BRIEF REPORT

The impact of learning of a genetic predisposition to nicotine dependence: an analogue study

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Objectives: To examine the consequences of informing smokers of a genetic predisposition to nicotine dependence and of providing treatment efficacy information tailored to genetic status.

Design: Analogue study using four vignettes; 2 (genetic status) $\times$ 2 (whether treatment efficacy information provided) between subjects design.

Participants: 269 British adult smokers.

Outcome measures: Preferred cessation methods and perceived control over quitting.

Results: Gene positive participants were significantly more likely to choose the cessation method described as effective for their genetic status, but significantly less likely to choose to use their own willpower. Providing tailored treatment information did not alter these effects. Perceived control was not significantly affected by either genetic status or information provision.

Conclusions: Learning of a genetic predisposition to nicotine dependence may increase desire for effective cessation methods, but may undermine the perceived importance of willpower in stopping smoking.

There is growing interest in identifying genetic markers that predict a heightened risk of nicotine dependence.^{1,2} A recent review suggested that the most likely benefit of this research would be an improvement in smoking cessation rates, achieved by tailoring cessation interventions to a smoker's genetic profile.¹ However, it is important to consider whether telling smokers that they are genetically predisposed to nicotine dependence will make them believe that their nicotine dependence is intractable. Research into reactions to genetic testing has largely focused on testing predictive of disease risk.³ Two studies have examined the impact on smokers' quitting behaviours of learning of a genetic vulnerability to lung cancer. The provision of high risk information did not increase cessation rates.⁴⁻⁶ It is possible that genetic testing predictive of cessation treatment response may more effectively promote smoking cessation than genetic risk information predictive of disease susceptibility. Genetic risks are sometimes seen as immutable and may engender a sense of fatalism.⁷ Given that perceived control is an important predictor of motivation for, and actual, addictive behaviour change,⁸ learning one has a genetic predisposition to nicotine dependence could adversely affect quitting.

Clinicians also need to know how the provision of information regarding genetic predisposition to dependence will affect smokers' choice of cessation methods. An individual's perception of a health problem, including its causes, influences their coping actions.⁹ Telling individuals that they have a genetic predisposition to nicotine dependence should influence actions taken to stop smoking. Clinicians can take advantage of this relation between perceived causes and actions by providing information about cessation methods

particularly suited to those with a genetic predisposition to nicotine dependence.

As research on this topic is at an early stage, smokers are not yet being offered information on their genetic predisposition to nicotine dependence. It is therefore timely to anticipate responses to providing such information in a clinical setting by using analogue methods. Hypotheses generated by such studies can then be tested in clinical contexts, as genetic testing for a predisposition to nicotine dependence becomes available. The current study focuses on providing information regarding genetic variation in dopamine concentrations and recommending bupropion as an appropriate cessation method for those with a genetic vulnerability to nicotine dependence, as hypothesised by Walton and his colleagues.² The study was designed to establish proof of principle regarding whether genetic risk information affected perceived control over quitting and choice of method, and so the pattern of results is more important than the proposed genetic mechanism of predisposition to nicotine dependence and the possible appropriate treatment.

The aim of the present analogue study is to examine the effects on perceived control and cessation method choice of telling smokers that they do or do not have a genetic predisposition to nicotine dependence, with or without the provision of tailored treatment efficacy information.

HYPOTHESES

This study tested the following hypotheses.

Perceived control

- (1) Participants in the gene positive conditions will have lower perceived control over smoking cessation than those in the gene negative conditions.
- (2) The provision of treatment efficacy information will increase perceived control over smoking cessation for participants in both the gene positive and gene negative conditions.

Choice of cessation method

- (3) Participants in the gene positive conditions will be more likely to choose bupropion than participants in the gene negative conditions.
- (4) Gene positive participants provided with treatment efficacy information will be more likely to choose bupropion than gene positive participants not provided with information.

METHODS

Interventions

The study used a 2 (genetic status) $\times$ 2 (treatment efficacy information provided or not provided) design. Participants were given vignettes (see appendix) which asked them to imagine that they had been tested for a genetic predisposition to nicotine dependence and received either gene positive or gene negative results. In order to test the impact of treatment

Table 1 Results of logistic regression on choice of willpower and bupropion

Method	Step	Predictor	OR	95% CI for OR
Willpower	1	Age	1.006	0.984 to 1.028
		Sex	0.724	0.421 to 1.244
		Time to first cigarette	1.270	0.982 to 1.642
	2	Considering quitting	1.355	0.784 to 2.341
		Educational qualifications	1.890	0.985 to 3.627
		Test result	0.302**	0.142 to 0.644
	3	Information provision	0.750	0.349 to 1.611
		Test result × information provision	1.175	0.400 to 3.452
Bupropion	1	Age	0.958**	0.934 to 0.983
		Sex	1.185	0.656 to 2.142
		Time to first cigarette	0.753	0.566 to 1.002
	2	Considering quitting	0.893	0.493 to 1.618
		Educational qualifications	0.679	0.325 to 1.420
		Test result	4.717***	2.043 to 10.891
	3	Information provision	1.279	0.526 to 3.111
		Test result × information provision	1.382	0.423 to 4.510

p<0.005; *p<0.001.

Ticking a cessation method was coded as 1.

Test result was coded 1 for gene positive and 0 for gene negative. Information provision was coded 1 for provided and 0 for not provided.

Predictors were evaluated at a p=0.0083 to correct for multiple comparisons.

CI, confidence interval; OR, odds ratio.

information, half of the vignettes in each condition also provided treatment efficacy information regarding particular cessation methods, given the individual's genetic status.

Participants

A total of 269 smokers were recruited from various cities around the UK using a market research agency in December 2000 and January 2001. While figures are not available, the research agency estimates that the response rate was 95%. Participants were approached in their homes, interviewed in person and reimbursed £2 (~US\$3/€3). Inclusion criteria were that individuals were aged over 21 years and smoked at least one cigarette a day. One hundred and thirty five men and 134 women participated. Their mean (SD) age was 41.5 (13.8) years; 77 participants (28.6%) had no formal educational qualifications, 144 participants (53.6%) smoked within 30 minutes of waking, and 106 participants (39.4%) said they smoked more than 20 cigarettes a day. The broad inclusion criterion of "at least one cigarette a day" was used to understand the impact of an increased awareness of a genetic predisposition to nicotine dependence across a broad population of smokers. Despite this criterion, the participants were actually slightly more dependent on nicotine than the general population of British smokers.¹⁰ There were no significant differences between the four experimental groups on any of these variables.

Measures

Perceived control over stopping smoking

This was assessed using three items, each with a seven point response format¹¹:

- (1) Having received this test result, I am confident that I can stop smoking during the next month (1, strongly disagree, to 7, strongly agree).
- (2) Having received this test result, for me to stop smoking during the next month is: (1, difficult, to 7, easy).
- (3) Having received this test result, how much control do you feel you have over stopping smoking during the next month (1, no control, to 7, complete control).

Choice of cessation methods

Respondents were asked: "Having received this test result, which of the following methods would you prefer to use to try to stop smoking?" The six response options were "using my own willpower", "contacting a telephone hotline such as

Quitline", "taking Zyban, a drug that reduces cravings for nicotine by increasing dopamine levels", "asking my family doctor for advice", "using nicotine replacement therapy, such as gum or patches", and "getting support from family and friends". Participants were asked to pick a maximum of three options, as pilot work demonstrated that otherwise individuals would endorse all the methods, rather than discriminate between them.

Demographic and smoking behaviour variables

In addition to demographic variables, data were collected on how soon after waking participants smoked their first cigarette, with the response options of "within five minutes", "between 6 and 30 minutes", "between 31 and 60 minutes", "after an hour or later". Readiness for quitting was assessed using a single item, asking, "are you seriously thinking about quitting?" with the response options, "yes, within the next 30 days", "yes, with in the next six months", and "no, not thinking of quitting".

RESULTS

Perceived control

The perceived control items summed to produce a reliable scale ($\alpha = 0.89$). Neither genetic status ($F(1,262) = 1.98$, ns) nor treatment information ($F(1,262) = 1.96$, ns) had significant main effects on perceived control. There was no significant interaction between genetic status and treatment information provision ($F(1,262) = 0.33$, ns). Mean (SD) values for the four groups were as follows: gene positive provided with treatment information 11.98 (5.58); gene positive not provided with treatment information 10.71 (5.19); gene negative provided with treatment information 12.52 (5.06); and gene negative not provided with treatment information 11.99 (5.11). The impact of learning of a genetic predisposition to nicotine dependence on perceived control may be restricted to those who are already thinking about quitting. However, when the analysis was restricted to those participants who were considering quitting in the next six months or sooner, the effects of genetic status ($F(1,127) = 0.382$), information provision ($F(1,127) = 0.048$), and their interaction ($F(1,127) = 0.373$) remained non-significant.

Choice of cessation method

Hierarchical logistic regression was used to examine whether choosing a particular cessation method could be predicted

from genetic status, treatment information provision, and their interaction, having first controlled for demographic and smoking behaviour variables. A Bonferroni correction was used to guard against type I error given that regression models were tested for all six cessation methods, resulting in predictors being evaluated at a significance level of $p = 0.0083$.

Participants in gene positive conditions were significantly more likely to choose bupropion, but significantly less likely to choose using their own willpower. Age was a significant predictor of choosing bupropion, older participants being less likely to choose this method. The two outcomes included in the regressions (willpower and bupropion) are not independent, given the instructions to select three cessation methods of the six, introducing a potential confound. However, if the choice of willpower can be significantly predicted by genetic status, first controlling for choice of bupropion, while the converse holds true for choice of bupropion, then we can be more confident that learning of a genetic predisposition to nicotine dependence affects choice of cessation methods. Two further logistic regression analyses were run based on these principles. Controlling for smoking behaviour and demographic variables as well as choice of willpower, genetic test results remained a significant predictor of choosing bupropion, such that those who received gene positive test results were more likely to say they would use bupropion, $\text{Exp}(B) = 4.086$, 95% confidence interval (CI) = 1.742 – 9.581, $p < 0.001$. Controlling for smoking behaviour and demographic variables in addition to choice of bupropion, the genetic test result remained a significant predictor of choice of willpower, such that those who received gene positive test results were less likely to say they would use their own willpower, $\text{Exp}(B) = 0.352$, 95% CI = 0.162 – 0.764, $p < 0.008$.

Choosing to consult one's family doctor, using nicotine replacement therapy, calling a helpline, and asking one's friends and family for support were not significantly predicted by any hypothetical situation variables in the regression equation. The interaction between genetic status and information provision was not a significant predictor of the choice of any cessation method. The details of the logistic regression analyses on choice of bupropion and willpower are shown in table 1.

DISCUSSION

This study was designed to test a number of hypotheses concerning the effects of learning of a genetic predisposition to nicotine dependence. The hypotheses that participants in the gene positive conditions would have lower perceived control over smoking cessation than participants in the gene negative conditions, and that the provision of tailored treatment efficacy information would increase perceived control for participants in both gene negative and gene positive conditions, were not supported. The prediction that participants in gene positive conditions would be more likely to choose bupropion than participants in gene negative conditions was supported. This is important as bupropion is considered a reasonably efficacious cessation method.^{12 13} However, participants in gene positive conditions were less likely to say that they would use their own willpower. This is potentially problematic, as it suggests that smokers have less faith in their own coping abilities when they learn that they have a genetic predisposition to nicotine dependence. This finding poses an apparent contradiction with the finding that genetic status had no impact on perceived control over quitting. The concept of using one's willpower involves resisting situation specific temptations and cravings, unlike the more general, non-specific perceived control over quitting measure. It is possible that while learning one has a genetic predisposition to nicotine dependence does not affect one's general perception

What this paper adds

There is considerable research interest in identifying genetic markers predictive of nicotine dependence. The most likely benefit of this research is improved cessation rates, achieved by using genotyping to match smokers to appropriate cessation interventions. However, it is not known how smokers will respond to learning of a genetic predisposition to nicotine dependence and whether this will affect their perceived control over quitting and choice of cessation method. This analogue study suggests that learning of a genetic predisposition to nicotine addiction makes smokers more likely to choose a genotype matched pharmacological treatment (bupropion), but less likely to say they will use their own willpower when quitting. We now need to determine whether the provision of stronger treatment efficacy information will minimise this potential disadvantage while allowing smokers to benefit from learning of their genetic predisposition, which may lead them towards more effective smoking cessation methods.

of control over quitting, it reduces belief in the effectiveness of one's abilities to withstand situation specific temptations and cravings.

The study has several limitations. The response option for Zyban (bupropion) included a phrase about its mechanism of action, as the drug had very recently become available on prescription in the UK at the time of the study and we wanted participants to believe it was a "real" smoking cessation therapy. There is the possibility that this choice of wording may have influenced results in the gene positive, treatment efficacy information condition, as it echoes the wording used in the treatment information and so may somewhat dilute its impact. The treatment efficacy information intervention, although more detailed than that provided by the response option, was brief. Examining the impact of more detailed and different information would be interesting. For choice of cessation therapy, the outcomes were not independent, creating interpretative difficulties. Future research may benefit from asking participants to rate the efficacy of different cessation therapies rather than simply choosing three of the six.

This analogue study has generated a number of hypotheses, which need to be tested in smokers provided with personalised information about genetic susceptibility to nicotine addiction, once such tests are available in a clinical context. This is one of the first studies to examine the impact upon smokers of learning that they have a genetic predisposition to nicotine dependence. Informing smokers that they have such a predisposition increases their desire to take bupropion, which is a fairly effective cessation method. Unfortunately, it may also undermine the likelihood of them using their own willpower to stop smoking. We now need to determine whether stronger treatment efficacy information will minimise this potential disadvantage while allowing smokers to benefit from learning of their genetic predisposition, which has the potential to lead them towards more effective smoking cessation methods.

APPENDIX: VIGNETTES USED IN THE STUDY

You are thinking of giving up smoking. You see an advertisement asking for smokers to take part in research aimed at finding out if they have a gene that makes them more likely to get addicted to nicotine.

This gene is found in people with low levels of dopamine, a natural pleasure chemical in the brain. Nicotine raises levels of dopamine resulting in feelings of pleasure. People with this gene are addicted to nicotine partly because it raises their naturally low dopamine levels. Some people have this gene and some people do not.

Gene positive

You have the test. One week later you receive a letter telling you that you DO have this gene.

Gene negative

You have the test. One week later you receive a letter telling you that you DO NOT have this gene.

Treatment efficacy information: gene positive

The letter tells you about recent research, which suggests that people with this gene can successfully stop smoking by taking Zyban, a drug that reduces nicotine cravings by increasing dopamine levels.

Treatment efficacy information: gene negative

The letter tells you about recent research, which suggests that people who do not have this gene can successfully stop smoking without using products that reduce dopamine related cravings for nicotine.

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