. Behav Genet 1997;27:113–120. [PubMed: 9145549]

Osler M, Holst C, Prescott E, Sorensen TIA. Influence of genes and family environment on adult smoking behavior assessed in an adoption study. Genet Epidemiol 2001;21:193–200. [PubMed: 11668576]

Perkins KA. Tobacco smoking is a ‘dependence’, not a ‘habit’. Nicotine Tob Res 1999;1:127–128. [PubMed: 11072393]

Plomin, R.; Chipuer, HM.; Loehlin, JC. Behavioral genetic and personality. In: Pervin, LA., editor. Handbook of personality theory and research. New York: Guildford; 1992.

Shadel WG, Shiffman S, Niaura R, Nichter M, Abrams D. Current models of nicotine dependence: what is known and what is needed to advance understanding of tobacco etiology among youth. Drug Alcohol Depend 2000;59 (Suppl 1):S9–S22. [PubMed: 10773435]

Shiffman S, Sayette MA. Validation of the nicotine dependence syndrome scale (NDSS): a criterion-group design contrasting chippers and regular smokers. Drug Alcohol Depend 2005;79:45–52. [PubMed: 15943943]

Shiffman S, Waters AJ, Hickcox M. The Nicotine Dependence Syndrome Scale: A multidimensional measure of nicotine dependence. Nicotine Tob Res 2004;6:327–348. [PubMed: 15203807]

True WR, Xian H, Scherrer JF, Madden PAF, Bucholz KK, Heath AC, Eisen SA, Lyons MJ, Goldberg J, Tsuang M. Common Genetic Vulnerability for Nicotine and Alcohol Dependence in Men. Arch Gen Psychiatry 1999;56:655–661. [PubMed: 10401514]

Walton R, Johnstone E, Munafo M, Neville M, Griffiths S. Genetic clues to the molecular basis of tobacco addiction and progress towards personalized therapy. Trends Mol Med 2001;7:70–76. [PubMed: 11286758]

Watkins SS, Koob GF, Markou A. Neural mechanisms underlying nicotine addiction: acute positive reinforcement and withdrawal. Nicotine Tob Res 2000;2:19–37. [PubMed: 11072438]

William RL. A note on robust variance estimation for cluster-correlated data. Biometrics 2000;56:645–646. [PubMed: 10877330]

Vink JM, Willemsen G, Boomsma DI. Heritability of smoking initiation and nicotine dependence. Behav Genet 2005;35:397–406. [PubMed: 15971021]

Table 1

Nicotine Dependence Syndrome Scale (NDSS) factor structure (N=1160 smokers)

Questionnaire item		Mean	(SD)	3-factor solution			Single factor solution
				Drive/ Priority	Stereotypy/ Continuity	Tolerance	
1 (1)	After not smoking for a while, I need to smoke to relive feelings of restlessness and irritability	2.35	(1.23)	**0.68**	0.32		**0.75**
2 (2)	Whenever I go without a smoke for few hours, I experience craving.	2.87	(1.33)	**0.58**	**0.51**	0.32	**0.83**
3 (3)	After not smoking for a while, I need to smoke in order to keep myself from experiencing any discomfort.	2.07	(1.17)	**0.72**			**0.75**
4 (4)	When I'm really craving a cigarette, it feels like I'm in the grip of some unknown force that I cannot control.	2.05	(1.23)	**0.65**			**0.63**
5 (5)	I feel a sense of control over my smoking. I can "take or leave it" at any time.	2.19	(1.38)	−0.40			**−0.55**
6 (6)	I tend to avoid restaurants that don't allow smoking, even if I would otherwise enjoy the food.	1.71	(1.13)	**0.50**			0.47
7 (7)	Sometimes, I decline offers to visit with my non-smoking friends because I know I'll feel uncomfortable if I smoke.	1.28	(0.71)	0.43			
8 (8)	Even if travelling a long distance, I'd rather not travel by airplane because I wouldn't be allowed to smoke.	1.48	(0.93)	**0.50**			0.45
9 (9)	Since the time when I became a regular smoker, the amount I smoke has either stayed the same or has decreased somewhat.	2.48	(1.32)			−0.44	
10 (10)	Compared to when I first started smoking, I need to smoke a lot more now in order to get what I really want out of it.	2.00	(1.21)	0.42		**0.63**	**0.68**
11 (11)	Compared to when I first started to smoking, I can smoke much, much more now before I start to feel nauseated or ill.	2.69	(1.43)	0.32		**0.68**	**0.67**
12 (12)	It's hard to estimate how many cigarettes I smoke per day because the number often changes.	2.23	(1.18)				
13 (15)	I smoke at different rates in different situations.	3.06	(1.25)			0.33	
14 (16)	My smoking is not much affected by other things. I smoke about the same amount whether I'm relaxed or working, happy or sad, alone or with others, etc.	2.84	(1.18)		0.43		
15 (17)	My cigarette smoking is fairly regular throughout the day.	2.95	(1.33)	0.36	**0.74**		**0.76**
16 (18)	I smoke consistently and regularly throughout the day.	3.01	(1.51)	0.37	**0.61**	0.43	**0.78**
17 (19)	I smoke about the same amount on weekends as on weekdays.	2.90	(1.28)		**0.66**		0.49
18 (20)	I smoke just about the same number of cigarettes from day to day.	3.03	(1.27)		**0.74**		**0.53**
19 (21)	Not even a torrential rainstorm could stop me – if I were out of cigarettes, I would be immediately on my way to the store to get some more.	2.29	(1.38)	**0.61**	0.32		**0.73**
20 (22)	Sometimes without realizing it, I go for several hours or more without smoking.	2.96	(1.36)	−0.33			−0.42
21 (23)	Where regulations require that I go outdoors to smoke, it's worth it to be able to smoke a cigarette, even in cold or rainy weather.	2.72	(1.35)	0.45	0.43	0.38	**0.73**
22 (24)	I rarely go for very long without smoking.	2.73	(1.30)	0.49	**0.53**	0.38	**0.80**
23 (25)	If I wake up during the night, I feel I need a cigarette.	1.51	(1.00)	**0.51**			**0.55**
24 (26)	I can function much better in the morning after I've had a cigarette.	2.26	(1.34)	**0.62**	0.36		**0.76**
25 (27)	Sometimes even when I'm telling myself I'm not going to have a cigarette, I find myself smoking anyway.	2.52	(1.30)	**0.50**			**0.62**
26 (28)	Whenever I quit or cut down on smoking, it is an unpleasant experience.	2.22	(1.25)	**0.51**	0.30		**0.62**

Questionnaire item		Mean	(SD)	3-factor solution			Single factor solution
				Drive/ Priority	Stereotypy/ Continuity	Tolerance	
27 (29)	The last time I quit (for 24 hours or more), when I went back to smoking it took a *LONG* time for me to build up to my old level of smoking.	1.92	(1.12)				
28 (−)	Since I started smoking, I have increased how much I smoke.	2.63	(1.52)			0.68	**0.60**
29 (−)	I don't ever crave cigarettes.	1.68	(1.09)	−0.33			−0.44
30 (−)	I can smoke more than I used to before it affects me.	2.11	(1.21)	0.37		0.59	**0.64**
31 (−)	When I smoke a cigarette I get less of an effect (good or bad) than when I first started.	2.62	(1.26)			0.38	0.36
Coefficient alpha (calculated by loadings above 0.40, except Single factor solution calculated with all 31 items)				**0.92**	**0.88**	**0.83**	**0.92**

Factor loadings above 0.5 are shown in bold. Factor loadings of 0.25 or less are not shown.

Item numbers in parenthesis are same as in Shiffman et al. (2004) in Table 6, page 340.

Table 2

Risk of DSM-IV nicotine dependence by the sum score in five groups (N=1259 smokers)

NDSS sum score groups (values in parenthesis)	Age-sex adjusted risk	Crude risk	% of DSM-IV nicotine dependent	% of subjects
Group 1(reference) (14–24)	1.00	1.00	21.3	17.3
Group 2 (25–32)	2.24 (1.49– 3.38)*	2.28 (1.54 – 3.39)	38.2	25.9
Group 3 (33–41)	4.79 (3.21–7.12)*	5.00 (3.39 – 7.38)	57.6	27.6
Group 4 (42–54)	11.9 (7.75 –18.4)*	12.4 (8.17 – 18.9)	76.9	24.5
Group 5 (55–70)	36.7 (13.0–103)*	39.2 (14.8 – 104)	91.4	4.6
Age (years)	0.97 (0.96 – 0.99)*			
Sex (1=men, 2=women)	0.96 (0.71– 1.21)*			

* Robust 95% confidence intervals in parentheses, i.e. adjusted for dependence of family members within families

Table 3

Pearson correlation of other smoking measures with the sum score and separate factors (N=1157; 95% confidence intervals in parenthesis)

Measurement	Sum score	Drive/Priority	Stereotypy/ Continuity	Tolerance
FTND	0.62 (.59–.66)	0.54 (.50–.58)	0.37 (.32–.42)	0.30 (.25–.35)
# of DSM-IV symptoms	0.51 (.47–.55)	0.49 (.45–.53)	0.16 (.10–.22)	0.30 (.25–.35)
Quantity of cigarettes smoked per day during period of heaviest smoking	0.45 (.40–.50)	0.34 (.29–.39)	0.30 (.25–.35)	0.27 (.22–.32)
Maximum cigarettes smoked in a 24 hour period	0.44 (.39–.49)	0.34 (.29–.39)	0.25 (.20–.30)	0.29 (.24–.34)

Table 4

The relationship of FTND with NDSS factors in linear regression models: regression coefficient (β; and 95% confidence intervals, CI) and model explanation (R^2) in models unadjusted and adjusted models for each NDSS factor (n=1155 smokers)

NDSS factor (continuous variables)	Unadjusted β (95% CI)	Unadjusted R^2	Adjusted B (95% CI)	Adjusted R^2
Drive/Priority	1.41 (1.28–1.53)	0.33	1.25 (1.14–1.36)	
Stereotypy/Continuity	0.92 (0.78–1.06)	0.16	0.76 (0.64–0.88)	0.46
Tolerance	0.79 (0.63–0.95)	0.13	0.60 (0.47–0.72)	

Adjusted for dependence of family members within families

Table 5

The risk of DSM-IV nicotine dependence associated with one unit change in NDSS factor scores in logistic regression models (odds ratio, OR and 95% confidence interval, CI) unadjusted and adjusted for each NDSS factor (n=1167 smokers)

	Risk for DSM-IV nicotine dependence	
NDSS factors (continuous variables)	**Factors singly in model OR (95% CI)**	**Factors jointly in model OR (95% CI)**
Drive/Priority	2.90 (2.42–3.49)	2.77 (2.31–3.32)
Stereotypy/Continuity	1.33 (1.15–1.52)	1.20 (1.04–1.39)
Tolerance	2.20 (1.88–2.58)	2.11 (1.79–2.48)

Adjusted for dependence of family members within families

Table 6

The intrapair correlations and 95% confidence intervals for the NDSS sum score, three NDSS factors and FTND in male and female regular smoking MZ and DZ twin pairs (N=291 pairs)

Variable	Men		Women		
	MZ	DZ	MZ	DZ	Opposite sex pairs
(N pairs)	47	96	18	33	97
Sum score	0.41 0.14, 0.62	0.22 −0.02, 0.40	0.34 −0.15, 0.69	−0.09 −0.42, 0.26	−0.08 −0.28, 0.12
Drive/Priority	0.24 −0.09, 0.51	0.26 0.05, 0.45	−0.03 −0.50, 0.46	0.04 −0.32, 0.40	−0.02 −0.24, 0.20
Stereotypy/Continuity	0.46 0.17, 0.68	0.21 −0.014, 0.40	0.20 −0.32, 0.62	0.21 −0.17, 0.53	0.06 −0.17, 0.27
Tolerance	0.26 −0.06, 0.53	0.28 0.071, 0.47	0.59 0.15, 0.82	0.19 −0.18, 0.52	−0.02 −0.22, 0.18
FTND	0.55 0.31, 0.72	0.21 0.01, 0.40	0.16 −0.34, 0.58	0.28 −0.07, 0.57	0.14 −0.6, 0.34