Review

Possible New Symptoms of Tobacco Withdrawal II: Anhedonia—A Systematic Review

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Abstract

Introduction: When animals undergo nicotine deprivation, rewards become less rewarding (ie, anhedonia occurs). We searched for tests of whether anhedonia occurs in abstinent smokers.

Methods: The major inclusion criterion was a within-participants comparison of behavioral measures of reward sensitivity or self-reported anhedonia during smoking versus during abstinence among daily smokers. A computerized search of PubMed, PsychInfo, and Cochrane databases and other methods located 13 studies. All but one were laboratory studies.

Results: The number of studies and participants were small and the results mixed. In terms of anticipatory anhedonia (ie, wanting a reward), abstinence appeared to decrease willingness to work for immediately available rewards, but did not appear to influence how much adding rewards to a task increased responding. Abstinence also appeared to produce small increases in self-reported anticipatory anhedonia. In terms of consummatory anhedonia (ie, liking a reward), self-report measures found anhedonia decreased pleasure from rewards in some but not all tests. In terms of learning (ie, learning to choose a more frequent reward), abstinence did not reliably decrease allocating responding to high versus low frequency reward options.

Conclusions: Although results were mixed, abstinence appears to increase anticipatory anhedonia. It is unclear if abstinence increases consummatory or reward learning-based anhedonia. Further studies of anhedonia in clinical settings are needed (1) to estimate the reliability and clinical significance of anhedonia as a symptom of tobacco withdrawal, (2) to assess if effects represent withdrawal versus offset processes, and (3) to assess if anhedonia interferes with the ability to stop smoking.

Implications: Anticipatory anhedonia appears to be a symptom of tobacco withdrawal and should be added to tobacco withdrawal checklists and diagnostic criteria. Further study of consummatory and learning-based anhedonia is warranted.

Introduction

In 1980s, tobacco withdrawal descriptions began to coalesce around the following eight symptoms: anxiety, anger/irritability, craving, depression, difficulty concentrating, hunger, insomnia, and restlessness.^{1,2} Most descriptions of tobacco withdrawal have not changed in the last 33 years; for example, the descriptions in DSM-III-R³ in

1980 and DSM-5 in 2013⁴ are identical. This article is the second of three papers assessing possible new symptoms. We have already reviewed data for including impulsivity⁵ and are currently examining positive affect as a possible symptom. The current article focuses on whether anhedonia should be added as a validated withdrawal symptom.

Anhedonia is a feature of several psychiatric disorders, including drug abuse.⁶ Definitions of anhedonia initially focused on decreased liking of reward; however, more recently the construct has been expanded to include decreased wanting for rewards and decreased reward learning.^{7,8} Anhedonia has been termed decreased reward sensitivity or responsiveness, or apathy.⁹ Anhedonia typically is distinguished from increased negative affect and decreased positive affect in that it focuses, not on a current internal state, but rather on the evaluation of a stimulus (ie, reward); for example, simply being unhappy does not necessarily imply anhedonia.^{7,10}

For this review, we will use the constructs of anticipatory, consummatory, and learning aspects of anhedonia.^{7,8} Anticipatory anhedonia is typically measured by willingness to work for a reward, ability of reward to increase responding, and self-report of degree of wanting a reward. Consummatory anhedonia is typically measured by self-report of current or past liking of rewards. Reward learning is typically measured by the degree to which participants learn to allocate responding to larger rather than smaller rewards.

In nonhumans previously administered nicotine chronically, nicotine deprivation decreases reward sensitivity; that is, increases the amount of electrical current necessary to engender self-stimulation.^{11,12} This finding has been interpreted to indicate that rewards become less rewarding during nicotine abstinence; that is, anhedonia occurs.

An effect of abstinence on anhedonia could be due to either of two processes.¹³ First, acute doses of nicotine increase the reinforcing effects of rewards^{14,15}; thus stopping nicotine should decrease reward sensitivity simply due to the “offset” of this effect. This decrease should continue until the predrug exposure baseline value is reached. How fast this process occurs depends both on the pharmacokinetics and pharmacodynamics of the drug. Second, chronic nicotine exposure in animals recruits an opponent¹⁶ or allosteric¹² process that produces a hypodopaminergic state. When chronic nicotine is stopped, the underlying opponent state persists that should temporarily decrease sensitivity to rewards; that is, withdrawal. The offset effect should result in a simple decrease in anhedonia over time; the withdrawal effect should result in an inverted U-shaped time pattern indicating an effect that occurs and then dissipates.¹⁷ Thus, it is only if there are several postabstinence values that one can distinguish between offset versus withdrawal types of abstinence effects.

If the evidence indicates abstinence decreases reward sensitivity this would suggest (1) adding anhedonia as a symptom of tobacco withdrawal to scales and diagnostic criteria, (2) undertaking tests of whether reductions in reward sensitivity/anhedonia during abstinence undermine the ability to quit and, if so, (3) development of treatments to combat anhedonia (eg, behavioral activation¹⁸). If abstinence does not reliably change reward sensitivity or anhedonia, this would suggest either more sensitive tests of reward sensitivity in humans are needed, or the animal models do not apply to humans.

Methods

The first author searched Pub Med, PsychInfo, Cochrane Controlled Trials Registry, and www.clinicaltrials.gov on several occasions until January 2018. The search strategy examined whether the following terms or their stems occurred in the title, abstract or keyword list: “(anhedonia OR apathy OR desire OR happiness OR reward OR wanting) AND (smoking OR tobacco) AND (cessation OR abstinence OR quit OR deprivation).” The search did not include year

or language restrictions. This resulted in 1258 articles in Pub Med and 972 in Psych Info. Among these 540 were duplicates, leaving 1690 articles. The first author also searched his personal files and the reference section of articles examined and requested articles from the Society for Research on Nicotine and Tobacco (www.srnt.org) list-serve. This added an additional 47 articles for a total of 1737 articles.

The major inclusion criteria were (1) a within-participant comparison of smoking and abstinence conditions, (2) a behavioral or self-report measure of anhedonia, (3) inclusion of daily smokers, (4) no active treatment during abstinence, (5) smokers did not have a psychiatric or neurological condition that would influence anhedonia, (6) assessment occurred within 30 days after abstinence began, and (7) published or in press manuscript in any language. We focused on within- rather than between-participant comparisons due to their greater internal validity.¹⁹ Within-participant comparisons included comparisons of outcomes before and after abstinence, or randomized crossover designs of smoking versus abstinence states. The review included studies of overnight abstinence because withdrawal symptoms can occur within a few hours of abstinence²⁰; however, whether the results of these designs represent true tests of withdrawal symptoms or a simple test of the direct effect of smoking is debatable¹³ as will be discussed later. The review included only dependent smokers and those without depressive disorders. In the spirit of transparency and comprehensivity, we also briefly report results of a few studies that could be thought relevant but were excluded.

The first author initially assessed the eligibility of the 1737 articles by reading their titles and abstracts to delete those articles that clearly did not report a within-participant comparison of anhedonia in smoking and abstinence states. This resulted in 36 articles that might be included. Then all three authors independently reviewed these 36 articles and excluded 23 based on the inclusion criteria cited earlier. The reasons for exclusion of each study are described in [Supplementary Appendix Table 1](#).

The three authors next independently coded the study characteristics of the resultant 13 articles ([Table 1](#)). Outcomes were obtained either via values in the text or estimated values from graphs using the Webplot Digitizer software (<https://automeris.io/WebPlotDigitizer>). Final entry both for inclusion and data coding was via consensus. Selection of studies and coding was not blind to authorship. No measures of inter-rater reliability were obtained. We did not include a measurement of the methodological quality of the studies because such measures are often not related to study outcomes.²¹ We did not register the review. We sent final drafts of the manuscript to first authors of included studies and asked for notification of errors or disagreements with our reasons for inclusion, coding, or interpretation of their results. Of the 10 authors, 7 responded.

Description of Studies

Prior articles have reviewed in some detail the optimal methods for withdrawal studies.^{2,17} Across the 13 studies ([Table 1](#)) the incidence of these were as follows: (1) a within-participant design ($n = 13$ studies), (2) smokers trying to quit (because this increases sensitivity)²² ($n = 3$), (2) two or more days of abstinence (to allow peak effects to occur) ($n = 2$), (3) measurements within the first week of abstinence (when effects typically occur) ($n = 13$), (4) multiple measurements during abstinence (to describe whether results appear to be due to simple offset of drug effects or a drug withdrawal syndrome) ($n = 2$), (5) biological verification of abstinence ($n = 13$), and (6) placebos during abstinence (to decrease biased self-report) ($n = 1$). Most of the studies ($n = 11$)

Table 1. Study Characteristics

Study	Design	Participants in analyses	CPD inclusion criteria	FTCD	Trying to quit	Duration of abstinence
Audrain-McGovern et al. ²⁹	Crossover	49	≥10 CPD	5.6	No	Overnight
Bühler et al. ³⁹	Crossover	21	"Dependent"	6.5	No	36 h
Cook et al. ⁴¹	Pre vs. post	189	≥10 CPD		Yes	10 days
Guillot et al. ⁴⁴	Crossover	125	≥10 CPD	5.2	No	Overnight
Hughes et al. ⁴⁰	Pre vs. post	61	≥10 CPD	5.0	Yes	28 days
Kalamboka et al. (Study 1) ⁴⁵	Crossover	32	CO > 15 ppm	3.5		Overnight
Lawn et al. ²⁷	Crossover	20	≥10 CPD	6.4	No	12 h
Pergadia et al. ³⁰	Crossover	31	≥15 CPD		No	24 h
Perkins and Karelitz ²⁸	Crossover	52 ^a	≥10 CPD or ≤5 CPD ^a	4.2		Overnight
Perkins et al. ⁴²	Crossover	5	>10 CPD	4.6	Yes	24 h
Perkins et al. ³⁷	Crossover	28	≥10 CPD	4.5		Overnight
Perkins and Karelitz ³⁸	Crossover	48	≥10 CPD	4.4	No	>12 h
Powell et al. ⁴³	Crossover	26	≥10 CPD	3.7		>10 h

CO = carbon monoxide; CPD = cigarettes/day; FTCD = Fagerstrom Test for Cigarette Dependence; ppm = parts per million.

^aCombined results for dependent and nondependent smokers.

used within-participants crossover designs. Most ($n = 10$) had sample sizes between 20 and 75. One author (K. Perkins) contributed 4 of the 13 studies, all of which used a similar procedure.

The studies used several different behavioral and self-report measures described in detail in [Supplementary Appendix Table 2](#). Behavioral tasks tested whether abstinence decreased the degree to which humans (1) are willing to work to obtain rewards or (2) work harder when assigned to a task more highly rewarded (anticipatory anhedonia). Behavioral tasks examined reward learning by testing a participant's ability to discriminate high versus low reward magnitude tasks and choosing to allocate more responding to the former (reward learning). Self-report tasks asked either about future rewards (anticipatory anhedonia) or current/past rewards (consummatory anhedonia).

Data Analysis

Given (1) the methodological heterogeneity in terms of selection criterion, procedures and measures, and (2) the relatively small sample sizes and number of studies, a meta-analysis was not undertaken. Instead, we used consistency of results across studies to estimate validity. We also wished to estimate the magnitude of any effects; however, none of the measures had clear algorithms for large versus small effects, or stated which effects would be considered clinically significant. Given this, as a substitute we calculated mean percent increase in anhedonia due to abstinence by taking the difference in smoking and abstinence periods and dividing this by the absolute value during the smoking condition. Readers should note that these difference scores are influenced by the absolute value in the smoking condition; that is, the same amount of change when the absolute score is high will be less than when the absolute score is low. Nevertheless, we include percent change results to provide readers with a rough approximation of the magnitude of effects.

Results

Behavioral Tasks

Anticipatory Anhedonia: Willingness to Work for Rewards

All four of the studies by Perkins found willingness to work on a computer task for a reward was less after overnight or short-term abstinence than during ad-lib smoking ([Table 2](#)). Abstinence

consistently decreased responding when an immediately available sensory reward (eg, music) was used, but not when a delayed general reward (ie, money) was used. The four studies used almost identical procedures, increasing the validity of comparing the magnitudes of effects across these studies. The percent decrease in willingness to work for rewards due to abstinence ranged from 18% to 49%. The Bühler study used a different computer task as part of a brain imaging study and did not find an effect of abstinence on willingness to work. This may be due to its use of a delayed monetary reward, small sample size, or more complicated computer task. The Lawn study reported data on willingness to work for a reward after choosing a given reward during a computer task. In this study, abstinence did not reduce willingness to work for sensory rewards. In summary, the consensus of these studies is that abstinence increases anticipatory anhedonia. Unfortunately, these studies do not allow one to determine if this is a simple offset effect or a true withdrawal effect.

Anticipatory Anhedonia: How Much Rewards Increase Responding

The Powell and Kalamboka studies compared responding on a task when no monetary reward for performance was available versus when monetary reward was available. The Powell study found that abstinence decreased the effect of monetary rewards to increase responding. The Kalamboka study used a similar task and did not replicate this result. That study suggested the positive result in the Powell study may have been due to an order effect. In summary, no definitive conclusions can be drawn from these two studies.

Reward Learning: Choosing More Frequent/Larger Rewards

The Audrain-McGovern and Pergadia studies had participants repeatedly undertake a discrimination task in which, unknown to participants, one version produced greater rewards than the other version. The outcome measure was how much participants allocated responding to the more rewarding version. The Pergadia study found a very large effect of abstinence to reduce this learning in both humans and nonhumans. The Audrain-McGovern study using the same task did not find this effect in humans. This may have been because it used less dependent smokers and examined a shorter abstinence period. The Hughes, Budney et al study used a different task that again examined learning to allocate responding to the

more rewarding option and failed to find an effect of abstinence, despite the fact that the study used smokers trying to quit and multiple testing over a long abstinence period. In summary, only one of the three tests of reward learning found an effect of abstinence. Thus, no definitive conclusion can be drawn from these studies.

Self-Reports

Consummatory Anhedonia

(Table 3) The Audrain-McGovern study described previously asked smokers 1–3 questions about current pleasure from rewards repeatedly during smoking and abstinence conditions using ecological momentary assessments (EMAs). It found no effect of abstinence. The Cook study was a clinical trial of medications for smoking cessation that collected EMA ratings for 5 days before and then 10 days after a quit attempt. We examined responses from the placebo group in that trial. The trial found an increased anhedonia beginning on the first day of abstinence in the placebo group. It found the anhedonia time pattern was the classic inverted U shape curve of a true withdrawal symptom. The study also found abstinence-induced

anhedonia was abated by nicotine replacement therapy and, importantly, predicted early relapse. The Guillot study had participants rate the pleasantness of various positive nonsmoking-related pictures and found no effect of abstinence. The Hughes and Lawn studies described earlier included previously validated anhedonia scales that ask about current or past anhedonia. The Hughes study found abstinence produced a small increase in consummatory anhedonia on the Apathy Evaluation Scale (AES)²³ but not the consummatory anhedonia subscale of the Temporal Evaluation of Pleasure Scale (TEPS)²⁴. The increase in AES and TEPS was so small that it was difficult to assess whether it showed the inverted U pattern. The Lawn study used ordinal ratings of current pleasure from chocolate and music rewards that were earned. It found no effect of abstinence. The Lawn study and the Powell study also employed the widely used Snaith-Hamilton Assessment of Pleasure Scale (SHAPS)²⁵ to assess anhedonia and both found large increases in anhedonia with abstinence. In summary, the Cook study was by far the most rigorous study and it found a significant effect of abstinence that was related to inability to stop smoking. This, plus the several other positive results

Table 2. Results of Behavioral Tests: Percent Increase in Anhedonia With Abstinence^a

Study	Anticipatory anhedonia reward (magnitude of effect)	Reward learning anhedonia (magnitude of effect)
Willingness to work for reward		
Bühler et al. ³⁹	Money (none)	
Lawn et al. ²⁷	Music (none)	Music (none)
	Chocolate (none)	Chocolate (none)
Perkins et al. ²⁸	Music (18%)	
	Money (none)	
Perkins et al. ⁴²	Music (49%)	
Perkins et al. ³⁷	Music (22%)	
	Video (31%)	
	Money (none)	
Perkins et al. ³⁸	Music (21%)	
	Video (25%)	
Rewards' influence on responding		
Kalamboka et al. ⁴⁵ Experiment 1	Money (none)	
Powell ⁴³	Money (15%)	
Choosing more frequent/larger rewards		
Audrain-McGovern et al. ²⁹		Money (none)
Hughes et al. ⁴⁰	Money (none)	Money (none)
Pergadia et al. ³⁰		Money (98%)

^aPositive numbers mean increased anhedonia.

Table 3. Results of Self-Report Measures: Percent Increase in Anhedonia With Abstinence^a

Study	Consummatory anhedonia	Anticipatory anhedonia
EMA ratings		
Audrain-McGovern et al. ²⁹	Self-selected reward ratings (none)	
Cook et al. ⁴¹	Ratings of rewards (20%)	
Ratings of lab stimuli		
Guillot et al. ⁴⁴	Ratings of positive pictures (none)	
Anhedonia scales		
Hughes et al. ⁴⁰	AES (6%)	REI enjoyment (5%)
	TEPS (none)	TEPS (6%)
Lawn et al. ²⁷	Ratings of rewards (none)	
	SHAPS (150%)	
Powell et al. ⁴³	SHAPS (71%)	

AES = Apathy Evaluation Scale; EMA = ecological momentary assessment; PRT = Picture Rating Task; REI = Rewarding Events Inventory; SHAPS = Snaith Hamilton Pleasure Scale; TEPS = Temporal Experience of Pleasure Scale.

^aPositive numbers mean increased anhedonia.

in this group of studies, suggest abstinence does increase subjective consummatory anhedonia. However, only the Cook study was able to assess offset versus withdrawal effects.

Anticipatory Anhedonia

The only two self-report measures of anticipatory anhedonia were from the Hughes study. It found a small decrease in anticipated pleasure using the Rewarding Events Inventory (REI), a 54 item inventory of common rewards,²⁶ and the anticipatory subscale of the TEPS. The changes in both were so small that it was difficult to determine whether their time pattern represented a withdrawal effect. Thus, the only two tests of self-reported anticipatory anhedonia suggest a small effect of unknown type.

Moderators

The results of the five studies in our analysis that used overnight abstinence did not appear to differ from the eight that used longer deprivation periods. The mean scores for FTCD were so similar that we could not test them as a moderator. Only three studies examined smokers trying to quit, so we could not test as a moderator as well.

Although the above analyses were based on dependent smokers defined as those smoking daily and nondepressed smokers, two studies included a separate group of nondependent smokers. One of these did not find an abstinence effect in either nondependent or dependent smokers²⁷ and the other found abstinence increased self-reported anhedonia in both nondependent and dependent smokers.²⁸ Also, two studies included participants with versus without depression history. Both found greater effects of abstinence on anhedonia in those with a history of depression.^{29,30} The validity of these moderator results is limited by the small sample sizes (20–49/group).

Studies Not Included in Main Analyses

Some of the excluded studies deserve comment. Two randomized controlled trials tested whether nicotine per se decreased abstinence-induced reduction of reward sensitivity compared to placebo.^{31,32} The initial analysis³² but not a later analysis³¹ found nicotine reduced anhedonia. One single-arm study of smokers in a cessation program asked them three questions to rate whether their pleasure from events had increased or decreased since becoming abstinent.³³ At both 1 week and 4 weeks after abstinence, smokers retrospectively reported more, not less pleasure from events after quitting. Other studies examined responses to positive stimuli in abstinent versus nonabstinent smokers. One of these reported that abstinent smokers reported less attractiveness of facial cues than smoking smokers.³⁴ Similarly, three studies reported in two articles^{35,36} found that abstinent smokers reported less happiness from positive film clips than smoking smokers.

Discussion

The number of studies addressing each of the three anhedonia domains was small, the number of participants was small and the results for each measure varied across studies. Nevertheless, we believe the findings suggest (1) abstinence appears to increase anticipatory anhedonia as measured both by behavioral and self-report tasks, (2) abstinence may increase consummatory anhedonia as measured by self-report tasks, (3) whether abstinence influences reward learning is unclear, and (4) whether any of the above effects represent true withdrawal versus offset effects is unclear. We believe

the weight of the evidence suggests abstinence increases anticipatory anhedonia because 7 of the 11 studies reported such a result on at least one outcome, and this occurred in 9 of the 16 outcomes. We also believe the evidence suggest abstinence may increase consummatory, though the evidence for it is less consistent; that is, four out of six studies and four out of eight outcomes.

The studies included had several methodological assets: within-participant comparisons (mostly randomized crossover designs), and biological verification of abstinence. Nevertheless, the validity of our conclusions is mitigated by several methodological concerns. First, most of the studies (8/13) examined only overnight deprivation. This short abstinence period may have produced false negative results because in some smokers withdrawal symptoms do not peak until the second or third day of abstinence. Second, almost all of these studies interpreted the difference between smoking and abstinence states, not as a withdrawal effect, but rather as a direct offset effect of stopping nicotine. Whether one should interpret differences in abstinence and smoking as agonist effects of smoking or an abstinence effects is debatable.¹³ Although recent studies suggest withdrawal symptoms can begin after short periods of deprivation,²⁰ it is unclear if these initial symptoms are offset or withdrawal effects. The studies by Perkins found that effects of abstinence on anhedonia occur independent of withdrawal effects, suggesting these effects are offset effects.^{21,37,38} Also, if abstinence increased anhedonia in “non-dependent” smokers (usually defined as nondaily smokers) who presumably have little withdrawal symptoms, this would support the interpretation that effects were offset effects. Although one study found this,²⁸ two others did not.^{27,39} The most direct method to distinguish withdrawal and offset effects is by collecting repeated measurements after abstinence to discern whether the typical transient (inverted U) pattern of effects occurred.¹³ Only 2 of the 13 studies did so. One study did not find sufficiently robust anhedonia effects to test this.⁴⁰ The other study found a clear inverted U pattern.⁴¹

Among the behavioral tests of anticipatory anhedonia, four of the eight studies came from one author and these produced six of the seven positive results. In the absence of the Perkins’s studies, only one of three behavioral tests were positive. The procedure used in the Perkins’s studies was a direct and face-valid procedure; however, it has not undergone a replication test from other researchers.

Twelve of the 13 studies were lab studies. The only clinical study by Cook et al. showed robust and clinically significant effects of abstinence on anhedonia. This may be, in part, because the study enrolled smokers who were trying to quit for good (a group shown to be more sensitive to abstinence effects²²) and the multiple testing across baseline and abstinence periods. Clearly, more studies of whether anhedonia occurs among smokers in clinical trials or in natural history studies who abstain are needed.

In the studies of reward learning, we have focused on learning as the process of interest; however, reward learning can be influenced by anticipatory or consummatory anhedonia. Only one of the four studies of whether abstinence reduces reward learning was positive. These negative results may have been because the tasks in the other three were too complex or the duration of the task was insufficient. Also, some of the learning studies did not provide sufficient detail on the task nor the data analytic methods to determine if this was a reason for the mixed findings. If reward learning cannot be reliably found in further studies this might not be unexpected as often the outcomes of behavioral and self-report measures of a construct differ. For example, in our prior review of whether abstinence increases

impulsivity, outcomes differed across response inhibition, delay discounting and self-report tests.⁵

Two of the studies that met our inclusion criteria^{28,37} and two that did not^{31,32} tested pharmacological specificity. Three^{32,37,42} of the four found nicotine per se reduced abstinence-induced anhedonia, suggesting abstinence-induced anhedonia is due to nicotine deprivation.

The Cook study was the only included study that tested the clinical significance of abstinence-induced anhedonia, and found increased anhedonia undermined quit success. Among two other studies not included, one found that scores on the SHAPS anhedonia did not prospectively predict relapse.⁴³ The other study asked recently abstinent smokers how much they enjoyed rewards compared with when they were smoking. The scores on this measure did not predict ability to remain abstinent.⁴³

In our prior review, we concluded impulsivity should be added as a withdrawal symptom, based on the following criteria: (1) it consistently increased in prospective within-participant comparisons, (2) it showed a true withdrawal time course, and (3) it was due to nicotine deprivation. In the current review, (1) in the majority of tests, abstinence increased anticipatory and consummatory anhedonia, but did not reduce reward learning, (2) during abstinence, anhedonia showed a withdrawal time course in the one adequate test of this, and (3) nicotine decreased abstinence-induced anhedonia in three of four nonincluded studies.

In summary, although the results are not entirely consistent across studies, we believe the weight of the evidence suggests anticipatory and consummatory anhedonia are abstinence effects, but whether they represent offset or withdrawal effects is unclear. We believe more data are needed to obtain more reliable findings on all three domains of anhedonia. Furthermore, we suggest future studies include the assets suggested in prior reviews of abstinence methodology.^{2,17} Given the several different conceptualizations of anhedonia, we suggest studies clearly state whether their outcomes represent anticipatory, consummatory, or learning aspects of anhedonia. Also, behavioral task measures of anhedonia can be complex and should be described with clear, jargon free language. We believe the most important future studies are those that test for (1) abstinence-induced anhedonia in clinical or naturalistic settings, (2) a withdrawal time course, (3) pharmacological specificity, and (4) whether anhedonia during abstinence undermines the ability to stop tobacco use.

Supplementary Material

Supplementary data are available at *Nicotine and Tobacco Research* online.

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Declaration of Interests

Dr Hughes has received consulting and speaking fees from several companies that develop or market pharmacological and behavioral treatments for smoking cessation or harm reduction, and from several nonprofit organizations that promote tobacco control. He has consulted with Swedish Match and Philip Morris on their efforts to develop less-risky tobacco products. Dr Peasley-Miklus's spouse works for Perrigo, who manufactures over-the-counter nicotine replacement products. Mr Klemperer has nothing to disclose.

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