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Experimentally exploring the potential behavioral effects of personalized genetic information about marijuana and schizophrenia risk

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ABSTRACT

Marijuana use may increase schizophrenia risk, and this effect may be genetically moderated. We investigated how hypothetical genetic test results indicating the presence or absence of heightened schizophrenia risk in reaction to marijuana use would affect attitudes toward marijuana use. In two experiments, participants were randomized to hypothetical scenarios in which genetic testing showed the presence or absence of a predisposition for marijuana use to increase their schizophrenia risk, or to a control condition with no mention of genetic testing. Experiment 1 used a sample of 801 U.S. young adults recruited via Amazon.com's Mechanical Turk platform. Experiment 2 replicated the same procedures with a nationally representative sample of 800 U.S. adults aged 18–30. In Experiment 1, those in the predisposition condition, compared to the control condition, rated the likelihood and importance of their avoiding marijuana as significantly higher, whereas those in the no-predisposition condition rated both as significantly lower. In experiment 2, these findings were largely replicated for the predisposition condition but not the no-predisposition condition, and prior marijuana use was a significant moderator, with the effects of the predisposition condition confined to participants who reported having used marijuana. If these results are predictive of responses to actual genetic testing, they suggest that genetic test results indicating that marijuana use will increase one's schizophrenia risk may incentivize abstinence, especially for those with prior marijuana use. Future research could further investigate whether genetic test results indicating the absence of such a predisposition might disincentivize abstinence from marijuana use.

1. Introduction

Substantial evidence has linked exposure to cannabis (e.g., marijuana) with heightened risk of psychotic disorders such as schizophrenia. Decades of longitudinal studies have identified an association between cannabis use and psychosis (Murray et al., 2017). Although the association between cannabis use and schizophrenia is likely not entirely causal (Gillespie and Kendler, 2021), a Mendelian randomization study indicated that cannabis use appears to cause a 37% increase in psychosis risk (Vaucher et al., 2017). Further supporting a causal relationship is the fact that a dose-response relationship has been found between cannabis use and psychosis risk (Marconi et al., 2016).

It has been estimated that approximately one in 12 Americans uses marijuana each month, and approximately 7,000 use marijuana for the first time each day (Azofeifa et al., 2016). It is clear that most individuals who use marijuana never go on to develop psychotic symptoms, and genetic differences may help to explain why some people develop psychosis after using marijuana while others do not (Zwicker et al., 2018). For instance, the finding of increased psychosis risk among cannabis-using carriers of the AKT1 rs2494732 C/C genotype (compared with cannabis-using T/T carriers) has been replicated in independent samples (Di Forti et al., 2012; Morgan et al., 2016). Although a single genetic variant alone clearly does not determine which cannabis users will develop psychosis, these kinds of findings highlight the prospect of specific, identifiable genetic signatures that could be used to identify individuals for whom cannabis use would significantly increase psychosis risk. Although no genetic test for this purpose currently exists, efforts to discover genetic variants and other biomarkers that can be used to guide psychiatric diagnoses and predict clinical outcomes are a key component of the current embrace of so-called "precision psychiatry" (Fernandes et al., 2017).

The development of genetic tests to predict whether marijuana use will increase risk of psychotic disorders such as schizophrenia could have weighty public health implications. Although some studies suggest

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that genetic test results are unlikely to promote healthy lifestyle choices (Hollands et al., 2016), other research suggests that when such results reveal risks that can be avoided through specific health behaviors, the frequency of those behaviors can increase (Aspinwall et al., 2013). Thus, it is plausible that genetic test results suggesting that marijuana would increase one's schizophrenia risk might motivate abstention from marijuana use. However, other research suggests possible pitfalls to the adoption of this kind of genetic testing. In particular, when individuals learn that they are not at heightened risk of a particular health problem, this may actually lead them to underrate the importance of preventive behaviors (Ahn and Lebowitz, 2018). This phenomenon, termed the "genetic invincibility effect," presumably occurs because people erroneously assume that a lack of heightened genetic susceptibility indicates invulnerability. Additionally, gene × environment interactions (e.g., psychosis resulting from the interaction of a genetic diathesis with exposure to cannabis) can be difficult to comprehend and may be fatalistically misinterpreted as implying that a particular outcome will inevitably occur due to genetics alone, regardless of environmental exposures (Dar-Nimrod and Heine, 2011). Thus, some individuals who learn from a genetic test that marijuana use would increase their risk of schizophrenia might misinterpret this information as implying heightened risk of developing the disorder regardless of cannabis exposure. Ironically, this could have the harmful effect of instilling a sense of fatalism and decreasing feelings of agency related to health behaviors.

To date, it is unclear whether personalized genetic information about the effect of marijuana use on schizophrenia risk has the potential to promote healthy behaviors (i.e., abstention from cannabis use among those with elevated risk), disincentivize healthy behaviors (e.g., through genetic invincibility effects among those without heightened risk), or both. Also unclear is how the effects of such information might depend on individual differences, such as past history of cannabis use. To investigate these questions, we conducted two randomized online survey experiments with large samples of American young adults (one of which was nationally representative). We hypothesized that genetic test results indicating that marijuana use would increase one's schizophrenia risk would lead participants to perceive avoiding marijuana as more important and to rate themselves as more likely to avoid marijuana use. By contrast, we hypothesized that genetic test results indicating that marijuana use would not increase one's schizophrenia risk would lead to a "genetic invincibility effect," in which participants would perceive avoiding marijuana as less important and view themselves as less likely to avoid marijuana use. We also sought to examine how any such effects might be moderated by a history of marijuana use. We concurrently explored how genetic test results might impact participants' feelings of self-efficacy (Bandura, 1977), locus of control beliefs (Wallston et al., 1976), and fatalism regarding their susceptibility to schizophrenia. On one hand, test results suggesting that one is genetically vulnerable to developing schizophrenia if one uses marijuana could be seen as providing a specific pathway to minimizing one's risk—i.e., by avoiding marijuana use. As such, this type of feedback could increase feelings of self-efficacy (i.e., belief in one's ability to successfully reduce one's risk) and internal locus of control (i.e., a sense that one has control over one's likelihood of developing the disorder). However, if the test results are instead interpreted merely as implying that one is genetically destined to develop schizophrenia, they might instead lead to increased feelings of fatalism. At the same time, test results suggesting that marijuana use would not increase one's risk of schizophrenia would likely not be expected to affect self-efficacy, locus of control, or fatalism, as the test results provide no indication about how one's own behavior might impact one's risk.

2. Methods

Both experiments were approved by the Institutional Review Board at the NY State Psychiatric Institute.

Design of the randomized online survey experiments. Procedures were identical for both experiments. After being recruited through an online platform (described below), participants were given basic information about schizophrenia, which was adapted from the National Institute of Mental Health's "What is Psychosis?" website. Schizophrenia was described as "a condition that affects the mind" in which "the person has had some loss of contact with reality" and potential symptoms of schizophrenia were listed (see Supplementary Material for more detail). Participants then completed measures of stigmatizing attitudes toward people with schizophrenia (which are not analyzed here) before being randomly assigned to one of three scenarios: a genetic test they hypothetically took revealed that marijuana use would greatly increase their risk of schizophrenia ("predisposition" condition); the test revealed the absence of such heightened risk ("no-predisposition" condition); or no genetic test result was mentioned (control condition). To accomplish the experimental manipulation, participants in all conditions were represented with the same background information about schizophrenia that was displayed at the start of the experiment, except the following was added at the beginning of the first sentence: "Scientists have found that for some people, using marijuana can increase the risk of developing schizophrenia." Then, those in the predisposition and no-predisposition conditions were presented with the following prompt: "In the general population, schizophrenia is thought to affect 1% of people or less. It is possible that in the near future, genetic tests could tell people whether or not marijuana use would increase their risk of schizophrenia. Imagine that you took a genetic test, and it found that because of your genetic makeup, using marijuana would [not] increase your risk of schizophrenia from 1% to 10%." The word "not" was included only for participants in the no-predisposition condition, and the entire prompt was omitted for participants in the control condition. Participants in the predisposition and no-predisposition conditions were shown reminders of their hypothetical genetic test result along with each set of measures.

Outcome measures. After the experimental manipulation, perceived likelihood and importance of avoiding/reducing marijuana use were gauged with two items adapted from prior research (Schiffman et al., 2016): "How likely [would you be] to reduce or completely avoid marijuana use?" and "How important [would it be] for you to reduce or completely avoid marijuana use?" (the bracketed phrases were replaced with "are you" and "is it" for the control condition, as these participants had not been prompted with a hypothetical scenario). Both items were answered on a scale from "1 (Not at all)" to "7 (Very)."

Fatalism was measured by asking participants, "Compared to the average person, how likely would you be to develop schizophrenia if you did NOT use marijuana?" The response scale ranged from "1 (Much less likely)" to "9 (Much more likely)." We reasoned that if the predisposition condition led participants to provider higher ratings of their likelihood of developing schizophrenia even in the absence of marijuana use, this could be understood as evidence that invoking genetics was interpreted fatalistically.

Locus of control was measured using a questionnaire adapted from the Health Locus of Control scale (Wallston et al., 1976) (see Supplementary Material). Possible scores on this measure ranged from 1 to 7, with higher scores indicating greater belief in one's ability to control one's risk of developing schizophrenia, referred to as an "internal" locus of control.

Self-efficacy was gauged using a measure adapted from the General Self-Efficacy Scale (Schwarzer, 1999) (see Supplementary Material). Possible scores ranged from 1 to 7, with higher scores indicating greater self-efficacy (i.e., belief in one's ability to successfully reduce one's risk of schizophrenia).

At the end of the procedures, participants were asked about their demographic details and their history of marijuana use.

Participants and recruitment. Participants in Experiment 1 were U.S. adults who were recruited using Amazon.com's Mechanical Turk (MTurk) platform (which allows individuals to complete online tasks in exchange for payment) (Buhrmester et al., 2011) and completed study

Table 1
Demographic details for Experiment 1 sample.

Variable	Condition			Full Sample (N = 801)
	Control (n = 267)	Predisposition (n = 267)	No-Predisposition (n = 267)	
Gender (%)				
Male	37.5	47.6	44.6	43.2
Female	61.4	51.7	52.8	55.3
Other or unknown	1.1	0.7	2.6	1.5
Ethnicity (%)				
Hispanic or Latino	10.5	11.6	8.2	10.1
Not Hispanic or Latino	86.1	84.6	87.6	86.1
Unknown (Hispanic or Latino)	3.3	3.7	4.1	3.7
Race[a] (%)				
American Indian or Alaska Native	0.4	1.5	2.6	1.5
Asian	12.0	10.1	10.5	10.9
Black or African American	8.6	9.4	10.5	9.5
Native Hawaiian or Pacific Islander	0	0	0.4	0.1
White	77.5	80.1	76.0	77.9
More than One Race	4.5	2.2	3.7	3.5
Prefer Not to Answer	2.2	1.1	2.2	1.9
Age (years): mean ± SD	26.7 ± 3.2	26.8 ± 3.4	26.7 ± 3.3	26.7 ± 3.3
Education (%)				
No high school diploma	0	0.4	0.4	0.2
High school diploma or equivalent	7.9	10.1	7.5	8.5
Some college, no bachelor's degree	33.0	29.6	32.6	31.7
Bachelor's degree or equivalent	46.8	40.4	46.4	44.6
Graduate degree	12.4	19.5	13.1	15.0
Annual household income (%)				
<$25,000	18.7	13.9	14.6	15.7
$25,000 - $49,999	31.5	28.1	28.1	29.2
$50,000 - $74,999	24.3	22.8	33.0	26.7
$75,000 - $99,999	10.5	16.1	12.7	13.1
≥ $100,000	14.6	19.1	11.6	15.1
Unknown	0.4	0	0	0.1
Reported any past marijuana use (%)	60.7	70.4	67.4	66.2
Reported past-year marijuana use (%)	40.8	40.4	42.7	41.3
Reported past heavy marijuana use (≥3x/week) (%)	31.8	34.5	33.3	33.2

[a] Percentages for racial categories do not sum to 100% because it was possible for participants to select multiple responses when indicating their race.

procedures via the Qualtrics.com online survey platform. Randomization was carried out in an automated manner by the Qualtrics.com online software, with participants randomly assigned to conditions in a 1:1:1 ratio. MTurk settings were used in an attempt to restrict eligibility to individuals aged 18–30, but 110 (13.6%) of the 806[1] individuals who initially completed the experiment reported ages above 30. To minimize the number of respondents who were excluded (to maximize sample size) while adhering reasonably closely to the intended age range, we included all participants who reported ages between 18 and 33, for a sample of 801 participants (99.4% of the initial respondents). This sample was 55.3% female, 43.2% male, and 1.5% other or unknown gender, with a mean age of 26.7 ± 3.3 years (see Table 1 for further demographic details).

Participants in Experiment 2 came from a nationally representative sample of Americans aged 18–30 years. As in Experiment 1, this age group was targeted because schizophrenia typically first emerges in adolescents and young adults. Participants for Experiment 2 were recruited by the survey research firm YouGov (http://www.yougov.com), which maintains a panel of participants who can be invited to complete online surveys. YouGov provided weights for each respondent that were used to weight the data for all analyses to achieve demographic representativeness of the national population of 18–30-year-olds (see Supplementary Material for additional information). The sample for Experiment 2 consisted of 800 U.S. adults aged 18–30 (weighted to 51.4% male, 48.6% female), with a weighted mean age of 23.9 ± 3.6 years (see Table 2 for further demographic details). Participants were randomized into one of the three conditions in a 1:1:1 ratio using block randomization based on entry time to the survey using Gryphon, YouGov's proprietary survey system.

Statistical analyses. For each experiment, we first analyzed the reliability of the multi-item measures (locus of control and self-efficacy). We then tested the effects of our experimental manipulation on each of our measures, as well as whether these were moderated by history of marijuana use, using 2 (ever used marijuana: yes vs. no) × 3 (condition) ANOVAs. When significant two-way (history of marijuana use × condition) interactions emerged, we decomposed them by conducting distinct one-way ANOVAs examining the main effect of condition separately for participants with and without a history of marijuana use. When significant main effects of condition were observed in these ANOVAs, we followed them up using Dunnett's test (two-sided) to conduct pairwise comparisons of the predisposition and no-predisposition conditions against the control condition. Main effects of history of marijuana use were not a focus of the present research.

3. Results

Experiment 1. Reliability was high both for the locus of control items (Cronbach alpha = .89) and self-efficacy items (Cronbach alpha = .92), so each set of items was averaged to compute a locus of control (LOC) score and self-efficacy score for each participant.

[1] A sample size of approximately 800 respondents per experiment was sought because an earlier pilot study had yielded an effect size of d = 0.37 for a two-group comparison, suggesting a sample size of at least 116 per group would be needed for 80% power with an alpha of .05. Rounding this number up to 125 resulted in a minimum sample of 375. Because we wished the subsamples of participants with and without marijuana use to both be adequately powered, we doubled this number to 750 and then rounded up to 800.

Table 2
Demographic details for Experiment 2 sample.

Variable	Condition			Full Sample (N = 800)
	Control (n = 233)	Predisposition (n = 304)	No-Predisposition (n = 263)	
Gender (%)				
Male	52.9	51.8	49.4	51.4
Female	47.1	48.2	50.6	48.6
Race/Ethnicity (%)				
White	55.6	58.9	48.0	54.4
Black	17.4	12.5	13.6	14.3
Hispanic	17.8	16.5	28.6	20.8
Asian	5.2	3.9	6.6	5.2
Native American	0	1.7	0.8	0.9
Two or more races	1.2	2.8	0.9	1.7
Other	2.5	2.4	1.2	2.1
Middle Eastern	0.3	1.3	0.3	0.6
Age (years): mean ± SD	23.9 ± 3.6	24.0 ± 3.7	23.7 ± 3.6	23.9 ± 3.6
Education (%)				
No high school diploma	7.2	7.0	6.5	6.9
High school graduate	28.4	33.6	31.9	31.5
Some college	26.5	27.6	33.8	29.3
Two-year college degree	13.1	8.9	6.1	9.2
Four-year college degree	21.1	17.5	16.5	18.2
Postgraduate education	3.8	5.4	5.2	4.9
Annual household income (%)				
< $30,000	38.9	29.0	35.2	33.9
$30,000 - $49,999	12.7	19.4	18.8	17.2
$50,000 - $79,999	18.9	20.2	22.3	20.5
$80,000 - $99,999	4.7	5.7	4.4	5.0
≥ $100,000	14.7	14.2	13.2	14.0
unknown	10.0	11.4	6.2	9.3
Reported any past marijuana use (%)	55.7	53.6	53.4	54.1
Reported past-year marijuana use (%)	38.8	36.9	39.8	38.4
Reported past heavy marijuana use (≥3x/week) (%)	36.3	34.9	34.4	35.1

Note: Values reflect weighted data.

The results of the ANOVAs (see Fig. 1), which included the 795 participants who answered the question about past marijuana use (99.3% of the sample), were consistent with our hypotheses. Relative to the control condition, the predisposition condition led participants to rate reducing/avoiding marijuana use as more important and to rate themselves are more likely to reduce/avoid marijuana use, whereas the no-predisposition condition led participants to rate reducing/avoiding marijuana as less important and themselves as less likely to reduce/avoid marijuana use. These effects were moderated by history of marijuana use, such that the effects of the predisposition condition were stronger among those with such a history, and the effects of the no-predisposition condition were strongest among those without one. There were significant two-way (history of marijuana use × condition) interactions for both likelihood of reducing/avoiding marijuana use, $F(2, 789) = 3.92$, $p = .02$, and perceived importance of reducing/avoiding marijuana use, $F(2, 789) = 4.33$, $p = .01$. The main effect of condition on both measures was significant for both participants with a history of marijuana use, $Fs(2, 527) > 85$, $ps < .001$, and those without, $Fs(2, 262) > 24$, $ps < .001$. Pairwise comparisons (see Table 3) revealed that compared to the control condition, regardless of history of marijuana use, both ratings were significantly higher in the predisposition condition (with larger effect sizes among participants with a history of marijuana use) and significantly lower in the no-predisposition condition (with larger effect sizes among participants with no history of marijuana use).

Compared to the control condition, the predisposition condition also yielded higher fatalism ratings, LOC scores, and self-efficacy scores, whereas the no-predisposition condition did not appear to affect these variables, and history of marijuana use was not a significant moderator. There was a significant main effect of condition for fatalism, $F(2, 789) = 9.58$, $p < .001$, LOC, $F(2, 789) = 62.87$, $p < .001$, and self-efficacy, $F(2, 789) = 21.41$, $p < .001$. Pairwise comparisons (see Table 3) revealed that compared to the control condition, participants in the predisposition condition scored significantly higher on all three of these measures, whereas the no-predisposition condition did not differ significantly. The two-way (history of marijuana use × condition) interactions were not significant for any of these three variables, $Fs<1.61$, $ps>.20$.

Experiment 2. Reliability was again high for the self-efficacy items (Cronbach alpha = .93) and LOC items (Cronbach alpha = .78).

The results of the ANOVAs (see Fig. 2), which were conducted among participants who answered the question about past marijuana use (more than 99% of the sample), largely replicated the results from Experiment 1 with regard to the effects of the predisposition condition, but not the no-predisposition condition (degrees of freedom vary slightly among analyses because of sample weighting and because some participants did not provide a response to some items). Relative to the control condition, the predisposition condition led participants with a history of marijuana use to rate reducing/avoiding marijuana as more important and to rate themselves as more likely to reduce/avoid marijuana use, whereas these measures showed no significant effects among participants without a history of marijuana use and no significant effects of the no-predisposition condition. LOC scores, relative to the control condition, were significantly elevated in the predisposition condition among participants with and without a history of marijuana use and in the no-predisposition condition among participants with a history of marijuana use, but not significantly different among those with a history of marijuana use in the predisposition condition. Self-efficacy scores, compared to the control condition, were significantly higher in the predisposition condition and not significantly different in the no-predisposition condition, and this was not significantly moderated by history of marijuana use. Fatalism ratings showed no effects of the experimental manipulations. There were significant two-way (history of

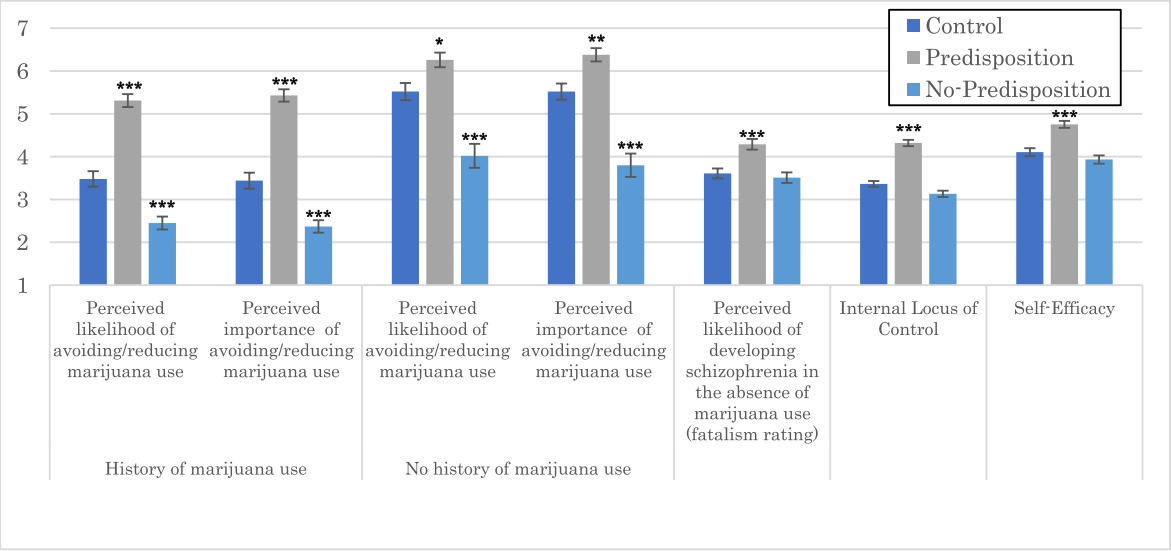

Fig. 1. Means of each dependent variable, by condition, in Experiment 1. Results are shown separately for participants with and without a history of marijuana use where this was a significant moderator of the effect of condition. Error bars represent one standard error above and below the mean. *p < .05 vs. control condition; **p < .01 vs. control condition; ***p < .001 vs. control condition.

Table 3
Pairwise comparisons versus the control condition in Experiment 1 among participants who indicated whether or not they had ever used marijuana.

Dependent Variable	Condition Compared to Control	Mean Difference	SE	p	d
Perceived likelihood of avoiding/reducing marijuana use (history of marijuana use)	Predisposition	1.83	.23	<.001	.84
	No-Predisposition	−1.03	.23	<.001	.48
Perceived importance of avoiding/reducing marijuana use (history of marijuana use)	Predisposition	1.98	.23	<.001	.91
	No-Predisposition	−1.07	.23	<.001	.49
Perceived likelihood of avoiding/reducing marijuana use (no history of marijuana use)	Predisposition	.74	.32	.038	.40
	No-Predisposition	−1.50	.31	<.001	.65
Perceived importance of avoiding/reducing marijuana use (no history of marijuana use)	Predisposition	.87	.30	.008	.51
	No-Predisposition	−1.72	.29	<.001	.78
Fatalism Rating	Predisposition	.68	.17	<.001	.35
	No-Predisposition	-.11	.17	.755	.06
Locus of Control Score	Predisposition	.96	.10	<.001	.83
	No-Predisposition	-.22	.10	.054	.19
Self-Efficacy Score	Predisposition	.65	.13	<.001	.45
	No-Predisposition	-.16	.13	.342	.11

Note: P-values are based on Dunnett's test (two-sided). Results are shown separately for participants with and without a history of marijuana use where this was a significant moderator of the effect of condition.

marijuana use × condition) interactions for likelihood of reducing/avoiding marijuana use, $F(2, 773) = 4.65$, $p = .01$, perceived importance of reducing/avoiding marijuana use, $F(2, 775) = 4.10$, $p = .02$, and LOC, $F(2, 776) = 4.78$, $p = .01$. The main effect of condition was significant for all three measures among participants with a history of marijuana use, $Fs > 7.45$, $ps \leq .001$, but only for LOC among those without a history of marijuana use, $F(2, 361) = 7.05$, $p = .001$ (other $Fs<1$, $ps>.37$). Pairwise comparisons (see Table 4) revealed that, compared to the control condition, ratings of the likelihood and importance of avoiding/reducing marijuana use were significantly higher in the predisposition condition among those with a history of marijuana use and not significantly different in the no-predisposition condition or among participants with no history of marijuana use. LOC scores were significantly higher, compared to the control condition, in both the predisposition and no-predisposition conditions among those without a history of marijuana use, as well as among those with a history of marijuana use in the predisposition condition, but not significantly different among those with a history of marijuana use in the no-predisposition condition. Self-efficacy scores showed a main effect of condition, $F(2, 776) = 4.09$, $p = .02$, and no significant two-way (history of marijuana use × condition) interaction, $F(2, 776) = 2.34$, $p = .10$. Pairwise comparisons (see Table 4) showed that compared to the control condition, self-efficacy was higher in the predisposition condition but not significantly different in the no-predisposition condition. For fatalism, there was no significant effect of condition, $F(2, 776) = 0.79$, $p = .45$, and no significant interaction, $F(2, 776) = 1.92$, $p = .15$.

Alternative analyses. Comparable patterns of responses emerged for both experiments when we calculated the percentage of participants with and without a history of marijuana use in each condition who scored above the scale midpoint on measures of their perception of the likelihood and importance of reducing/avoiding marijuana use (see Supplementary Material).

4. Discussion

The present research investigated how exposure to a hypothetical genetic test result indicating the presence or absence of a predisposition to develop schizophrenia in response to cannabis exposure would affect attitudes and beliefs among young adults. In particular, we measured how these scenarios affected perceptions of the likelihood and importance of avoiding marijuana use and perceptions about the likelihood of developing schizophrenia in the absence of marijuana use, as well as self-efficacy and feelings of control over one's schizophrenia risk.

The results of Experiment 1 suggested that learning that one had a genetic predisposition to develop schizophrenia in response to cannabis use could have positive effects, with participants reporting that they would consider it more important to reduce or avoid marijuana use and

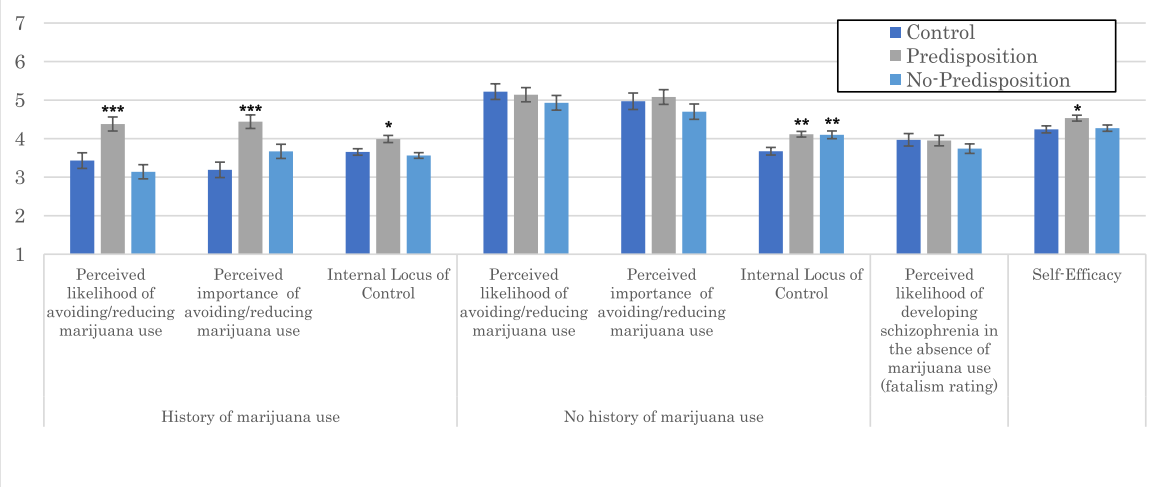

Fig. 2. Means of each dependent variable, by condition, in Experiment 2. Results are shown separately for participants with and without a history of marijuana use where this was a significant moderator of the effect of condition. Error bars represent one standard error above and below the mean. *p < .05 vs. control condition; **p < .01 vs. control condition; ***p < .001 vs. control condition.

Table 4
Pairwise comparisons versus the control condition in Experiment 2, among participants who indicated whether or not they had ever used marijuana.

Dependent Variable	Condition Compared to Control	Mean Difference	SE	p	d
Perceived likelihood of avoiding/reducing marijuana use (history of marijuana use)	Predisposition	.94	.27	<.001	.41
	No-Predisposition	-.29	.28	.457	.13
Perceived importance of avoiding/reducing marijuana use (history of marijuana use)	Predisposition	1.25	.26	<.001	.55
	No-Predisposition	.48	.27	.141	.21
Locus of Control Score (history of marijuana use)	Predisposition	.34	.12	.010	.31
	No-Predisposition	-.09	.12	.678	.10
Perceived likelihood of avoiding/reducing marijuana use (no history of marijuana use)	Predisposition	-.08	.28	.944	.04
	No-Predisposition	-.29	.28	.480	.14
Perceived importance of avoiding/reducing marijuana use (no history of marijuana use)	Predisposition	.12	.29	.886	.05
	No-Predisposition	-.27	.30	.565	.12
Locus of Control Score (no history of marijuana use)	Predisposition	.44	.13	.001	.47
	No-Predisposition	.43	.13	.003	.40
Self-Efficacy Score	Predisposition	.27	.12	.046	.21
	No-Predisposition	-.01	.12	.984	.02

Note: P-values are based on Dunnett's test (two-sided). Results are shown separately for participants with and without a history of marijuana use where this was a significant moderator of the effect of condition. Pairwise comparisons were not conducted for fatalism ratings, as this variable showed no significant effects of the experimental manipulations.

would be more likely to do so, as well as that they would feel a greater sense of self-efficacy and control over their schizophrenia risk. However, they also indicated that they would perceive their risk of schizophrenia as somewhat higher even if they did avoid cannabis exposure, perhaps suggesting a somewhat fatalistic understanding of the role of genes in schizophrenia susceptibility. Moreover, there was also evidence that learning that one lacked such a genetic predisposition could have negative consequences: participants assigned to such a scenario gave significantly lower ratings, compared to a control condition, of the likelihood and importance of their avoiding marijuana use, suggesting that a "genetic invincibility effect" could be at play, disincentivizing healthy behavioral choices among participants who view their genetic risk as low. A moderation analysis in Experiment 1 suggested that the beneficial effects of the "predisposition" feedback on perceptions of marijuana use might have been strongest among participants with a history of marijuana use. At the same time, it appeared that the negative impacts of the "no-predisposition" feedback may have been strongest among those without a history of marijuana use, perhaps because the genetic invincibility effect counteracted their naturalistic reticence to experiment with cannabis.

Experiment 2 replicated Experiment 1's finding that a scenario in which one learns of a genetic predisposition to develop schizophrenia in the context of marijuana use can have a positive impact, especially on individuals with a history of marijuana use. In particular, among participants with a history of marijuana use, those assigned to such a scenario again reported that they would consider it more important to reduce or avoid marijuana use and that they would be more likely to do so, as well as that they would feel a greater sense of self-efficacy and control over their schizophrenia risk, although effect sizes were generally smaller than in Experiment 1. However, Experiment 2 found no evidence of any genetic invincibility effects in the "no-predisposition" condition, and unlike in Experiment 1, the significant beneficial effects of the "predisposition" condition on ratings of the likelihood and importance of avoiding/reducing marijuana use were largely limited to participants with a history of marijuana use.

One limitation of the present research is that it measured self-reported reactions to hypothetical scenarios, rather than actual behavior in response to real genetic test results. While it is thus not possible to be certain of how our findings would translate into real-world behavior, multiple meta-analyses have found that self-reported intentions are a significant, if imperfect, predictor of substance use behavior (Cooke et al., 2016; Topa and Moriano, 2010). Additionally, the use of hypothetical scenarios allowed us to achieve a high level of experimental control, ensuring that all participants in each condition received exactly the same stimuli. It also allowed for participants to be randomly assigned to the conditions, permitting us to conclude that the (hypothetical) genetic tests results themselves, rather than actual genetic differences between the participants, accounted for our findings—without requiring the use of deceptive methods (e.g., leading

participants to believe that their randomly assigned test results were real). Additionally, while the use of an experimental manipulation that was delivered via a self-administered online survey minimized the threat of experimenter effects, it is impossible to rule out the possibilities that demand characteristics could have affected how participants reacted to the hypothetical scenarios or that the hypothetical scenarios may not have affected participants as strongly as real genetic test results would. As such, our findings may be considered somewhat preliminary and should be confirmed with research examining reactions to the delivery of actual genetic test results. However, studies using hypothetical scenarios like the ones reported here can function as a sort of early-warning mechanism, helping to identify potential risks and benefits of healthcare practices (such as specific types of genetic testing) before they are in widespread use.

Given the areas in which the findings of our two experiments converged, an important conclusion from the present research appears to be that for young people who have a history of marijuana use, the return of genetic test results may be a useful way to encourage abstinence among those who learn that they are genetically predisposed to increase risk of schizophrenia with cannabis exposure. This could be especially valuable considering that schizophrenia is generally considered to be a disorder of neurodevelopment that is difficult (if not impossible) to cure after onset, highlighting the importance of prevention. Thus, if such a genetic test is developed, it may be reasonable to consider providing such testing to young people with a history of marijuana use.

The effects of learning that one lacks such a genetic predisposition were less clear, with Experiment 1 suggesting that genetic invincibility effects could result, especially among young people with no history of marijuana use, while Experiment 2 found no such evidence. However, across both experiments, no beneficial effects of the "no-predisposition" feedback were observed. This is notable, considering that if genetic testing for heightened susceptibility to schizophrenia in response to marijuana use were to become more widespread, this type of "no-predisposition" feedback would likely be common; our findings suggest that these kinds of results may be of limited benefit and may even have the potential for harm. Given this, caution may be advisable in deciding whether to test individuals with no history of marijuana use (who are presumably not at risk of negative cannabis-associated psychiatric outcomes anyway), at least until more evidence about the effects of this kind of feedback can accumulate.

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Author statement

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Declaration of competing interest

All authors declare that they have no conflict of interest.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jpsychires.2021.05.066.

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