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

A J Wright, J Weinman, T M Marteau

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) × 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.

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) × 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...
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$3.63). 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. 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 format: (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 ($F(1,262) = 0.53$, ns). Mean (SD) values for the four groups were as follows: gene positive provided with treatment information 11.99 (5.11); gene positive not provided with treatment information 12.52 (5.06); gene negative provided with treatment information 11.99 (5.11); 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

<table>
<thead>
<tr>
<th>Method</th>
<th>Step</th>
<th>Predictor</th>
<th>OR</th>
<th>95% CI for OR</th>
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<td>Sex</td>
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<td>0.985 to 3.627</td>
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<td></td>
<td>2</td>
<td>Test result</td>
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<td>Information provision</td>
<td>0.750</td>
<td>0.349 to 1.6111</td>
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<td></td>
<td>3</td>
<td>Test result × information provision</td>
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<td>0.400 to 3.552</td>
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<td>Bupropion</td>
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<td></td>
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<td>0.656 to 2.142</td>
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<tr>
<td></td>
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<td>Time to first cigarette</td>
<td>0.753</td>
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<td>Considering quitting</td>
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<tr>
<td></td>
<td>3</td>
<td>Test result × information provision</td>
<td>1.382</td>
<td>0.423 to 4.510</td>
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</table>

* *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.
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, 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, 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 effective 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.

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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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