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## Experimental manipulations of behavioral economic demand for addictive commodities: a meta-analysis

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### Abstract

**Background and Aims**—Reinforcing value, an index of motivation for a drug, is commonly measured using behavioral economic purchase tasks. State-oriented purchase tasks are sensitive to phasic manipulations, but with heterogeneous methods and findings. The aim of this meta-analysis was to characterize the literature examining manipulations of reinforcing value, as measured by purchase tasks and multiple-choice procedures, to inform etiological models and treatment approaches

**Methods**—A random-effects meta-analysis of published findings in peer-reviewed articles. Following the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) protocol, studies were gathered through searches in PsycINFO and PubMed/MEDLINE (published 22 May 2018). Searches returned 34 unique studies (aggregate sample  $n = 2402$ ; average sample size = 68.94) yielding 126 effect sizes. Measurements included change (i.e. Cohen's  $d$ ) in six behavioral economic indices (intensity, breakpoint,  $O_{\max}$ ,  $P_{\max}$ , elasticity, cross-over point) in relation to six experimental manipulations (cue exposure, stress/negative affect, reinforcer magnitude, pharmacotherapy, behavioral interventions, opportunity cost).

**Results**—Cue exposure ( $d$  range = 0.25–0.44, all  $P$ s < 0.05) and reinforcer magnitude [ $d = 0.60$ ; 95% confidence interval (CI) = 0.18, 1.01;  $P < 0.005$ ] manipulations resulted in significant increases in behavioral economic demand across studies. Stress/negative affect manipulations also resulted in a small, significant increase in  $O_{\max}$  ( $d = 0.18$ ; 95% CI = 0.01, 0.34;  $P = 0.03$ ); all other effect sizes for negative affect/stress were non-significant, albeit similar in size ( $d$  range = 0.14–0.18). In contrast, pharmacotherapy ( $d$  range = –0.37 to –0.49;  $P$ s < 0.04), behavioral intervention ( $d = -0.36$  to –1.13) and external contingency ( $d = -1.42$ ; CI = –2.30, –0.54;  $P = 0.002$ ) manipulations resulted in a significant decrease in intensity. Moderators (substance type) explained some of the heterogeneity in findings across meta-analyses.

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Declaration of interests

The authors declare no conflicts of interest, except for J.M. who is a principal in BEAM Diagnostics, Inc.

**Conclusions**—In behavioral economic studies, purchase tasks and multiple-choice procedures appear to provide indices that are sensitive to manipulations found to influence motivation to consume addictive substances in field experiments.

### Keywords

Alcohol purchase task; behavioral economics; behavioral intervention; craving; cue exposure; demand; pharmacotherapy; reinforcer pathology; reinforcing value; stress

## INTRODUCTION

Understanding the behavior-strengthening properties of a commodity, known as reinforcing value, is important for understanding addictive behaviors, as it quantifies the degree of motivation to consume the addictive substance. Reinforcing value has been operationalized using a variation of fixed-ratio tasks known as behavioral economic (BE) demand curves. Demand curves can be derived from hypothetical behavioral tasks that ask participants to purchase and consume a substance across a series of escalating prices [1]. During an alcohol hypothetical purchase task (HPT), for example, participants are presented with a brief hypothetical drinking scenario, after which they report the number of drinks they would consume across a series of escalating prices. HPTs provide an efficient, reliable and valid alternative to estimating reinforcing value using actual drug self-administration paradigms [2,3]. Although purchase task methodology follows a basic pattern, there is wide variability in methodological characteristics and data analysis, as outlined in recent reviews [4,5].

Consumption decisions are plotted on curves that illustrate consumption and expenditure values as a function of drink price (Fig. 1). These curves are used to estimate demand indices, including intensity (consumption when cost is zero), breakpoint (price at which consumption reaches zero), elasticity (rate of decline in consumption as prices increase),  $O_{\max}$  (maximum expenditure) and  $P_{\max}$  (price at which demand becomes elastic). Each index represents a theoretically distinct aspect of demand and loads onto one of two factors [7,8]: amplitude, reflecting absolute level of hypothetical consumption (e.g. intensity,  $O_{\max}$ ) and persistence, reflecting sensitivity to price (e.g.  $P_{\max}$ , elasticity, breakpoint,  $O_{\max}$ ). Elasticity is thought to represent the ‘essential value’ of the reinforcer [9] and is typically derived from an exponential or exponentiated equation [9,10]. A related measure, known as the multiple-choice procedure, asks participants to choose between a unit of a substance and increasing amounts of money. The price at which choices switch from the substance to money is known as the cross-over point, and is another index of reinforcing value. These indices are correlated with actual behavior and thus represent an efficient way to measure the reinforcing effects of a substance [11–16].

BE demand aggregates a series of cost–benefit decisions between a commodity and ascending monetary values and has typically functioned as a tonic (trait) level index of motivation to use a commodity [17]. Thus, consistent with theory, greater demand amplitude or persistence demarcates greater severity of engagement in a range of substances and behaviors, including alcohol [18–20], cigarettes [21], cannabis [22], opioids [23], heroin [24], cocaine [25], gambling [26], tanning [27,28] and internet use [29,30]. Demand indices,

and intensity and  $O_{max}$  in particular, are also associated with a variety of clinical outcomes [31,32]. Although individual differences in demand are generally stable over time [17,33], BE theory recognizes that phasic (state-like) factors may acutely influence demand. For example, several studies have found that the presence of a next-day responsibility, which introduces an opportunity cost for the drinking behavior, decreases alcohol demand [34,35]. Other research suggests that manipulations such as cue exposure [36], stress [37], behavioral therapy [32] pharmacotherapy [38] and reinforcer magnitude [39] also dynamically influence demand.

Effect sizes for studies examining manipulations of demand have also demonstrated wide heterogeneity across indices and commodities [37,40]. Understanding conditions that acutely influence delay discounting, a behavioral economic measure of impulsivity, has long been of interest [41] and has recently been clarified through a meta-analysis [42]. Thus, it is also necessary to systematically quantify the impact of manipulations intended to increase or decrease substance demand. This would aggregate effects of various phasic factors (e.g. cue exposure, stress/negative affect, reinforcer magnitude, pharmacotherapy, behavioral interventions and opportunity costs) which could, in turn, increase understanding of conditions that influence reinforcer value and contribute to the identification of state-level demand indices as surrogate end-points for screening novel interventions. Indeed, change in demand has been shown to predict changes in subsequent alcohol consumption [31,32]. Thus, the aims of this study were to: (1) meta-analyze the published peer-reviewed findings on manipulations of demand (including moderation by substance type and demand parameter) and (2) examine the presence of publication bias (i.e. bias of strength of effect size due to lack of unpublished studies) in this literature.

## METHOD

### Study selection

Studies were identified using PubMed and PsycINFO (to 22 May 2018) meeting the following inclusion criteria: (i) published, peer-reviewed studies on humans written in English; (ii) within- or between-subjects experimental designs utilizing at least two groups; (iii) reported BE demand, operationalized as indices extracted from purchase tasks (actual or hypothetical) or multiple choice procedure questionnaires, measured before and after (for within-subjects designs) or after manipulation (for between-subjects designs); and (iv) examined substances or drugs. No inclusion restrictions were made on timing or setting.

One author (S.A.) performed all searches. After removing duplicates, two reviewers (S.A. and A.D.) independently screened titles and abstracts of all articles returned in the database searches for clearly eligible or ineligible studies and compared results. Studies that were not marked clearly eligible or ineligible by both reviewers were discussed. Next, a reviewer (S.A.) reviewed the full manuscript of any study in the eligible group and provided brief justification for removal of any studies deemed ineligible at this stage. A second reviewer (A.D.) reviewed each decision, and the two reviewers came to an agreement before studies were removed. Finally, the authors checked reference lists of any recent systematic reviews or meta-analyses examining BE demand (S.A.). Figure 2 depicts the study selection procedure, which followed the Preferred Reporting Items for Systematic Reviews and Meta-

Analysis (PRISMA) standards [43], This review was pre-registered in PROSPERO (CRD42017062 501). The analyses for the current study were not pre-registered.

### Meta-analytical sample characteristics

Primary meta-analyses were conducted for manipulations with at least three studies. Characteristics of the studies included can be found in Table 1. There were 34 unique studies that met the inclusion criteria, yielding a total of 126 effect sizes. A subgroup of studies were eligible, but data were unavailable [13,60,68–81]. Further, several studies did not fit into a manipulation category with enough effect sizes and were thus not included [47,48,82–95]. Each study reported an average sample size of 68.94 (range = 7–328; aggregate sample = 2402). Studies reported demand effect sizes for alcohol ( $k = 78$ ), cigarettes/nicotine ( $k = 27$ ), cannabis/tetrahydrocannabinol (THC) ( $k = 7$ ), cocaine ( $k = 7$ ), methylphenidate ( $k = 3$ ), hydromorphone ( $k = 1$ ), triazolam ( $k = 1$ ), nabilone ( $k = 1$ ) and gamma hydroxybutyrate (GHB) ( $k = 1$ ) using the following indices: intensity ( $k = 35$ ), cross-over point ( $k = 22$ ),  $O_{\max}$  ( $k = 20$ ), elasticity ( $k = 20$ ), breakpoint ( $k = 18$ ) and  $P_{\max}$  ( $k = 11$ ).

### Meta-analytical approach

The primary effect size was Cohen's  $d$ . Results were calculated using a random-effects model based on major differences in study designs. Effects for within-subjects studies were quantified with a modified Cohen's  $d$  effect size that accounts for the shared variance between measurement points [96]. Elasticity effect sizes were multiplied by  $-1$  before use in analyses due to inverse relations with other demand indices. For studies reporting more than one effect size, individual meta-analyses were performed to acquire a pooled effect size for use in primary meta-analyses.

Meta-analyses for each demand index with three or more independent effect sizes were performed for six theoretically distinct manipulation conditions: (1) controlled exposure to substance cues (e.g. holding a lit cigarette; inhaling the smell of a beer), intended to induce craving (i.e. cue exposure [97]); (2) exposure to stress induction (e.g. guided imagery or Trier Social Stress Test paradigms [98,99]); (3) increases in the magnitude of the dose of the active ingredient (reinforcer magnitude); (4) pharmacotherapies (i.e. targeting pharmacological mechanisms to influence substance use); (5) behavioral interventions (i.e. episodic future thinking interventions, brief motivational interventions and cognitive behavioral therapy for smoking); and (6) introduction of a potential loss from an alternative when choosing to engage with the substance (e.g. drinking and driving or a next-day class or test; opportunity cost). Moderator analyses examined unique effects between commodities (alcohol, cigarettes, etc.) when two or more separate studies contributed effect sizes.<sup>1</sup> Moderators were tested using the  $Q$  statistic, which measures the between-group difference in a mixed-effects analysis [100]. To examine the influence of each individual effect size on the aggregate Cohen's  $d$  for each meta-analysis, we conducted sensitivity analyses that re-

<sup>1</sup>Further moderator analyses examining differences in effect sizes by study design (within versus between) and measure type (purchase task versus multiple-choice procedure) are reported in Supporting information, Table S5. Most studies ( $k = 28$ ) used within-subjects designs, and most studies used purchase tasks outside reinforcer magnitude analyses. Thus, moderator analyses for these two variables were performed in analyses pooling all effect sizes from single study into a single effect size and recoding all effects in the same direction.

estimate the overall effect with each effect size systematically excluded (i.e. jack-knife analysis [101]). Publication bias was assessed based on four indices (Table 3): (1) the classic fail-safe  $n$ , (2) Orwin's fail-safe  $n$  at 50% of the reported effect size [102]; the two-tailed Begg–Mazumdar test [103]; and (4) the one-tailed Egger's test [104]. Results for Hedge's  $g$  and publication bias are reported in the Supporting information, in addition to all forest plots and sensitivity analyses.

## RESULTS

### Cue exposure

Cue exposure was associated with significant, small-to-medium magnitude increases in intensity, breakpoint,  $O_{\max}$ ,  $P_{\max}$  and elasticity (Table 2). There was significant heterogeneity across cue exposure effect sizes for all demand indices except breakpoint; moderator analysis for studies examining alcohol demand demonstrated larger, significant effect sizes for intensity ( $d = 0.34$ ), breakpoint ( $d = 0.39$ ),  $O_{\max}$  ( $d = 0.51$ ),  $P_{\max}$  ( $d = 0.31$ ) and elasticity ( $d = 0.77$ ); there were not enough effect sizes to examine moderator analyses for other commodities. There was mixed evidence of publication bias across demand indices (Table 3). The fail-safe  $n$  estimates indicated that a large number of studies would need to be unpublished for the aggregate two-tailed  $P$ -value to exceed 0.05 for intensity, breakpoint,  $O_{\max}$  and elasticity. The fail-safe  $n$  was smaller for  $P_{\max}$ , indicating a greater likelihood of publication bias for this index ( $> 13$ ). The Orwin's fail-safe  $n$ , however, indicated that a small number of studies would need to be unpublished to reduce effect sizes in half, which was consistent across demand indices (range = 5–7). The Begg–Muzumdar and Egger's tests were non-significant for all demand indices except for  $P_{\max}$ , suggesting that results for  $P_{\max}$  may be biased.

### Negative affect/stress

Negative affect/stress was associated with significant, small changes in demand  $O_{\max}$ . The effect of negative affect/stress was not significant for any other demand index (Table 2). There was significant heterogeneity in effect sizes for intensity, breakpoint and elasticity, but not for  $O_{\max}$ . Moderator analysis for studies examining alcohol demand demonstrated larger and significant effect sizes for intensity ( $d = 0.31$ ,  $P = 0.001$ ), breakpoint ( $d = 0.25$ ,  $P = 0.003$ ),  $O_{\max}$  ( $d = 0.26$ ,  $P = 0.002$ ) and elasticity ( $d = 0.26$ ,  $P = 0.04$ ); there were not enough effect sizes to examine moderator analyses for other commodities. There was evidence of potential publication bias for stress/negative affect studies. The fail-safe  $n$  and Orwin's fail-safe  $n$  was low across demand indices. The Begg–Muzumdar test was non-significant for all demand indices. The Egger's test was also non-significant for all demand indices except for intensity.

### Reinforcer magnitude

Reinforcer magnitude was associated with a significant, medium magnitude increase in the cross-over point index of reinforcing value (Table 2). There was significant heterogeneity across reinforcer magnitude effect sizes. Moderator analysis demonstrated a large effect of reinforcer magnitude on the cross-over point for alcohol ( $d = 1.42$ ,  $P < 0.001$ ), a medium-to-large effect on the cross-over point for cocaine ( $d = 0.64$ ,  $P < 0.001$ ) and a small, non-

significant effect on the cross-over point for methylphenidate ( $d = 0.11$ ,  $P = 0.17$ ). Publication bias indices suggested a lack of publication bias for reinforcer magnitude studies. The fail-safe  $n$  was robust, and Orwin's fail-safe  $n$  indicated that 10 studies would need to be unpublished for the cross-over point effect size to be reduced by half. Further, both Begg–Muzumdar and Egger's tests were non-significant.

### Pharmacotherapy

Pharmacotherapy interventions examined effects of bupropion (dopamine and norepinephrine agonist; used for smoking cessation and depression), isradipine (anti-hypertensive; high blood pressure treatment), naltrexone (opioid antagonist; alcohol or opioid dependence maintenance) and varenicline (partial nicotinic agonist; smoking cessation). Pharmacotherapy interventions were associated with significant, small-to-medium magnitude reductions in demand intensity and breakpoint (Table 2). There was significant heterogeneity among pharmacotherapy effect sizes for intensity, but not for breakpoint. Moderator analysis for studies examining cigarette demand demonstrated the same effect size for intensity ( $d = -0.49$ ,  $P = 0.16$ ) and a slightly smaller effects size for breakpoint ( $d = -0.33$ ,  $P = 0.31$ ), although both were non-significant due to limited power. The fail-safe  $n$  values were large for intensity and small for breakpoint. Orwin's fail-safe  $n$  values were small for both intensity and breakpoint. The Begg–Muzumdar's test was significant for intensity; both the Begg–Muzumdar and Egger's tests were non-significant for breakpoint.

### Behavioral interventions

Behavioral interventions were associated with significant, medium magnitude reductions in  $O_{\max}$  and large effect size reductions in intensity (Table 2). The effect of behavioral interventions on demand elasticity was non-significant. There was significant heterogeneity across effect sizes for intensity,  $O_{\max}$  and elasticity. Moderator analysis for studies examining alcohol demand demonstrated smaller effect size for intensity ( $d = -0.70$ ,  $P = 0.003$ ),  $O_{\max}$  ( $d = -0.28$ ,  $P = 0.005$ ) and elasticity ( $d = -0.14$ ,  $P = 0.27$ ). Moderator analysis for studies examining cigarette demand demonstrated larger, albeit non-significant, effect sizes for both intensity ( $d = -2.02$ ,  $P = 0.22$ ) and elasticity ( $d = -0.80$ ,  $P = 0.22$ ). Fail-safe  $n$  estimates were large for intensity and moderate for  $O_{\max}$  and elasticity. Across demand indices, Orwin's fail-safe  $n$  indicated that a small number of effect sizes would be necessary to reduce the effect size by half. The Begg–Muzumdar and Egger's tests were non-significant for all demand indices, with the exception of the Egger's test for intensity.

### Opportunity cost

Opportunity costs were associated with significant, medium-to-large magnitude reductions in demand intensity (Table 2). There was significant heterogeneity across opportunity cost effect sizes. All studies examined changes in alcohol demand; thus, moderator analyses were not explored. Fail-safe  $n$  estimates were large for intensity. Orwin's fail-safe  $n$  indicated that a small number of effect sizes would be necessary to reduce the effect size by half. Both the Begg–Muzumdar and Egger's tests were non-significant.

## DISCUSSION

Our results suggest that behavioral economic demand is sensitive to a variety of experimental manipulations that directly result in significant fluctuations in demand and, theoretically, strength of motivation to use substances. Thus, although when measured as a general trait-like property, demand is a stable individual difference measure of substance use severity [5], these results suggest that there are a variety of contextual factors that can contribute to dynamic within-person fluctuations in demand. Our findings suggest that cue exposure increases phasic motivation (across demand indices) for drugs, possibly resulting in triggered episodes of use/relapse even in the context of a more general desire to abstain. Negative affect/stress effect sizes for alcohol demand were significant, suggesting that negative affect increases motivation to consume alcohol. These results are consistent with research elucidating a small effect of negative affect on drug craving [105], and with novel perspectives highlighting the positively reinforcing aspects of alcohol as a pathway connecting internalizing psychopathology and alcohol misuse [106–108]. Negative affect/stress effect sizes for tobacco demand were small and non-significant, although not enough studies were available to examine aggregate effect sizes. Reinforcer magnitude had a medium effect on demand for alcohol and cocaine, suggesting that more potent forms of these substances may result in greater consumption for these substances.

The opportunity cost meta-analysis indicated that increasing the response costs of drinking (e.g. by stipulating a next-day academic responsibility) may effectively compete with the immediate reinforcement associated with alcohol. It is unclear if this effect is specific to alcohol or if opportunity costs may also have an effect on motivation for other substances, as the current analyses only examined alcohol. Our results also supported the efficacy of interventions to decrease demand for both alcohol and cigarettes. Interestingly, many of the interventions we examined were brief (i.e. typically no longer than two 1-hour sessions) and resulted in subsequent change in actual alcohol consumption following the intervention [31,32]. It is possible that more intensive treatments would result in even greater decreases in demand. Indeed, one reviewed study found a large reduction in demand among patients in a smoking cessation treatment program [59].

The studies that examined the effects of pharmacotherapy on demand for alcohol or cigarettes generally observed reductions. Naltrexone (target substance alcohol) and bupropion (target substance nicotine) were each associated with reductions in a single study; thus, these promising results require replication. Varenicline was effective in one study but not in another, and also requires additional research. Although further research is required, these results imply that purchase tasks are consistently sensitive to manipulations that influence motivation for substances and may be viable surrogate end-points for drugs seeking Food and Drug Administration or Health Canada approval as a means of decreasing substance misuse, and more generally to help guide regulatory decision-making [109].

The meta-analysis revealed differences in effect size by demand index, possibly suggesting different mechanistic properties across manipulations. For example, our results suggest that demand intensity is sensitive to change in manipulations attempting to reduce demand, but less likely to increase among during manipulations trying to increase demand (indicating a

possible ceiling effect). Further, persistence indices (breakpoint, elasticity and  $O_{max}$ ) are generally more susceptible to increases in demand from cue exposure compared to intensity. Most interventions attempting to reduce demand target peak level consumption, the aspect of consumption most related to harm. In contrast, cue exposure may reflect a strong desire to consume at least some of the substance, rather than a high total amount *per se*, and thus manifest in change in persistence. More research should be performed throughout demand indices in each manipulation condition in order to extend our understanding of how different manipulations influence theoretically distinct aspects of motivation to consume a substance.

Taken together, our results extend knowledge of behavioral economic models of substance misuse by characterizing phasic factors that reliably change reinforcing value for different commodities, suggesting that a tonic- phasic reinforcer pathology approach may best fit models of substance use. More specifically, an individual's demand may have a fixed set point, or base rate, but may also vary substantially in response to various contextual factors, including those examined in the current meta-analysis. Thus, these variables may precipitate clinically meaningful changes in motivation to use drugs that may inform models of recovery and relapse [110–112]. Although our study describes the aggregate effects of these unique conditions, there is probably considerable within-subject variability in the malleability of demand, which may represent an important risk factor for greater severity of substance misuse. A few studies have begun to investigate these individual differences; for example, those with a family history of alcohol use are less sensitive to next-day responsibilities among college students [113]. Further, those high in drinking to cope demonstrate a greater increase in reinforcing value following a stress induction [50]. An extension of these findings might use an aggregate of purchase task data across manipulations. Individual differences in the change in demand from one context to another could be conceptualized as a 'meta-elasticity' that accounts for change in demand not only as a function of price, but also as a function of other environmentally relevant factors.

### Limitations and future directions

First, several of our moderator meta-analyses only included a small number of studies and were not adequately powered to detect differences in effect sizes with null hypothesis significance testing. Secondly, many of the studies explored manipulations of demand among heavy drinking college students or adult community smokers, which precludes examination of moderating effects of population type and dependence level. Thirdly, studies examined a limited number of commodities including alcohol, cigarettes and cannabis, and some manipulations (i.e. opportunity cost) only examined one of these commodities. Studies should test the effect of these manipulations on demand for other drugs, including opioids. Fourthly, the variability in measurement time-frame and intervention type for behavioral and pharmacotherapy manipulations should be considered. Fifthly, recent work has considered the effect of task differences on purchase task results and should be considered in future analyses [4,93,114]. Sixthly, evidence was mixed for most publication bias indices, with results of the negative affect/stress manipulation suggesting possible publication bias. It should be noted that the studies did included exhibit significant heterogeneity, which could contribute to higher levels of detected publication bias using these indices. Seventhly,



although the meta-analytical method was pre-registered, the analyses were not, and the results should be considered exploratory.

Although the results explored the effect of six manipulations on demand, the search also returned studies of other phasic factors that could not be aggregated due to the small number of studies, including pain induction [82], happy-hour beer purchasing (more broadly, value framing; [91], excise tax increases on cigarette purchasing [92], cannabis quality [90], devaluation (i.e. substance that turns beer bitter [47]), time constraints on alcohol consumption [93], alcohol administration [83], self-control depletion [94], sexual arousal [48], availability of concurrent commodities [84,85,95,115], deprivation from the addictive commodity [86,94] and income constraint [87,88]. Many of these studies report a statistically significant effect of the manipulation on BE demand and may ultimately be included in future meta-analyses. Other potential manipulations also exist, such as the number of peers present during drinking [116] or the economy type (open versus closed), which could extend basic research into applied domains. Examining the reinforcing value of candidate addictive behaviors (e.g. tanning, internet use) under such conditions would be a further test of their addictive properties [117]. Given the presumed difference in pharmacological potency between substance and behavioral addictions [118], graded effect sizes may exist between manipulations and demand for different indices, which future moderator analyses across commodities could illuminate empirically. Further, changes in some demand indices for the manipulations reported in the current analyses have not been reported often enough for inclusion, and thus future studies should fully report all demand indices to more adequately determine the extent of heterogeneity across different aspects of demand.

### Clinical implications

Our results suggest that behavioral and pharmacological interventions, along with opportunity costs, decrease motivation to consume a range of substances. Further, the results provide an empirical basis for identifying situations that increase substance motivation which could be targeted with intervention. More generally, this study supports the utility of ongoing assessment of demand as a dynamic indicator of motivation that could identify high- risk moments (elevated demand) when individuals may be especially receptive to intervention. Brief demand measures [83,119] may be useful in daily diary or ecological momentary assessment studies to more efficiently track the clinical utility of these shifts in motivation. If successful, these could eventually be useful within the context of a personalized treatment protocol delivered remotely that can react spontaneously to changes in demand reported by the client in real time. The results also highlight opportunities for public health-level interventions that change the context through increasing the response costs, decreasing the reinforcing magnitude and minimizing cues associated with use (i.e. advertising). For example, significant changes in behavioral economic demand due to differences in reinforcer magnitude demonstrate support for policy decisions attempting to control alcohol and other regulated drugs by reducing the levels of the addictive compound available in each unit of the substance (US FDA 83 FR 11818). Results also appeared similar to cannabis demand which, if replicated with further studies, could inform policy decisions regarding regulation of cannabis.

## CONCLUSION

The results provide meta-analytical evidence for significant effects of six manipulations that either increase or decrease motivation to consume a substance, albeit of varying magnitude. A number of other manipulation conditions were retrieved through the search with only one or two studies available, suggesting that the literature is inchoate but growing. Nonetheless, the results provide support for a tonic-phasic reinforcer pathology approach and, more generally, for the utility of HPTs for revealing acute effects of diverse experimental manipulations on the reinforcing value of different addictive commodities.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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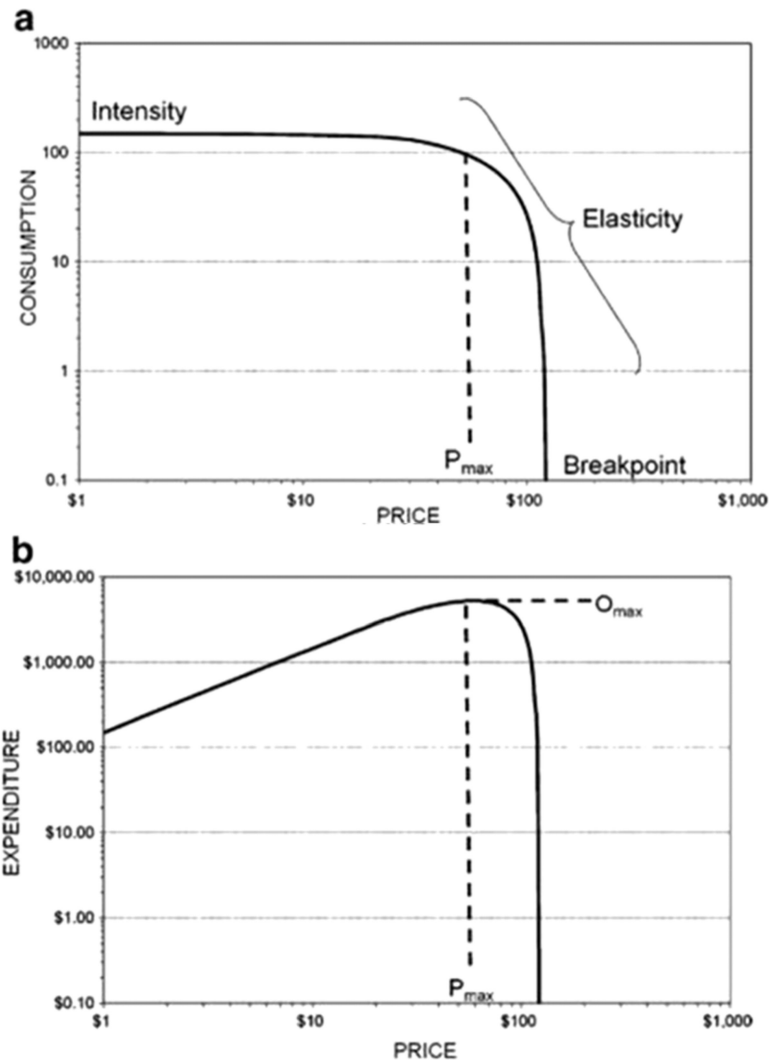
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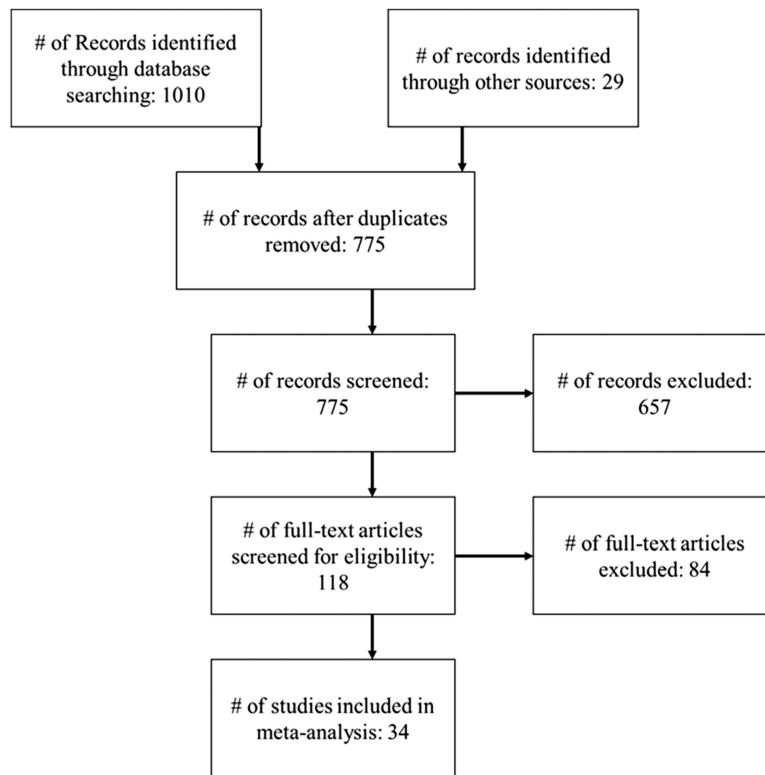
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**Figure 1.** Conceptual representation of prototypical demand curves elicited by a hypothetical purchase task. Curves are presented in logarithmic units for visual presentation. (a) The demand curve, with average consumption values at each price graphed in logarithmic units. The demand curve captures intensity (consumption when the commodity is free), elasticity (the sensitivity of consumption as a function of increasing price) and breakpoint (the price at which consumption reaches zero). (b) The expenditure curve, with average expenditure (price  $\times$  consumption) plotted at each price in logarithmic units. The expenditure curve captures  $O_{max}$  (maximum expenditure) and  $P_{max}$  (the price at which demand becomes elastic). Figures were originally published in MacKillop et al. [6]



**Figure 2.** Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) inclusion flow diagram

Table 1

Studies meeting criteria for inclusion.

Study	Within versus between	Group	n	Commodity	Manipulation	Number of indices	Number of prices	Price range
Acker <i>et al.</i> 2013 [44]	Within	Adult smokers	47	Cigarettes	Cue exposure	5	18	\$0–5
MacKillop <i>et al.</i> 2010 [36]	Within	Heavy drinking college students	92	Alcohol	Cue exposure	5	19	\$0–1120
Metrik <i>et al.</i> 2016 [45]	Within	Emerging adult cannabis users	88	Cannabis	Cue exposure	4	22	\$0–10
Owens <i>et al.</i> 2015 [46]	Within	Adult heavy drinkers	84	Alcohol	Cue exposure	3	10	\$0–40
Rose <i>et al.</i> 2018 [47]	Within	Social drinkers	32	Alcohol	Cue exposure	5	25	£0–15
Spelman & Simons, 2018 [48]	Between	Heavy drinking college students	58	Alcohol	Cue exposure	5	24	\$0–15
Amlung & MacKillop, 2014 [37]*	Within	Emerging adult heavy drinkers	84	Alcohol	Negative mood induction	5	18	\$0–15
Dahne <i>et al.</i> 2016 [40]	Within	Emerging adult smokers	73	Cigarettes	Negative mood induction	5	48	\$0–9
Owens <i>et al.</i> 2015 [49]	Within	Emerging adult heavy drinkers	62	Alcohol	Negative mood induction	4	16	\$0–1120
Rousseau <i>et al.</i> 2011 [50]*	Between	Heavy drinking college students	44	Alcohol	Negative mood induction	1	42	\$0–20
Bujarski <i>et al.</i> 2012 [38]	Within	Heavy drinking Asian Americans	32	Alcohol	Pharmacotherapy	4	16	\$0–120
Madden & Kalman, 2010 [51]	Between	Adult smokers	60	Cigarettes	Pharmacotherapy	2	26	\$0–1120
Murphy <i>et al.</i> 2017 [52]	Within	Adult smokers with a SUD	110	Cigarettes	Pharmacotherapy	3	41	\$0–\$64
Roache <i>et al.</i> 2005* [53]	Within	Adult cocaine users	11	Cocaine	Pharmacotherapy	2	70	\$0.25–25
Schlienz <i>et al.</i> 2014 [54]	Between	Adult treatment-seeking smokers	60	Cigarettes	Pharmacotherapy	3	19	\$0–1120
Gentile <i>et al.</i> 2012 [55]	Between	College students	230	Alcohol	Opportunity cost	6	19	\$0–15
Gilbert <i>et al.</i> 2014 [34]	Within	Heavy drinking college students	78	Alcohol	Opportunity cost	8	1	\$0
Skidmore & Murphy, 2011 [35]	Within	Heavy drinking college students	207	Alcohol	Opportunity cost	10	17	\$0–20
Teeters & Murphy, 2015 [20]	Within	Drinking college students	328	Alcohol	Opportunity cost	3	17	\$0–20
Bulley & Gullo, 2017 [56]	Within	College students	42	Alcohol	Behavioral intervention	5	19	\$0–1120
Denhardt <i>et al.</i> 2015 [31]	Within	Heavy drinking college students	97	Alcohol	Behavioral intervention	6	19	\$0–20

Study	Within versus between	Group	n	Commodity	Manipulation	Number of indices	Number of prices	Price range
Murphy <i>et al.</i> 2015 [32]	Between	Heavy drinking college students	133	Alcohol	Behavioral intervention	4	17	\$0–20
Snider <i>et al.</i> 2016 [57]	Within	Adult smokers	39	Alcohol	Behavioral Intervention	2	5	\$0–1
Stein <i>et al.</i> 2018 [58]	Between	Adult smokers	117	Cigarettes	Behavioral intervention	2	13	\$0–64
Weidberg <i>et al.</i> 2018 [59]	Within	Treatment-seeking smokers	92	Cigarettes	Behavioral intervention	5	19	€0–1000
Benson <i>et al.</i> 2009 [39]*	Within	Drinking college males	27	Alcohol	Magnitude	1	17	\$0–20
Johnson <i>et al.</i> 2013 [60]*	Within	Adult drinkers	14	GHB, ethanol	Magnitude	2	70	\$0.25–25
Johnson <i>et al.</i> 2010 [61]*	Within	Adult cocaine users	14	Nicotine, cocaine	Magnitude	2	65	–\$40 to 40
Lile <i>et al.</i> 2010 [62]*	Within	Adult cannabis users	7	THC, nabilone, methylphenidate	Magnitude	3	9	\$0.10–632
Lile <i>et al.</i> 2010 [63]*	Within	Adult cannabis users	8	THC, triazolam, hydromorphone, methylphenidate	Magnitude	4	9	\$0.25–64
Lile <i>et al.</i> 2013 [64]*	Within	Adult cannabis users	7	THC	Magnitude	1	9	\$0.25–64
Roache <i>et al.</i> 2005 [53]*	Within	Adult cocaine users	11	Cocaine	Magnitude	1	70	\$0.25–25
Rush <i>et al.</i> 1999 [65]*	Within	Adult cocaine users	9	Cocaine	Magnitude	1	48	\$0.05–5.45
Stoops <i>et al.</i> 2003 [66]*	Within	Adult stimulant users	8	Methylphenidate	Magnitude	1	9	\$0.25–64
Walsh <i>et al.</i> 2010 [67]*	Within	Adult cocaine users	8	Cocaine	Magnitude	2	48	\$0.05–5.45

Sample size reflects combined sample for between-subjects studies; for all studies, the largest sample size analyzed was reported. Individual effect sizes for all indices reported in each study can be found in the Supporting information. For studies reporting the same demand index multiple times at various magnitudes (e.g. cigarette demand for cigarettes with low, medium and high amounts of nicotine), we only included effect sizes for the greatest magnitude difference to minimize violations of the assumptions of independence. Where two separate versions of a multiple-choice procedure or purchase task was used, the largest price range and number of prices were reported in the far-right columns.

\*These studies included a multiple-choice procedure and reported an effect size for cross-over point.

GHB = gamma hydroxybutyrate; THC = tetrahydrocannabinol.

Table 2

Meta-analytical results for the effect of each manipulation on changes in each demand index, random effects.

	k	d	SE	variance	Lower limit	Upper limit	Z-value	P-value	Heterogeneity statistics			
									Q	pQ	I <sup>2</sup>	
Cue exposure												
Intensity	6	0.29	0.09	0.01	0.12	0.45	3.35	0.001	18.12	0.003	72.41	
Breakpoint	6	0.33	0.08	0.01	0.18	0.48	4.34	<0.001	9.13	0.10	45.26	
O <sub>max</sub>	6	0.44	0.09	0.01	0.27	0.62	4.98	<0.001	12.89	0.02	61.22	
P <sub>max</sub>	5	0.25	0.12	0.01	0.02	0.48	2.09	0.04	11.94	0.02	66.49	
Elasticity	4	0.43	0.16	0.03	0.11	0.75	2.65	0.008	15.11	0.002	80.14	
Stress/negative affect												
Intensity	3	0.17	0.16	0.03	-0.14	0.49	1.08	0.28	16.25	<0.001	87.69	
Breakpoint	3	0.14	0.11	0.01	-0.08	0.36	1.26	0.21	6.54	0.04	69.40	
O <sub>max</sub>	3	0.18	0.08	0.007	0.01	0.34	2.13	0.03	3.41	0.18	41.39	
Elasticity	3	0.16	0.12	0.01	-0.07	0.39	1.35	0.18	8.01	0.03	75.00	
Reinforcer magnitude												
Cross-over Point	10	0.60	0.21	0.04	0.18	1.01	2.82	0.005	46.86	<0.001	80.80	
Pharmacotherapies												
Intensity	4	-0.49	0.24	0.06	-0.96	-0.02	-2.04	0.04	15.90	0.001	81.13	
Breakpoint	3	-0.37	0.17	0.03	-0.70	-0.04	-2.21	0.03	4.56	0.10	56.10	
Behavioral interventions												
Intensity	6	-10.13	0.32	0.10	-1.75	-0.51	-3.56	<0.001	84.42	<0.001	94.08	
O <sub>max</sub>	4	-0.48	0.20	0.04	-0.87	-0.09	-2.42	0.02	15.63	0.001	80.80	
Elasticity	5	-0.36	0.25	0.07	-0.86	0.14	-1.43	0.15	37.44	<0.001	89.32	
Opportunity costs												
Intensity	4	-1.42	0.45	0.20	-2.30	-0.54	-3.15	0.002	196.05	<0.001	98.47	

k = number of effect sizes; d = Cohen's d effect size; SE = standard error.

**Table 3**

Publication bias results for each manipulation, split by demand index.

	<b>k</b>	<b>Fail-safe n</b>	<b>Orwin's fail-safe n</b>	<b>Kendall's <math>\tau</math> (P-value)</b>	<b>Egger's test (P-value)</b>
<b>Cue exposure</b>					
Intensity	6	> 56	7	0.07 (0.85)	2.40 (0.05)
Breakpoint	6	> 53	7	0.33 (0.35)	2.29 (0.15)
O <sub>max</sub>	6	> 100	6	0.20 (0.57)	3.56 (0.08)
P <sub>max</sub>	5	> 13	5	0.40 (0.33)	1.31 (0.33)
Elasticity	4	> 27	5	1.00 (0.04)	5.42 (< 0.001)
<b>Stress/negative affect</b>					
Intensity	3	> 1	3	1.00 (0.12)	6.54 (0.02)
Breakpoint	3	> 1	4	0.33 (0.60)	6.57 (0.20)
O <sub>max</sub>	3	> 4	4	0.33 (0.60)	4.64 (0.33)
Elasticity	3	> 2	3	1.00 (0.12)	5.34 (0.09)
<b>Reinforcer magnitude</b>					
Cross-over point	10	> 65	10	0.24 (0.33)	1.78 (0.07)
<b>Pharmacotherapies</b>					
Intensity	4	> 26	5	1.00 (0.04)	6.97 (0.08)
Breakpoint	3	> 7	4	1.00 (0.12)	0.67 (0.15)
<b>Behavioral interventions</b>					
Intensity	6	> 170	7	-0.33 (0.35)	-7.05 (0.04)
O <sub>max</sub>	4	> 27	4	-0.67 (0.17)	-10.61 (0.25)
Elasticity	5	> 21	6	0.20 (0.62)	-0.33 (0.48)
<b>Opportunity costs</b>					
Intensity	4	> 344	5	-0.33 (0.50)	-9.46 (0.15)

*k* = number of effect sizes; *d* = Cohen's *d* effect size; SE = standard error.