Original investigation

A Preliminary Exploration of College Smokers' Reactions to Nicotine Dependence Genetic Susceptibility Feedback

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Abstract

Introduction: Many young smokers underestimate their risk for becoming addicted to cigarettes. We explored whether informing light college smokers (i.e., fewer than 5 cigarettes/day) of their genetic predisposition to nicotine dependence influenced their perceived risks and worry about becoming addicted, their ability to quit (i.e., self-efficacy), their desire to quit, and smoking cessation.

Methods: College smokers ($n = 142$) received educational materials on mechanisms and consequences of nicotine addiction and were offered genetic susceptibility testing for nicotine dependence. Participants who accepted testing were randomized to receive feedback or no feedback (i.e., control). Tested participants learned they were above or not above average genetic risk for nicotine dependence. All participants responded to questions about perceived risks and worry about becoming addicted, efficacy to quit, and desire to quit. Cessation was assessed during a 1-month follow-up.

Results: Efficacy beliefs, worry about becoming addicted, and desire to quit did not differ by study condition or feedback. Perceived risk for becoming addicted was highest among tested participants informed they were above average risk for nicotine dependence. Overall, self-reported 30-but not 7-day quit rate was higher among participants who underwent genetic testing compared with control participants.

Conclusions: This pilot study is the first to show that among light college smokers, receipt of genetic susceptibility feedback to nicotine dependence potentially curbs smoking without producing detrimental effects.

Introduction

Cessation interventions targeting college smokers often do not address in depth addiction to smoking. Young smokers, including college smokers,¹ often believe they will not become addicted and can quit readily.^{2–5} These optimistic beliefs are often misplaced as indicated by inaccuracies between the number of youth who say they will quit and the number who do.^{6,7} Overcoming these beliefs may be

critical to motivate cessation. To this end, conveying to college smokers the result of genetic susceptibility testing for nicotine dependence may overcome optimistic beliefs about addiction and possibly influence their smoking. However, researchers have not explored college smokers' reactions to actual genetic testing for nicotine dependence.

We begin to address whether informing light college smokers of their genetic predisposition to nicotine dependence influences their perceived risks and worries about becoming addicted, efficacy to

quit, desire to quit, and cessation. Whether such feedback has positive or negative effects is a point of debate.⁸ For example, informing young smokers they have a genetic predisposition to nicotine dependence may undermine their efficacy to quit and amount of effort spent on planning and trying to quit.⁸ Consistent with this view, using hypothetical vignettes, smokers informed they had a genetic variant related to increased nicotine dependence reported less use of willpower as a means to quit,⁹ although perceived control over their ability to quit was not influenced by the feedback. In another study, adult smokers who attributed their smoking to genetic causes reported lower control over smoking, although such attribution did not predict cessation success.¹⁰ Lastly, college smokers who read an article concerning a genetic variation linked with increased risk of both severe nicotine dependence and lung cancer did not express lower efficacy in being able to quit relative to participants in an attention control condition or participants informed such a genetic variant did not exist.⁸ Thus, it remains unclear how actual nicotine dependence susceptibility feedback influences beliefs about quitting and how these beliefs affect desire to quit and cessation.

In addition to efficacy beliefs, we explore whether susceptibility feedback influences perceived risk and worry about becoming addicted and, in turn, desire to quit and cessation. Heightened risk perceptions, negative outcome expectancies, and worry about health are positively related to intention and commitment to quit.¹¹⁻¹⁸ Informing college smokers of a higher predisposition toward nicotine dependence should increase perceived risk and worry about becoming addicted resulting in a higher desire to quit. Conversely, informing smokers of a lower predisposition may decrease perceived risk and desire to quit.

Exploring reactions to genetic susceptibility feedback to nicotine dependence is now possible due to identification of several genetic markers of risk. Genome-wide association studies provide independent confirmation of the role of variation in the *CHRNA5-CHRNA3-CHRNA4* nicotinic acetylcholine receptor gene cluster on chromosome 15 in nicotine addiction. Berrettini *et al*,¹⁹ Bierut,²⁰ and Saccone *et al*²¹ first identified rs16969968, a mis-sense [398 Asp/Asn] single nucleotide polymorphism (SNP) in *CHRNA5*, as conferring heightened risk for nicotine addiction. This initial finding was later confirmed in independent European samples.²² Weiss *et al*²³ extended these findings showing that variants in *CHRNA3* and *CHRNA5* were associated with nicotine addiction only in individuals who started smoking by age 16, defined as “early onset” smoking. Based on these findings, we selected for this study rs16969968 for genotyping. Individuals with the risk allele for rs16969968 self-report higher levels of nicotine dependence and report consuming more cigarettes per day.²⁴⁻²⁹

In sum, feedback on genetic susceptibility to nicotine dependence can serve as a “teachable moment” acting as a warning sign to some college smokers, and as an indicator to others, that cessation is easier before addiction sets in. This approach may be most effective among light college smokers. Before this strategy is implemented on a larger scale, it is critical to establish whether this feedback is interpreted correctly and influences mediators of health behavior change, such as perceived risk and worry, efficacy beliefs, and desire to quit. We predicted that college smokers who receive feedback indicating they are at above average genetic risk for nicotine dependence, compared with college smokers who receive no genetic risk feedback or who receive feedback of not being at above average in genetic risk for nicotine dependence, would report

1. higher perceived risk and worry for becoming addicted,
2. lower efficacy beliefs about being able to quit,
3. a greater desire to quit, and
4. Higher quit rates at follow-up.

Methods

Participants

We recruited smokers from seven college campuses in central North Carolina. The eligibility requirements included enrollment in a 4-year college or university, aged ≥18 years, having smoked at least one cigarette during the last week but less than 5 cigarettes/day during the last week, and willing to review information about undergoing genetic susceptibility testing for nicotine dependence.

Overview of Procedures

Students who responded to advertisements were provided with an overview of the study and screened for eligibility. Eligible students interested in participation were consented verbally on the phone and completed a baseline phone survey; at times, the baseline was completed a few days after being screened. After baseline, participants met in-person with a genetic counselor to review online science education materials on mechanisms of nicotine addiction (Session 1). During this session, the counselor discussed genetic susceptibility testing and offered participants genetic susceptibility testing. Participants who accepted testing were randomized in a 2:1 to either receipt of feedback (i.e., testing) or no feedback (i.e., control), respectively. About one month later, all participants attended a second in-person session (Session 2). Participants not tested first completed questions pertaining to their reactions to hypothetical testing results (e.g., interpretation and evaluation of hypothetical test feedback, emotional reactions to test feedback) and then answered questions about smoking beliefs unconditional on test results; tested participants received their feedback and completed measures about the feedback. All participants completed a phone survey 1 month after Session 2. This study was approved by the Duke University Medical Center institutional review board.

Procedures: Session 1

Providing a scientific basis for disease risk, especially conferred by a genetic mutation, can influence beliefs conducive to motivate protective action.³⁰ Hence, participants used a laptop to review an online module covering mechanisms and consequences of nicotine addiction. The main concepts covered were overview of nicotine, how nicotine affects the brain, development of addiction to nicotine, brain changes with repeated use of nicotine, role of genetics in nicotine addiction, and summary of key points. With respect to genetics, the module mentioned that a person's risk of becoming addicted to nicotine depends, in part, on his/her genes. Thus, environmental risk factors, along with a person's genetic predisposition, influence the chance of becoming addicted. The module reviewed single nucleotide polymorphisms (e.g., what they are and their importance), and specifically rs16969968. For example, participants read about allele frequencies in different racial groups and degree of heightened risk. After reviewing the module, participants were offered genetic testing and all accepted. Participants next swished 10ml of mouthwash for 30 s and spit the mouthwash into a tube, then completed a survey.

Procedures: Session 2

Meeting with a genetic counselor, tested participants received their result in a sealed envelope. Participants were informed that based on

rs16969968 they were above or not above average risk for nicotine dependence. Participants then completed measures concerning their test result, smoking beliefs, and attitudes. Participants who were assigned randomly not to receive feedback were asked to imagine being told that they were above or not above average genetic risk for nicotine dependence. These participants then responded to questions for each hypothetical outcome (not reported here), and general questions pertaining to smoking beliefs and attitudes unconditional on hypothetical test results (see Measures section).

Measures

The following questions were asked at baseline, during Sessions 1 and 2, and at the 1-month follow-up among those who did not report quitting—because of our interest in immediate responses to testing, we do not report the 1-month follow-up reactions related to perceptions of risk and worry about becoming addicted, efficacy beliefs, and desire to quit. During Session 2, control participants were not asked to answer any of the questions below based on hypothetical scenarios of being at above or not above average genetic risk, other than interpretation and evaluation of hypothetical feedback test results—their data are not reported here but available from the first author upon request.

Perceived Risk of Becoming Addicted. “What do you think is the chance of you becoming addicted to nicotine in cigarettes if you continue to smoke?” (1 = *no chance*, 2 = *very unlikely*, 3 = *unlikely*, 4 = *moderately likely*, 5 = *likely*, 6 = *very likely*, 7 = *certain to happen*).

Worry About Becoming Addicted. “How worried are you about becoming addicted to nicotine in cigarettes if you continue to smoke?” (1 = *not at all* to 7 = *very much*).

Perception of Being Addicted. “To what extent do you think you are addicted to cigarettes?” (1 = *not at all* to 7 = *extremely*).

Efficacy Beliefs. We measured perceived ability to quit with three items³¹: “How confident are you that you can stop smoking in the next month” (1 = *not at all* to 7 = *extremely*); “I have the ability to stop smoking in the next month” (1 = *strongly agree* to 7 = *strongly disagree*); and “How easy would it be for you to stop smoking in the next month” (1 = *not at all* to 7 = *extremely*). The items were summed and averaged across the three timepoints (Cronbach's alpha = 0.71–0.80).

Desire to Quit. “How strong is your desire to quit smoking right now?” (1 = *not at all* to 7 = *very*).

Cessation. At the 1-month follow-up, we asked participants if they had smoked a cigarette, even a puff, during the last 30 days (no/yes). If participants smoked during the last 30 days, they were asked if they smoked a cigarette, even a puff, during the last 7 days.

During the second session, we asked the following questions about the test result.

Interpretation of Feedback. We asked participants tested to check whether their test result indicated they were or were not at above average risk for nicotine dependence and to estimate their risk of becoming addicted to nicotine if they continued to smoke (1 = *much lower than average* to 7 = *much higher than average*).

Evaluation of Feedback Result. Participants evaluated their result pertaining to relevance, accuracy, credibility, trustworthiness, and usefulness (1 = *extremely* to 7 = *not at all*).

Defining Levels of Risk

We defined risk levels based on rs16969968 as follows. There are two variant alleles, G and A, with A being the minor allele with

increased risk for dependence (G allele frequency is about two-thirds and A is about one-third), resulting in three genotypes: G/G, G/A, and A/A. The approximate frequencies of these three genotypes in Europeans based on two populations in dbSNP³² are 40%, 45%, and 15%, respectively. In African Americans, the expected frequencies are about 70%, 30%, and 0%, respectively. For this study, individuals with the G/A or A/A genotype were placed in the above average risk group; those with G/G genotype were placed in the not above average risk group.

Statistical Methods

We tested hypotheses regarding differences in the outcomes between the three testing/feedback groups across the three timepoints using hierarchical linear modeling (HLM).^{33,34} HLM allows analyses of growth trajectories of effects across time by treating observations nested within individuals. The nested-structure growth analysis allows examination of linear (growth rate) and quadratic (acceleration) growth trajectories over time.^{33,34} Specifically, at the first level, HLM models outcomes (or repeated observations) as a function, with linear and quadratic terms, of time. Coefficients of the linear and quadratic terms are the growth rate and the acceleration, respectively, of trajectories of outcomes over time. At the second level of HLM analyses, the growth rate and the acceleration are modeled as functions of the grouping variable (i.e., testing/feedback groups). The coefficients (e.g., β s) of the grouping variable are used to determine group difference in the changes (trajectories) of outcomes over time. In all HLM analyses, we controlled for perceptions of being addicted as a time-varying covariate due to significant positive relationships (all but one with desire to quit at Session 2) across time between this perception and the four outcomes ($r = .21$ – $.63$, all $ps < .05$; for desire to quit at Session 2, $r = .10$, $p = .338$); mean values of this covariate did not statistically change across time or by the testing/feedback groups ($ps = .195$ – $.765$).

As main tests of hypotheses, we conducted cross-sectional analysis of variances to explore effects of feedback during the second session. Overall, because the observed means closely matched the means adjusting for perceptions of being addicted, we present the unadjusted means during the second session with the 95% confidence intervals (CIs). Logistic regression analysis was used to determine predictors of cessation at the 1-month follow-up, using those who did not quit as the reference group.

Unlike their response during the screener, three participants reported at baseline smoking more than 5 cigarettes/day (one dropped from the study after baseline, one was not tested, and one tested at above average risk). Eliminating these participants from analyses did not change results appreciably, except for desire to quit. Hence, we report findings involving the entire sample and discuss how desire to quit changed when these three participants were dropped from the analyses.

Results

Participant Characteristics

Figure 1 displays the study flow diagram. Overall, 168 college smokers completed baseline, of which 142 and 132 attended Sessions 1 and 2, respectively; 128 completed the 1-month survey. Among the 90 participants who, during Session 1, were randomized to testing, 42 were at above average genetic risk and 48 were not above average risk. Among these, 40 and 45 attended Session 2, respectively; 39 and 42 completed the 1-month follow-up, respectively. Among those

Figure 1. Study flow diagram. At each timepoint, participants completed measures of current perception of being addicted, perceived future risk and worry about becoming addicted, efficacy beliefs, and desire to quit.

not tested, 47 attended Session 2 and 47 completed the 1-month follow-up. There were no differences in demographic (year in college: $p = .384$; sex: $p = .106$; race: $p = .075$) or smoking profiles (years smoked: $p = .474$; amount smoked: $p = .332$; desire to quit: $p = .321$) among those who attended Session 1 and those who dropped out after baseline, nor on perceived risk ($p = .592$) and worry for becoming addicted ($p = .516$) and efficacy beliefs ($p = .406$).

Baseline characteristics of the 168 participants are shown in Table 1. Most participants were freshman, smoked less than one cigarette a day and for less than a year. The sample was racially diverse with about equal numbers of men and women. Perception of being addicted was low. Mean perceived risk and worry of becoming addicted was around average, as was their desire to quit. The sample expressed relatively higher efficacy beliefs.

Interpretation of Feedback Among Tested Participants

The interpretation of genetic risk feedback was as intended. All participants checked accurately being at above or not above average risk. Further, participants informed they were at higher risk perceived themselves at higher risk for becoming addicted than participants informed they were not at above risk ($M = 5.70$ vs. 3.14 , $p < .001$).

Evaluation of Feedback Among Tested Participants

Participants at above and not above average risk evaluated the test result as relevant ($M = 2.92$, $SD = 1.58$ vs. $M = 2.86$, $SD = 1.62$, respectively; $p = .872$), accurate ($M = 2.42$, $SD = 1.33$ vs. $M = 2.35$, $SD = 1.36$, $p = .810$), credible ($M = 2.13$, $SD = 1.07$ vs. $M = 2.23$, $SD = 1.26$, $p = .714$), trustworthy ($M = 2.42$, $SD = 1.29$ vs. $M = 2.66$, $SD = 1.18$, $p = .385$), and useful, although participants at higher risk viewed their finding as more useful than participants informed they were not at above average risk ($M = 2.42$, $SD = 1.55$ vs. $M = 1.80$, $SD = 1.25$, respectively; $p < .05$).

Table 1. Baseline Characteristics of the Study Participants (N = 168)

Characteristic	M (SD)/Frequency (%)
Age (years)	18.95 (0.99)
Years smoked	0.18 (0.17)
Number of cigarettes/day	0.75 (2.12)
Year in college ^a	
Freshman	76 (48.1%)
Sophomore	45 (28.5%)
Junior	24 (15.2%)
Senior	12 (7.65%)
Refused	1 (0.6%)
Sex ^a	
Male	86 (54.4%)
Female	72 (45.6%)
Race ^a	
African American	26 (16.5%)
White	95 (60.1%)
Hispanic	9 (5.7%)
Asian	9 (5.7%)
Other	19 (12.0%)
Perceptions of being addicted	2.83 (1.42)
Perceived risk of becoming addicted	4.16 (1.55)
Worry of becoming addicted	3.76 (1.72)
Efficacy beliefs	5.66 (1.14)
Desire to quit	3.55 (1.53)

^aOnly 158 participants provided demographic information.

Effects of Feedback on Perceptions of Risk and Worry

We expected participants who received feedback of being at higher genetic risk would report during the second session the highest mean perceived risk and worry of becoming addicted. The HLM trajectory analysis revealed no overall linear or quadratic trajectory of feedback on perceived risk ($p = .377$ and $p = .796$, respectively) and

Figure 2. Perceived risk, worry, efficacy beliefs, and desire to quit (means with 95% confidence limits), by study condition and feedback at Session 2.

worry over time ($p = .105$ and $p = .423$, respectively). The trajectories also did not differ between groups for perceived risk ($p = .195-.900$) or worry ($p = .445-.835$).

The cross-sectional analysis of variance on Session 2 data revealed a group difference in perceived risk by feedback ($F = 6.08$, $p < .005$, $\eta^2 = .09$). Participants informed they were at above average risk perceived themselves as having a higher chance of becoming addicted than participants informed they were not above average risk ($t = 3.46$, $p < .001$, $d = 0.79$); perceived risk did not differ between other testing/feedback groups (see Figure 2a). For worry, the cross-sectional means immediately after feedback did not differ between the testing/feedback groups ($F = 1.65$, $p = .196$, $\eta^2 = .03$, see Figure 2b).

Effects of Feedback on Efficacy Beliefs

We expected participants who received feedback of being at higher genetic risk would report during the second session the lowest mean efficacy beliefs. The HLM trajectory analysis revealed significant overall linear and quadratic trajectories over time. The linear growth rate significantly decreased over time ($\beta = -0.93$, $p < .001$) and the quadratic growth rate significantly increased over time ($\beta = -0.39$, $p < .01$) or the trajectory was concave upward (i.e., U shape). However, trajectories did not differ between the testing/feedback groups at any timepoint ($p = .400-.523$). Further, the cross-sectional

means during Session 2 did not differ between the testing/feedback groups ($F = 0.44$, $p = .646$, $\eta^2 = .01$, see Figure 2c).

Effects of Feedback on Desire to Quit

No significant overall trajectories or differences in trajectories between groups were found for desire to quit ($p = .335-.834$). The cross-sectional means during Session 2 did not differ between the testing/feedback groups ($F = 2.90$, $p = .058$, $\eta^2 = .04$, see Figure 2d). However, when the three participants who reported smoking more than 5 cigarettes/day were removed, group differences became significant ($F = 3.25$, $p < .05$, $\eta^2 = .05$). Participants informed they were at above average risk had a higher desire to quit than participants informed they were not above average risk ($t = 2.38$, $p < .05$, $d = 0.53$).

Effects of Feedback on Quit Rates

At follow-up, 20.3% (26 of 128) of participants reported not having smoked during the last 30 days. Quit rate was highest among those at above average risk (42.3%), followed by not being at above average risk (38.5%) and not being tested (19.2%; $\chi^2 = 4.54$, $p = .104$). Thus, quitting was highest among those tested versus not tested ($\chi^2 = 4.29$, $p < .04$). Among the remaining 102 participants who smoked during the last 30 days, 22% ($n = 23$) reported not having smoked within the last 7 days. Among them, 43.5% were not tested,

26.1% were above average risk, and 30.4% were not above average risk ($\chi^2 = .067, p = .967$).

We explored whether perceived risk and worry, desire to quit, and efficacy beliefs predicted 30-day and 7-day quit rates, controlling for group. Logistic regression analyses show that desire to quit (odds ratio = 1.831, 95% CI = 1.241–2.702, $p < .01$) and efficacy beliefs (odds ratio = 2.049, 95% CI = 1.126–3.717, $p < .05$) significantly predicted 30-day quit rate. None of the four variables predicted 7-day quit rates.

Discussion

To the best of our knowledge, this is the first study to examine reactions to genetic susceptibility feedback to nicotine dependence among light college smokers. Being informed that one is at above average risk increases perceived risk of becoming addicted relative to being informed one is not at above risk, but not more than not knowing one's susceptibility status. Importantly, these findings were obtained after controlling for current perceptions of being addicted—that did not differ between groups across timepoints. Although we did not find any statistical significant group differences for worry about becoming addicted and desire to quit in the total sample, the same pattern of results held. Undergoing and receiving feedback resulted in higher self-reported 30-day, but not 7-day, cessation rates, regardless of test result.

We found no evidence that being informed one is at higher risk of nicotine dependence lowers perceived efficacy to quit compared with other conditions. The stability of relatively high-efficacy beliefs across time may reflect the failure of feedback to alter perceptions of being addicted. That is, if feedback was interpreted to reflect degree of addiction, this interpretation may have altered efficacy beliefs. This did not occur. Moreover, participants with higher efficacy beliefs had lower odds of smoking. Thus, provision of materials to reinforce and increase young smokers' efficacy beliefs can be useful adjuncts to genetic feedback of susceptibility to nicotine dependence. Further, informing light smokers of not being at above average risk did not lower appreciably perceived risk and worry compared with participants who did not receive feedback.

Being informed that one is not at higher genetic risk did not lower quit rates. Rather, these participants reported higher 30-day quit rates than participants not informed of their susceptibility. In general, participants who underwent genetic testing reported higher 30-day, but not 7-day, quit rates than participants not tested. Testing may sensitize participants to the detrimental consequences of nicotine dependence. It would be important to replicate these findings in a larger sample of light college smoker to strengthen the conclusion that undergoing genetic testing for nicotine dependence improves quit rates.

Our findings need to be interpreted cautiously. First, our control group responded early-on to questions conditional on a hypothetical test result of being at above and not above average genetic risk. Thus, our control participants may have reacted similarly to subjects in analog studies rather than as "pure" controls.³⁵ Although having participants answer questions under hypothetical scenarios may have influenced our findings, we believe the effects are negligible or small for the following reasons. First, participants were not instructed to consider the hypothetical scenarios when they addressed questions about global perceived risk and worry of becoming addicted, self-efficacy, desire to quit, and 30- and 7-day quit rates at follow-up. Second, questions posed under the hypothetical scenarios assessed

different constructs than those mentioned previously. Third, there are very few significant associations between responses to the hypothetical scenarios (e.g., evaluation of feedback, emotional reactions) and outcomes reported in this paper; when associations occurred, they were generally small (i.e., below absolute correlation of .30)—findings available from the first author. Nonetheless, future studies should try to replicate these findings without having control participants consider hypothetical findings. Second, the moderate sample size resulted in limited power to detect moderate and especially small effect sizes. Third, results apply to very light college smokers with an interest in undergoing genetic testing and may not be generalizable to other populations. Fourth, we used a single gene to determine susceptibility to nicotine dependence. The clinical and public health use of a single gene is simplistic compared with newer and more predictive algorithms that determine susceptibility to nicotine addiction and subsequent behaviors.³⁶ Fifth, feedback was based on the crude dichotomy of being at above or not above average risk. Gradations of risk, such as being at above average, average, and lower risk, may produce different results. Lastly, cessation was based on self-report only.

Based on our findings, undergoing genetic testing can modify personal beliefs about risk of addiction and motivate cessation. This approach differs from studies that explore how genetic/genomic markers of nicotine dependence predict quitting success.^{37–39} Further, our approach differs from genetic feedback studies targeting smokers in that we used a genetic marker of dependence, whereas other studies have focused on genetic risk of developing cancer, heart disease, and Alzheimer's disease in adult smokers, with many finding no effects of feedback on cessation.^{35,40,41} Future research should focus on replicating our findings using larger samples of college smokers as well as testing effects of feedback among noncollege smokers. Such research should explore mediators of effects. Indeed, understanding how best to educate and convey risks of nicotine dependence to youth poses significant challenges. This study helps to fill gaps in this limited literature.

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Declaration of Interests

None declared.

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