Social Cognitive and Affective Neuroscience, 2020, 725–732

doi: 10.1093/scan/nsaa108
Advance Access Publication Date: 30 July 2020
Original Manuscript

Effects of acetaminophen on risk taking

Alexis Keaveney[1], Ellen Peters[2] and Baldwin Way[1]

[1]Department of Psychology, The Ohio State University, Columbus, OH 43210, USA and [2]School of Journalism and Communication, University of Oregon Eugene, OR 97403, USA

Correspondence should be addressed to Baldwin M. Way, Department of Psychology, The Ohio State University, 1835 Neil Avenue, Columbus, OH 43210, USA. E-mail: way.37@osu.edu

Abstract

Acetaminophen, an analgesic and antipyretic available over-the-counter and used in over 600 medicines, is one of the most consumed drugs in the USA. Recent research has suggested that acetaminophen's effects extend to the blunting of negative as well as positive affect. Because affect is a determinant of risk perception and risk taking, we tested the hypothesis that acute acetaminophen consumption (1000 mg) could influence these important judgments and decisions. In three double-blind, placebo-controlled studies, healthy young adults completed a laboratory measure of risk taking (Balloon Analog Risk Task) and in Studies 1 and 2 completed self-report measures of risk perception. Across all studies (total $n = 545$), acetaminophen increased risk-taking behavior. On the more affectively stimulating risk perception measure used in Study 2, acetaminophen reduced self-reported perceived risk and this reduction statistically mediated increased risk-taking behavior. These results indicate that acetaminophen can increase risk taking, which may be due to reductions in risk perceptions, particularly those that are highly affect laden.

Key words: NSAID; decision-making; risk perception; anti-inflammatory

Acetaminophen, the active ingredient in Tylenol® and nearly 600 other medicines, is taken each week by an estimated 23% of the US adult population (Kaufman *et al.*, 2002). Recent research has demonstrated that acetaminophen's effects on pain and fever reduction extend to psychological processes. For example, acetaminophen reduces hurt feelings (Dewall *et al.*, 2010), meaning threats (Randles *et al.*, 2013), distress over another's suffering (Mischkowski *et al.*, 2016), loss aversion (DeWall *et al.*, 2014) and affective reactivity to negatively valenced images (Durso *et al.*, 2015). In this latter study, acetaminophen also blunted affective reactivity to positively valenced images, suggesting that it may reduce affective reactivity more generally, rather than solely influencing negative experiences. Because risk judgments and decisions rely on both positive and negative affect (Loewenstein *et al.*, 2001; Slovic *et al.*, 2004), it is reasonable to hypothesize that acetaminophen may influence them.

Affect and decision-making

Work on the 'affect-heuristic' and 'risk-as-feelings' hypothesis have demonstrated a key role for affect in risk judgments and decisions (Loewenstein *et al.*, 2001; Slovic *et al.*, 2004). In particular, when faced with a complex decision, people often use their feelings about an option as information, substituting it for the more difficult probabilities and outcomes that accurately describe risks. This affect then serves as a simple cue, allowing people to avoid hazards quickly and efficiently. As a result, affect manipulations, perhaps including acetaminophen, should influence decisions about risks.

Received: 19 October 2019; **Revised:** 28 May 2020; **Accepted:** 24 June 2020

Affect heuristic and risk taking

The affect heuristic predicts that individuals will use affect as information to guide decisions, especially in risky tasks that are affectively stimulating and experientially engaging (Figner and Weber, 2011). The Balloon Analog Risk Task (BART; (Lejuez *et al.*, 2002)), for example, is such an experiential task; performance on it predicts drug and alcohol use, delinquent behavior and risky sexual behavior (e.g. (Lejuez *et al.*, 2004 2007; Aklin *et al.*, 2005)). The BART is a computerized task in which participants inflate balloons to earn money, but each pump risks them losing all of their prior earnings. The task is probabilistic although it does not provide explicit information about the probability of loss events. It is also visual and experiential, making it a strong candidate for a task in which participants are likely to use the affect heuristic.

Indeed, experimentally induced increases to participant's negative affect have reduced risk taking on the BART (Yuen and Lee, 2003; Heilman *et al.*, 2010; Parkinson *et al.*, 2012). This research suggests that negative affect experienced during the BART signals one to engage in less risk taking. Because the BART negative loss events are more visually and auditorily salient than its win events and because manipulations of negative affect had significant influences on task performance, it seems likely that negative affect toward potential or experienced losses exerts a stronger influence on BART decisions than does positive affect toward potential or experienced gains. Therefore, acetaminophen's blunting of negative affect may lead to a reduction in this negative affect signal and an increase in risk taking. These considerations led to our first hypothesis: Acetaminophen will increase risk taking on the BART (Hypothesis 1).

Affect heuristic and risk and benefit judgments

Affect-heuristic use also has also been explored in the context of risk and benefit judgments (Slovic and Peters, 2006). Individuals appear to rely on affect to infer the risks and benefits offered by activities and hazards. Objects that elicit positive affect, say alcoholic beverages, tend to be judged as having high benefits and low risks. Conversely, objects that elicit negative affect, say nuclear power, tend to be judged as low in benefit and high in risk. Because acetaminophen appears to reduce the extremity of affective reactions to stimuli, it may reduce perceived risk and perceived benefit of a behavior or policy. Therefore, our second hypothesis is: acetaminophen will reduce the negative affect elicited when considering potential risk, leading to reduced risk perception (Hypothesis 2A). The corollary of this hypothesis is that acetaminophen will reduce the positive affect elicited when considering potential benefits, leading to reduced benefit perception (Hypothesis 2B).

To test these hypotheses, we used an acute, double-blind, placebo-controlled, parallel-arm design with acute administration of the standard extra-strength dosage (1000 mg) of acetaminophen.

Study 1

Method

Participants. Participants were 142 undergraduate volunteers (76 men, 64 women, 2 nonresponses) with a mean age of 19.36 years (s.d. = 1.68). Sample size was determined a priori based on the expectation of a similar effect size as that found in previous acetaminophen and affect research (Durso *et al.*, 2015) and acetaminophen and decision-making research (DeWall *et al.*, 2014). All research reported herein was approved by the Ohio State University Institutional Review Board.

Acetaminophen. A double-blind, placebo-controlled design was used. Participants were randomly assigned to drug condition using a random number generator ($n = 69$ placebo, $n = 73$ acetaminophen). Participants were given a placebo or 1000 mg of acetaminophen, the recommended extra strength dosage for a headache and the dosage commonly used in studies of acetaminophen's psychological effects (Durso *et al.*, 2015). Acetaminophen and placebo solutions were prepared by Pharmacy Specialists Compounding Pharmacy (Altamonte Springs, Florida; http://www.makerx.com/). The drug solution consisted of acetaminophen (100 mg/ml) suspended in Ora-Plus suspension liquid and flavored with Fagron Simple Syrup. The placebo solution consisted of Avicel Microcrystalline powder (100 mg/ml) dissolved in Ora-Plus suspension liquid and flavored with Ora-Sweet Syrup. After consuming the assigned solution, participants were given a small cup of water to wash it down. At the conclusion of the experiment, participants were asked to guess which drug condition they were in (acetaminophen, placebo, or 'no idea'); thus, participants could opt out of guessing their condition, or guess between drug and placebo conditions, a 50% chance of guessing correctly. In the acetaminophen condition, 46.6% of participants correctly guessed which condition they were in (i.e. choosing 'acetaminophen' and not 'placebo' or 'no idea'). A one-sample t-test for proportions reveals that this was not significantly different from chance, $t = -0.58$, $P = 0.56$. In the placebo condition, 34.8% of participants correctly guessed which condition they were in (i.e. selecting 'placebo' and not 'acetaminophen' or 'no idea'), a proportion that was significantly worse than chance, $t = -2.64$, $P = 0.01$, suggesting that participants did not accurately predict their experimental condition (the most common response in this group was 'no idea', 41%).

Risk taking. To measure risk taking, the BART was used (Lejuez *et al.*, 2002). In this task, participants complete 30 trials, each of which includes 1–128 participant responses. A trial begins with a small, uninflated balloon on a computer screen. Participants can inflate the balloon, with each pump earning $0.05. Though they played this game for imaginary money, they were told their goal was to earn as much money as possible in the task. Participants can collect their total trial earnings and move them to a permanent bank at any point by pressing a button saying 'Collect $$$'. However, participants also are told that the balloon can burst as early as the first trial and as late as when the balloon fills the entire computer screen. Bursts are accompanied by a bursting sound and popping animation. If the balloon bursts prior to the participants pressing the 'Collect $$$' button, they lose any money earned thus far on that trial, and must move on to the next trial having added no money to their permanent bank.

Participants are not told about the maximum number of pumps, the likelihood of bursts, nor that, for each balloon, the first pump has a 1/128 probability of bursting, the second pump 1/127, and so on until on the 128th pump there is a 1/1 probability of bursting.

Risk and benefit perception. To assess acetaminophen's impact on use of the affect heuristic in risk judgments, participants

completed the risk and benefit perceptions questionnaire used by Finucane *et al.* (2000). Participants were asked to make risk and benefit judgments of various activities and technologies for US society as a whole. They made these judgments on a 7-point scale ranging from *not at all risky (beneficial)* to *very risky (beneficial)*. To enhance affect-heuristic use, participants were put under time pressure with a countdown clock on the screen while making judgments, with 5.2 s for each item (as in Finucane *et al.*, 2000). The scale consisted of 23 items (e.g. 'Pesticides', 'Nuclear Power Plants'), presented one at a time on the screen. Items were presented in randomized order. After completing ratings of all 23 items on the first scale (either risk or benefit), participants then received instructions for completing the second scale (benefit or risk), with all items presented again in a different random order. Order of the benefit and risk perception tasks was counter-balanced.

Procedure. After signing up for the experiment, participants received an email informing them that 'Half of the participants will receive a liquid dose of acetaminophen (i.e. Tylenol) and half of the participants will receive a liquid dose of placebo (i.e. a sugar pill or inactive liquid). Therefore, there is a 50% chance you will be in the group that receives acetaminophen'. The email informed them about the risk factors associated with acetaminophen (e.g. currently taking a drug containing acetaminophen, a history of liver disorder, an allergic reaction to acetaminophen, currently taking an anticoagulant, or a history of alcohol abuse) and asked them to refrain from participation if they met any of these risk factors. To facilitate drug absorption, we also asked participants to refrain from consuming food for three hours before the experiment. Upon arrival at the laboratory and after providing informed consent (which repeated the information in the email described above), participants consumed either the drug or placebo, based on random assignment. To allow for sufficient drug uptake into the brain (Singla *et al.*, 2012), we waited 45 min to begin the main tasks of the study. During drug uptake, participants completed a number of background personality and health measures. At 45 min, participants began completing decision-making tasks. At approximately 50 min after the drug consumption, participants completed the risk and benefit perception task using the online survey program Qualtrics (Qualtrics, Provo, UT). Immediately following and approximately 60 min after the drug consumption, participants completed the BART task, implemented using the Psychology Experiment Building Language (PEBL) package and prepackaged BART script (Mueller and Piper, 2014; http://pebl.sourceforge.net/). Following the BART, participants answered a short survey, which included demographic information, then were debriefed and thanked.

Results

Risk-taking main effect. To analyze the BART data, we computed participants' adjusted average number of pumps across the 30 trials, according to methods in prior work (Lejuez *et al.*, 2002). Specifically, trials on which a balloon burst occurred were excluded, as the number of pumps completed on this trial reflected balloon bursts rather than the participant's desired amount of risk taking had a burst not occurred. After those trials were excluded, averages across the remaining trials were computed.

Consistent with our first hypothesis that acetaminophen would increase BART risk taking, a t-test revealed a significant difference in risk taking between those on acetaminophen and those on placebo, $t(140) = -2.29$, $P = 0.023$, 95% CI [−10.94, − 0.81], Cohen's $d = 0.38$ (Figure 1A, left panel). As hypothesized, those in the placebo condition engaged in significantly less risk taking as indexed by adjusted average number of pumps ($M = 33.10$, s.d. = 15.75) than those on acetaminophen ($M = 38.98$, s.d. = 14.80). Hierarchical linear modeling techniques demonstrated similar results, but did not identify further psychological mechanisms driving these effects (see supplementary material). There was also a significant difference ($t(140) = -2.02$,

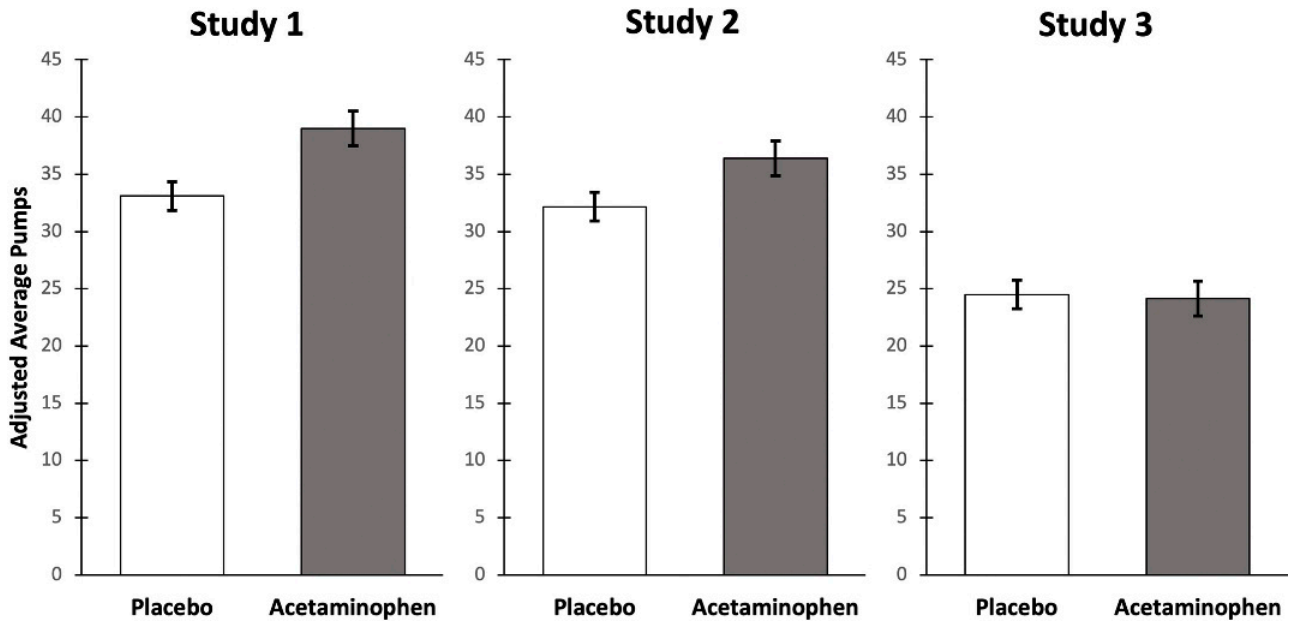


Fig. 1. Graphs of the adjusted average number of pumps for each study (error bars denote standard error of the mean). In Studies 1, 2 and the combined analysis of all three studies, the acetaminophen group had significantly more adjusted average pumps.

$P = 0.045$, 95% CI [−2.95, −0.033]) in the number of balloons that burst as a function of drug condition with more balloons bursting in the acetaminophen condition ($M = 10.07$, s.d. = 4.13) than the placebo condition ($M = 8.58$, s.d. = 4.64).

Risk and benefit perception. To assess risk perception, average ratings were computed across the 23 items. The same process was used for benefit perception. Our second hypothesis that acetaminophen would decrease risk and benefit perceptions was not supported. A t-test for average risk perception revealed no significant difference between drug conditions, $t(140) = 1.48$, $P = 0.14$, 95% CI [−0.05, 0.34]. Descriptively, those on placebo perceived more risk ($M = 3.93$, s.d. = 0.62) than those on acetaminophen ($M = 3.78$, s.d. = 0.56). A t-test for average benefit perception also revealed no significant difference between drug conditions, $t(140) = 0.74$, $P = 0.46$, 95% CI [−0.13, 0.28]. Descriptively, those on placebo perceived more benefit ($M = 4.58$, s.d. = 0.61) than those on acetaminophen ($M = 4.50$, s.d. = 0.62). We also examined acetaminophen's impact on the correlation between risk and benefit judgments; these analyses are described in the supplementary online material.

Study 1 discussion

Study 1 provided initial support for our first hypothesis; those on acetaminophen, relative to placebo, engaged in significantly more risk taking on the BART. Little evidence emerged, however, for our second hypothesis that acetaminophen would reduce risk and benefit perceptions. We speculated that our participants perceived these items to be less affectively stimulating than those in the original Finucane *et al.* (2000) affect-heuristic study. Indeed, in our placebo group, negative correlations between risk and benefit perceptions were obtained ($r = -0.23$), but were much weaker than those in the same time-pressure condition of the original study ($r = -0.80$). If participants had weaker negative affect to these risks in our study, acetaminophen may not have exerted much effect on judgments because acetaminophen has weaker effects on stimuli that are less affective compared to more affective (Durso *et al.*, 2015).

Study 2

In Study 2, we attempted a direct replication with the BART task and used a risk-perception scale with items that may be more affectively stimulating than those of Study 1 to re-test our second hypothesis.

Method

Participants. One-hundred eighty-nine undergraduates volunteered (109 men, 79 women, 1 nonresponse) and had a mean age of 19.49 years (s.d. = 2.89). We aimed for 200 participants based on a power analysis of Study 1 (Cohen's $d = 0.38$); data collection ended at the end of the semester.

Acetaminophen. As in Study 1, we used a double-blind, placebo-controlled design with random assignment to 1000 mg of acetaminophen or placebo ($n = 95$ and 94, respectively). Participants were asked to guess which drug condition they were in (acetaminophen or placebo). A total of 54.7% of participants in the acetaminophen condition correctly guessed which condition they were in, a proportion that was not significantly different from chance, $t = 0.92$, $P = 0.36$. A total of 52.1% of participants in the placebo condition correctly guessed which condition they were in, a proportion that was not significantly different than chance, $t = 0.41$, $P = 0.68$.

BART. The same behavioral measure of risk taking, the BART, was used in Study 2. Participants completed 30 trials. Following this, participants answered self-report questions about their experience and perception of balloon bursts during the task (see supplementary material for full materials and analysis).

Risk and benefit perceptions. To examine acetaminophen's effect on risk and benefit perceptions, we used the revised Domain Specific Risk-Taking Scale (DOSPERT; Blais and Weber, 2006). This 30-item scale provides behavioral scenarios (e.g. 'Betting a day's income on the outcome of a sporting event') for which participants were then asked for their gut-level perception of the riskiness of each behavior as well as the expected benefits that would be obtained from enacting each behavior. Participants responded on a 7-point scale ranging from *not at all risky (no benefits at all)* to *extremely risky (great benefits)*. Because these items are more experientially descriptive and participants are asked to judge risk and benefit personally rather than for society, we thought they would be more affectively stimulating than Study 1's items. We found support for this hypothesis in an additional study described in the supplemental materials. In brief, the DOSPERT items were rated as significantly more emotional and negative than the Finucane items. Participants also reported feeling more worried when thinking about those items than the Finucane items.

The DOSPERT scale can be analyzed both for general risk and benefit perceptions as well as domain-specific perceptions in ethical ('passing off somebody else's work as your own'), financial ('betting a day's income at a high-stake poker game'), health ('driving a car without a seatbelt'), recreational ('Bungee jumping off a tall bridge B') and social ('moving to a city far away from your extended family') domains. We analyzed the data for average risk/benefit overall and separately within each of the five domains.

Procedure. Study 2's procedure was nearly identical to Study 1 and used the same software. Participants gave informed consent, consumed drug or placebo, and waited 45 min while completing background measures. Approximately 50 min after drug administration, participants completed the DOSPERT. Following this and approximately 60 min after drug administration, participants completed the BART, followed by the self-report items concerning recalled affective experience during the BART task (see supplemental material).

Results

Risk-taking main effect. As in Study 1, we computed participants' adjusted average number of pumps across the 30 trials. A t-test revealed a significant difference in risk taking between those on placebo and those on acetaminophen, $t(187) = -2.14$, $P = 0.033$, 95% CI [−8.11, −0.34], Cohen's $d = 0.31$. Those on acetaminophen ($M = 36.38$, s.d. = 14.79) engaged in significantly more risk taking than those on placebo ($M = 32.15$, s.d. = 12.14) (Figure 1, middle panel), thus replicating Study 1's effect. As in Study 1, more balloons burst in the acetaminophen condition ($M = 9.54$, s.d. = 4.29) than the placebo condition ($M = 8.73$,

s.d. = 4.43). However, the difference was not statistically significant ($t(187) = -1.27$, $P = 0.21$, 95% CI [−2.06, 0.45]).

Risk and benefit perception. To test the second hypothesis that acetaminophen would decrease risk and benefit perceptions, we used t-tests to compare placebo and acetaminophen groups' summed risk and summed benefit perception across all 30 DOSPERT items, as is typically done when analyzing the DOSPERT scale. A t-test revealed a significant difference in risk perception between conditions, $t(187) = 2.72$, $P = 0.007$, 95% CI [1.93, 12.19], Cohen's $d = 0.40$. Those on acetaminophen ($M = 133.89$, s.d. = 18.03) perceived significantly less risk than those on placebo ($M = 140.96$, s.d. = 17.71). Thus, Hypothesis 2A was supported for risk perceptions. When analyzed separately by domain, this effect held for risk perception in the social ($P = 0.005$) and recreational ($P = 0.025$) domains was marginally significant in the financial ($P = 0.069$) domain and was nonsignificant but in the hypothesized direction in the health ($P = 0.12$) and ethical ($P = 0.67$) domains.

For benefit perception (Hypothesis 2B), a t-test revealed no significant difference in summed benefit perception between conditions, $t(187) = 0.10$, $P = 0.92$, 95% CI [−4.85, 5.35]; this null effect existed for each of the five domains when analyzed separately. Thus, Hypothesis 2B was not supported.

Risk-taking mediation. The finding that acetaminophen significantly reduced perceived risk (measured with the DOSPERT) could account for the drug's effect on BART risk taking. We explored whether acetaminophen's effect on risk taking was mediated by the drug's effect on DOSPERT risk perception by using PROCESS Model 4 (Hayes, 2012). This analysis revealed a significant indirect effect of acetaminophen on risk taking through risk perception (point estimate: 0.88, 95% bootstrap CI = 0.14 to 2.31); acetaminophen no longer had a direct effect on risk taking (direct effect = 3.34, $P = 0.09$, 95% CI = −0.58 to 7.26). No evidence existed of an indirect effect through benefit perception (point estimate: −0.03, 95% bootstrap CI = −0.88 to 0.66).

Study 2 discussion

Study 2 replicated and extended Study 1's risk-taking result: Again, acetaminophen increased risk taking, supporting our first hypothesis. Furthermore, there was also support for hypothesis 2A: acetaminophen reduced risk perceptions (but not benefit perceptions) on the DOSPERT. These effects of acetaminophen on risk perceptions in Study 2, but not Study 1, are likely due to the greater negative emotion elicited by the DOSPERT items than Finucane *et al.* (2000) items (see supplementary material for the aforementioned additional study demonstrating greater emotionality of the DOSPERT items).

In addition, the acetaminophen-caused reduction in risk perceptions mediated increased risk taking on the BART, suggesting that acetaminophen may reduce negative affect to options and thereby how risky they seem.

Study 3

The goal of Study 3 was to replicate and extend Study 2.

Method

Participants. Two-hundred fifteen undergraduates volunteered (91 men, 122 women, 1 selected 'prefer not to answer') and had a mean age of 19.49 years (s.d. = 2.89). Like in Study 2, we aimed for 200 participants; data collection ended at the end of the semester. The sample was 69% white, 10% Asian, 8% Black or African American, and 14% Mixed race or some other origin.

Drug preparation. As in the prior studies, we used a double-blind, placebo-controlled design with random assignment to 1000 mg of acetaminophen or placebo ($n = 109$ and 106, respectively). It should be noted that a different preparation procedure and vehicle were used for acetaminophen administration than in the prior studies. Drug suspension was prepared in the laboratory by adding 40g of acetaminophen powder with 0.6 g Vivasol® GF to 400 ml of Flavor Blend™ suspending vehicle from which 10 ml (1000 mg) aliquots were administered to participants. Placebo solutions were prepared in the same manner by adding 40 g of Avicel® PH-105 microcrystalline cellulose powder with 0.6 g Vivasol® GF to 400 ml of Flavor Blend™ suspending vehicle. All products were prepared and provided by Pharmacy Specialists Compounding Pharmacy (Altamonte Springs, Florida; http://www.makerx.com/).

Procedure. The procedure was similar to prior studies. After consenting and consuming drug or placebo, participants completed background questionnaires. At least 45 min later, participants completed two tasks (Columbia Card Task (Figner *et al.*, 2009) and the Iowa Gambling task (Bechara *et al.*, 1994); these data have not been analyzed and will be reported separately) followed by the BART. A different software platform (Inquisit, www.millisecond.com) was used to implement the BART. An additional change in procedure was that after the first 15 balloons, participants completed the same self-report items as in Study 2, which were repeated after the final 15 balloons. Participants did not complete any self-reported risk perception items in this study.

Results and discussion

Unlike the prior studies, participants in the acetaminophen condition were better at guessing their condition; 61.2% correctly guessed their condition, a proportion significantly better than chance, $t = 2.45$, $P = 0.02$.

As measured by the average number of pumps on nonbursting trials, we did not find a significant difference in risk taking on the BART between the acetaminophen ($M = 24.13$, s.d. = 12.56) and placebo condition ($M = 24.49$, s.d. = 13.30), $t(213) = 0.20$, $P = 0.84$, 95% CI [−3.11, 3.83] in this study (Figure 1, right panel). Although we thought it plausible that guessed drug condition might have predicted performance, according to an ANOVA, no main effect existed of guessed drug condition ($F(1,210) = 1.59$, $P = 0.21$) nor was there an interaction effect of guessed drug condition ($F(1,210) = 0.32$, $P = 0.57$) with actual drug condition (one subject did not guess condition). There was a greater number of balloon bursts in the acetaminophen ($M = 6.56$, s.d. = 3.60) than the placebo condition ($M = 6.17$, s.d. = 3.47); however, the difference was not significant ($t(213) = -.81$, $P = 0.42$, 95% CI [−1.34, 0.56]).

It should be noted that the average number of pumps in this study (across both conditions), which used the Inquisit software ($M = 24.31$, s.d. = 12.90) was significantly less ($F(2,543) = 39.88$,

$P < 0.0001$) than that from the prior two studies that used the PEBL software (Study 1, $M = 36.12$ s.d. $= 15.50$; Study 2 $M = 34.28$, s.d. $= 13.66$). Similarly, the number of bursts in this study ($M = 6.37$, s.d. $= 3.53$) was significantly lower ($F(2,543) = 2185.73$, $P < 0.001$) than those in the prior two studies (Study 1: $M = 9.35$, s.d. $= 4.34$; Study 2: $M = 9.14$, s.d. $= 4.37$). Consistent with these differences, significant differences existed in earnings ($F(2,545) = 31.5$, $P < 0.001$), with lower earnings in Study 3 (Study 1: $M = \$34.27$, s.d. $= 10.14$ Study 2: $M = \$34.02$, s.d. $= 10.37$; Study 3: $M = \$26.53$, s.d. $= 11.95$).

Combined analysis of studies 1, 2 and 3

As compilation of results across studies can lead to improved interpretation of effects (Braver *et al.*, 2014; Fabrigar and Wegener, 2016), we combined data from all three studies. In this compilation, there was a significant main effect of acetaminophen on BART risk taking ($t(544) = -2.26$, $P = 0.024$, 95% CI [−5.35, −0.38], Cohen's $d = 0.19$) with a greater average number of pumps on nonbursting balloons in the acetaminophen condition ($M = 32.24$, s.d. $= 15.40$) than the placebo condition ($M = 29.37$, s.d. $= 14.11$). Consistent with the acetaminophen group engaging in greater risk taking, there was a greater number of balloon bursts ($t(544) = -2.237$, $P = 0.026$, 95% CI [−1.543, −0.100]) in the acetaminophen condition ($M = 8.51$, s.d. $= 4.28$) than the placebo condition ($M = 7.68$, s.d. $= 4.30$). This provides strong evidence that acetaminophen increases risk-taking on the BART.

General discussion

Across three separate studies, acetaminophen increased risk taking on the BART. In Study 2, acetaminophen also reduced perceived risk on the DOSPERT, and this experimentally induced reduction in perceived risk accounted for increased risk taking on the BART, suggesting acetaminophen may reduce negative affect and risk perception in turn and, thereby, increase risk taking.

Acetaminophen did not reduce risk perceptions using the Finucane items (Study 1) in contrast to the effects seen with the DOSPERT risk perception items (Study 2). Motivated by prior work showing that acetaminophen has greater effects on affective stimuli rated to be more extreme in negative or positive valence than less extreme stimuli (Durso *et al.*, 2015), our additional online study (see supplementary material) provided evidence that Study 2's items were more affectively stimulating (e.g. they were rated more emotional and negative) than Study 1's items These findings provide initial evidence that acetaminophen can influence risk judgments, especially for more affectively stimulating stimuli.

Interestingly, although acetaminophen significantly reduced perceived risk in Study 2, it did not reduce perceived benefit. One potential explanation for the lack of effect on benefit items is that their phrasing may have elicited more cognitive evaluation, whereas the risk questions may have been more affectively stimulating. The risk questionnaire asked participants to rate 'your gut level assessment of how risky each situation or behavior is' whereas the benefit scale asks for 'the benefits you would obtain from each situation'. An emphasis on gut level risk assessment may increase reliance on the affect heuristic. This difference may account for Study 2's acetaminophen-caused reduced risk perceptions and its lack of effect on perceived benefits.

Although not all studies were independently significant, when treated in aggregate, a significant relation emerged between taking acetaminophen and choosing more risk. Multiple studies with effects in the same direction, even if not significant, reduce the probability that the population effect is zero (Braver *et al.*, 2014; Fabrigar and Wegener, 2016), suggesting that this is a reliable effect. Potential factors contributing to the lack of an effect in Study 3 could be the different drug formulation that led to greater awareness of drug condition as well as the differences in software used to implement the BART. Each inflation of the balloon using the software in Study 3 was larger, leading to fewer pumps being necessary to fill the screen and thus less overall pumps and bursts. Such reduced range may have impaired the ability to detect a drug effect.

Another consideration is whether or not playing the BART with actual money would have changed the results. Although some controversy exists about the differential role of hypothetical relative to monetary reinforcers on decision-making tasks (Johnson and Bickel, 2002; Madden *et al.*, 2003; Hinvest and Anderson, 2010), it appears that when real monetary reinforcers have differential effects they tend to amplify the differences between conditions (Bowman and Turnbull, 2003). For example, large monetary losses in a modified form of the BART led to greater neural reactivity and reductions in risk behavior than hypothetical losses (Xu *et al.*, 2018). Thus, employing a BART with real money could potentially enhance the effects of acetaminophen.

Future directions

In addition to decreases in risk perception, other psychological processes are likely involved in acetaminophen's effects on risk taking. One possible unexplored mechanism is anticipatory experienced anxiety. It may be that as the balloon increases in size, those on placebo feel increasing amounts of anxiety about a potential burst. When the anxiety becomes too much, they end the trial. Acetaminophen may reduce this anxiety, thus leading to greater risk taking. As indicated in the supplement, self-reported affective experiences to the BART did not differ between conditions, but these recalled emotions may not reflect affective responses experienced in the moment.

Additionally, there are many potentially interesting ways in which we might examine the impact of risk taking on tasks that involve stronger positive affect. It may be the case that risk-taking tasks that focus on the positive affect associated with gains may actually show reverse effects of acetaminophen due to acetaminophen's affect-blunting effects. For instance, if we manipulated the BART to make gain events more salient (adding sounds and visuals) or more intense (larger payoffs), acetaminophen may decrease risk taking.

Alternatively, acetaminophen's effects on risk taking may be driven less by affective influences on judgment than by effects on another psychological process such as learning during the task (Pearson *et al.*, 2018) or error monitoring. Event-related potentials (ERPs) recorded during a Go/No-Go task, for example, showed that acetaminophen reduced the error positivity (Pe), which partially mediated acetaminophen-induced increases in omission errors (Randles *et al.*, 2016). The Pe is a signal that appears to be associated with the emergence of conscious awareness of committing an error (Nieuwenhuis *et al.*, 2001; Murphy *et al.*, 2012) and highly correlated with activity in the anterior insula (Ullsperger *et al.*, 2010). Of note, the association of greater anterior insula activation with anticipated risk is one of the most reliable findings in the neural decision-making literature (Knutson and Huettel, 2015). Because acetaminophen

blunts activity in the anterior insula (Dewall *et al.*, 2010) as well as the Pe, it may be influencing risk-related processing particularly at a conscious level. Dissecting such influences on the BART could provide insight into additional psychological mechanisms accounting for the drug-induced increase in risk taking.

Another question for future research will be identifying the biological mechanisms responsible for these effects of acetaminophen. Like more conventional nonsteroidal anti-inflammatory drugs (NSAIDs) such as ibuprofen and aspirin, acetaminophen inhibits the production of prostaglandins in the brain (Flower and Vane, 1972). The administration of such drugs might provide insight into whether the prostaglandins are involved in risk judgments as well as which enzymes producing prostaglandins (cyclooxygenase 1 and cyclooxygenase 2) are greater contributors to the effect. Alternatively, acetaminophen may exert its effects on risk taking through a different biological pathway than the prostaglandins, potentially through the vanilloid, cannabinoid or serotoninergic systems (Graham *et al.*, 2013).

Potential implications

With nearly 25% of the population consuming acetaminophen each week (Kaufman *et al.*, 2002), reduced risk perceptions and increased risk taking could have important societal effects. Many areas of daily life require making decisions that involve the processes examined here. For example, many patients in the hospital have acetaminophen in their systems when presented with risk information and asked to make potentially life-changing risk assessments such as whether or not to do an invasive surgery. Similarly, when driving, one is regularly presented with decisions that involve risk perception and assessment. Thus, it is imperative that we understand acetaminophen's effects on choices made and risks taken. Risk perception and risk taking are judgments and decisions that can affect many aspects of our lives, and this common, over-the-counter drug may influence this process, unbeknownst to the millions taking the drug.

Acknowledgements

We would like to acknowledge the helpful assistance of Liv Bobb, Amanda Brown, Brittany Boltz, Michael Butrey, Japera Benson, Nicole Hadjisofocli, Catie Johnson, Elianna Miller, Cori O'Boyle, Maggie Walsh and Zachary Weisenseel.

Supplementary data

Supplementary data are available at *SCAN* online.

Open practices

The consent form completed by participants in these studies stated, 'Only the investigators and their research assistants will have access to the original research data'. As a consequence, we cannot share the original data publicly at this time. However, for anyone interested in accessing the data for verifying our analyses, please contact the authors. Study 1 (https://osf.io/p2e5c/) and the online study reported in the supplemental material (https://osf.io/496rc/) were preregistered with the Open Science Framework.

Funding

This research was generously supported by funds from the Ohio State University as well as the National Science Foundation (Award #1558230; Peters (PI), Way (Co-I)). The funders had no influence on the design, collection, analysis and interpretation of the data, writing of the report and decision to submit this article for publication.

Conflict of interest

The authors do not have any conflicts of interest.

References

Aklin, W.M., Lejuez, C.W., Zvolensky, M.J., et al. (2005). Evaluation of behavioral measures of risk taking propensity with inner city adolescents. *Behaviour Research and Therapy*, *43*, 215–28.

Bechara, A., Damasio, A.R., Damasio, H., et al. (1994). Insensitivity to future consequences following damage to human prefrontal cortex. *Cognition*, *50*, 7–15.

Blais, A.-R., Weber, E.U. (2006). A domain-specific risk-taking (DOSPERT) scale for adult populations. *Judgment and Decision Making*, *1*, 33–47.

Bowman, C.H., Turnbull, O.H. (2003). Real versus facsimile reinforcers on the Iowa Gambling Task. *Brain and Cognition*, *53*, 207–10.

Braver, S.L., Thoemmes, F.J., Rosenthal, R. (2014). Continuously cumulating meta-analysis and replicability. *Perspectives on Psychological Science*, *9*, 333–42.

DeWall, C.N., Chester, D.S., White, D.S. (2014). Can acetaminophen reduce the pain of decision-making? *Journal of Experimental Social Psychology*. *56*, 117–120.

Dewall, C.N., Macdonald, G., Webster, G.D., et al. (2010). Acetaminophen reduces social pain: behavioral and neural evidence. *Psychological Science*, *21*, 931–7.

Durso, G.R.O., Luttrell, A., Way, B.M. (2015). Over-the-counter relief from pains and pleasures alike: acetaminophen blunts evaluation sensitivity to both negative and positive stimuli. *Psychological Science*, *26*, 750–8.

Fabrigar, L.R., Wegener, D.T. (2016). Conceptualizing and evaluating the replication of research results. *Journal of Experimental Social Psychology*, *66*, 68–80.

Figner, B., Mackinlay, R.J., Wilkening, F., et al. (2009). Affective and deliberative processes in risky choice: age differences in risk taking in the Columbia Card Task. *Journal of Experimental Psychology. Learning, Memory, and Cognition*, *35*, 709.

Figner, B., Weber, E.U. (2011). Who takes risks when and why? Determinants of risk taking. *Current Directions in Psychological Science*, *20*, 211–6.

Finucane, M.L., Alhakami, A., Slovic, P., et al. (2000). The affect heuristic in judgments of risks and benefits. *Journal of Behavioral Decision Making*, *13*, 1–17.

Flower, R.J., Vane, J.R. (1972). Inhibition of prostaglandin synthetase in brain explains the anti-pyretic activity of paracetamol (4-acetamidophenol). *Nature*, *240*, 410–1.

Graham, G.G., Davies, M.J., Day, R.O., et al. (2013). The modern pharmacology of paracetamol: therapeutic actions, mechanism of action, metabolism, toxicity and recent pharmacological findings. *Inflammopharmacology*, *21*, 201–32.

Hayes, A.F. (2012). *PROCESS: A Versatile Computational Tool for Observed Variable Mediation, Moderation, and Conditional Process Modeling*. KS: University of Kansas.

Heilman, R.M., Crişan, L.G., Houser, D., et al. (2010). Emotion regulation and decision making under risk and uncertainty. *Emotion*, *10*, 257.

Hinvest, N.S., Anderson, I.M. (2010). The effects of real versus hypothetical reward on delay and probability discounting. *The Quarterly Journal of Experimental Psychology*, *63*, 1072–84.

Johnson, M.W., Bickel, W.K. (2002). Within-subject comparison of real and hypothetical money rewards in delay discounting. *Journal of the Experimental Analysis of Behavior*, *77*, 129–46.

Kaufman, D.W., Kelly, J.P., Rosenberg, L., et al. (2002). Recent patterns of medication use in the ambulatory adult population of the United States. *JAMA: The Journal of the American Medical Association*, *287*, 337–44.

Knutson, B., Huettel, S.A. (2015). The risk matrix. *Current Opinion in Behavioral Sciences*, *5*, 141–6.

Lejuez, C.W., Aklin, W., Daughters, S., et al. (2007). Reliability and validity of the youth version of the balloon analogue risk task (BART–Y) in the assessment of risk-taking behavior among inner-city adolescents. *Journal of Clinical Child and Adolescent Psychology*, *36*, 106–11.

Lejuez, C.W., Read, J.P., Kahler, C.W., et al. (2002). Evaluation of a behavioral measure of risk taking: the Balloon Analogue Risk Task (BART). *Journal of Experimental Psychology Applied*, *8*, 75–84.

Lejuez, C.W., Simmons, B.L., Aklin, W.M., et al. (2004). Risk-taking propensity and risky sexual behavior of individuals in residential substance use treatment. *Addictive Behaviors*, *29*, 1643–7.

Loewenstein, G.F., Weber, E.U., Hsee, C.K., et al. (2001). Risk as feelings. *Psychological Bulletin*, *127*, 267–86.

Madden, G.J., Begotka, A.M., Raiff, B.R., et al. (2003). Delay discounting of real and hypothetical rewards. *Experimental and Clinical Psychopharmacology*, *11*, 139–45.

Mischkowski, D., Crocker, J., Way, B.M. (2016). From painkiller to empathy killer: acetaminophen (paracetamol) reduces empathy for pain. *Social Cognitive and Affective Neuroscience*, *11*, 1345–53.

Mueller, S.T., Piper, B.J. (2014). The psychology experiment building language (PEBL) and PEBL test battery. *Journal of Neuroscience Methods*, *222*, 250–9.

Murphy, P.R., Robertson, I.H., Allen, D., et al. (2012). An electrophysiological signal that precisely tracks the emergence of error awareness. *Frontiers in Human Neuroscience*, *6*, 65.

Nieuwenhuis, S., Ridderinkhof, K.R., Blom, J., et al. (2001). Error-related brain potentials are differentially related to awareness of response errors: evidence from an antisaccade task. *Psychophysiology*, *38*, 752–60.

Parkinson, B., Phiri, N., Simons, G. (2012). Bursting with anxiety: adult social referencing in an interpersonal Balloon Analogue Risk Task (BART). *Emotion*, *12*, 817.

Pearson, R., Koslov, S., Hamilton, B., et al. (2018). Acetaminophen enhances the reflective learning process. *Social Cognitive and Affective Neuroscience*, *13*, 1029–35.

Randles, D., Heine, S.J., Santos, N. (2013). The common pain of surrealism and death: acetaminophen reduces compensatory affirmation following meaning threats. *Psychological Science*, *24*, 966–73.

Randles, D., Kam, J.W., Heine, S.J., et al. (2016). Acetaminophen attenuates error evaluation in cortex. *Social Cognitive and Affective Neuroscience*, *11*, 899–906.

Singla, N.K., Parulan, C., Samson, R., et al. (2012). Plasma and cerebrospinal fluid pharmacokinetic parameters after single-dose administration of intravenous, oral, or rectal acetaminophen. *Pain Practice*, *12*, 523–32.

Slovic, P., Finucane, M.L., Peters, E., et al. (2004). Risk as analysis and risk as feelings: some thoughts about affect, reason, risk, and rationality. *Risk Analysis: An International Journal*, *24*, 311–22.

Slovic, P., Peters, E. (2006). Risk perception and affect. *Current Directions in Psychological Science*, *15*, 322–5.

Ullsperger, M., Harsay, H.A., Wessel, J.R., et al. (2010). Conscious perception of errors and its relation to the anterior insula. *Brain Structure & Function*, *214*, 629–43.

Xu, S., Pan, Y., Qu, Z., et al. (2018). Differential effects of real versus hypothetical monetary reward magnitude on risk-taking behavior and brain activity. *Scientific Reports*, *8*, 1–9.

Yuen, K.S., Lee, T.M. (2003). Could mood state affect risk-taking decisions? *Journal of Affective Disorders*, *75*, 11–8.

Effects of Acetaminophen on Risk Taking: Online Supplement

Alexis Keaveney, Ellen Peters, and Baldwin Way

The Ohio State University

Table of Contents

Supplemental Online Study: Comparing DOSPERT and Finucane Risk Perception Scales:

Do the risk items on the DOSPERT elicit greater affective reactions than those used by Finucane and colleagues?

To test of the prediction that the DOSPERT items (Blais and Weber, 2006) were more affectively stimulating than the Finucane items (Finucane *et al.*, 2000), we recruited 202 participants on Amazon's Mechanical Turk (mTurk) website. The sample was 48% Female, with 89% having attended at least one year of post-high school education, and an average age of 22 (SD = 1.91 years; ranging from 18 to 27). Of the 202 participants, 77% resided in North America, 15% in India, 5% in Europe and then one participant each from Kenya, Jamaica, Mexico, Nepal, and the Philippines.

After consenting, participants rated each of the 23 items used in Study 1 that came from Finucane et al. (2000) as well as the 30 DOSPERT items used in Study 2. The Finucane and DOSPERT items were presented in blocks, which were presented in randomized order. After each item, participants responded on a 7-point scale (1=*not at all* to 7=*very*) to each of the following four questions: "How emotional do you feel when thinking about this?", "How vividly can you imagine this?", "How worried or concerned would you feel about this?", and "How does thinking about this make you feel?" (from very negative (-3) to very positive (+3)). Participants responded to each of the four questions before progressing to the next item. After rating the 53 items used in Studies 1 and 2 on each of the 4 questions, participants were thanked and paid ($1).

Results and Discussion. According to paired t-tests (Supplemental Table 1), the DOSPERT items were perceived as significantly more emotional and more negative. Participants also reported feeling more worried when thinking about them compared to the Finucane items (all *p's* <.001). However, participants reported being able to more vividly imagine the Finucane

items than the DOSPERT ones ($p < .001$). Thus, the DOSPERT scale appears to evoke more emotional response, though not more vivid imagination. The stronger effect of acetaminophen on ratings of riskiness for the DOSPERT items (Study 2) than the Finucane items (Study 1) is consistent with acetaminophen having more robust effects on more affectively stimulating stimuli (Durso *et al.*, 2015).

Supplementary Table 1**.**

Attribute	DOSPERT items	Finucane items
Emotion	4.30 (1.12)***	3.24 (1.35)
Vividness	4.51 (1.14)	4.86 (1.09)***
Worry	4.61 (0.94)***	3.21 (1.03)
Valence	3.47 (0.78)***	4.24 (0.58)

Means and standard deviations (in parentheses) of responses to DOSPERT and Finucane Scales (n=202). All differences were significant at the p < .001 level (denoted by ***) according to paired t-test.

Studies 1 and 2 Additional Analyses and Results

Correlation between risk and benefit

Although in the real world, risk and benefit tend to be positively correlated such that objects or behaviors that are associated with greater risk are often also associated with greater benefit, risk and benefit seem to be negatively correlated in people's minds (Fischhoff *et al.*, 1978). It has since been demonstrated that the strength of one's affective reaction to the judged object predicts the inverse relationship between perceived risk and perceived benefit (Alhakami and Slovic, 1994). Thus, in addition to our hypothesis that acetaminophen may reduce the perceived risk and benefit, we also considered the possibility that acetaminophen would reduce the correlation between perceived risk and perceived benefit that results from the use of the affect heuristic.

Study 1 risk and benefit correlation. As in Finucane et al. (Finucane *et al.*, 2000), within the placebo group, 22 of the 23 items showed negative correlations between perceived risk and perceived benefit, though these were substantially weaker than the correlations in the Finucane study (average r = -.23 in the placebo group in present study compared to average r = -.80 in Finucane's congruent time-pressure condition). The correlations between risk and benefit perception for each item, separated by drug condition, can be found in Supplementary Table 2. To assess whether acetaminophen reduced the inverse relationship between perceived risk and perceived benefit, we used a moderation approach. Average perceived risk was used to predict average perceived benefit, and then we tested whether this relationship was moderated by drug condition. PROCESS Model 1 was used (Hayes, 2012). This revealed a non-significant interaction between risk perception and drug condition predicting benefit perception, b = -0.07, $t(138)$ = -0.37, p =0.71. Thus, the correlation between average risk rating and average benefit rating did not depend on drug condition.

We also examined this interaction for each individual item on the 23-item scale. The interaction between drug condition and risk perception predicting benefit perception was non-significant for all items, except solar power, b = 0.43, $t(138)$ = 2.31, p =0.02. For solar power, risk rating significantly inversely predicted benefit rating for those on placebo, b = -0.50, $t(67)$ = -4.46, p <.001, but risk rating did not significantly predict benefit rating for those on acetaminophen, b = -0.07, $t(71)$ = -0.49, p = .62. Overall, no support existed for the hypothesis that acetaminophen would dampen the inverse relationship between risk and benefit perception. Supplementary Table 2.

Scale Item	Placebo	Acetaminophen	Interaction p-value
Alcoholic Beverages	-.09	-.34**	.12
Water Fluoridation	-.31*	-.60**	.05
Chemical Plants	-.20†	-.21†	.94
Eating Beef	-.40**	-.46**	.45
Food Preservatives	-.28*	-.31*	.93
Cars	-.35**	-.08	.12
Cigarettes	-.16	-.44**	.38
Pesticides	-.29*	-.27*	.94
Natural Gas	-.24†	-.20†	.75
Chemical Fertilizers	-.09	-.42**	.06
Explosives	-.26*	-.23†	.59
Cellular Phones	-.41**	-.29*	.42
Food Irradiation	-.31*	-.38**	.50
Roller Blades	-.25*	.02	.17
Nuclear Power Plants	-.32*	-.44**	.14
Surfing	-.09	.05	.82
Swimming Pools	-.12	-.12	.17
Solar Power	-.48**	-.06	.02
Railroads	-.16	-.27*	.58
Air Travel	-.18	-.23†	.88
Motorcycles	-.12	-.12	.96
Microwave Ovens	-.26*	-.29*	.70
Bicycles	.14	-.03	.31
Average Correlation	-.23†	-.25*	

The correlation between risk and benefit on the Finucane items (Finucane et al., 2000) in Study 1. Pearson's r values reported in table (acetaminophen group n = 73; placebo group n = 69), p <.10 = †, p<.05* p<.01**

Study 2 risk and benefit correlation. For Study 2, we used a moderation approach to test whether the relationship between summed overall risk perception and benefit perception was moderated by drug condition. As in Study 1, we used PROCESS Model 1 (Hayes, 2012). This analysis revealed a trend toward the hypothesized interaction, $b = 0.22$, $t(185) = 1.52$, $p = .13$. Although summed risk perception was a marginally significant predictor of summed benefit perception for those on placebo, $b = -0.18$, $t(92) = -1.69$, $p = .09$, it was not a significant predictor of benefit perception for those on acetaminophen, $b = 0.04$, $t(93) = 0.44$, $p = .66$.

We then used the same moderation model for each domain of the DOSPERT separately. As shown in Supplementary Table 3, negative correlations between risk and benefit perception

were reduced in all domains. A significant interaction existed between risk perception and drug condition predicting benefit perception in the health domain, with a stronger negative association between risk and benefit perception for those on placebo than those on acetaminophen. Analysis revealed a marginally significant interaction between risk perception and drug condition predicting benefit perception in the ethical domain, with a stronger negative association between risk and benefit perception for those on placebo than those on acetaminophen. There were no significant interactions between risk perception and drug condition predicting benefit perception in the financial, recreational, or social domains. Overall, this provides support for the hypothesis that acetaminophen may reduce the inverse relationship between risk and benefit perception and it appears to do so for the domains which show a stronger inverse correlation between risk and benefit perception in the placebo groups (ethical: r = -.44; health: r = -.45).

Supplementary Table 3.

Domains	Placebo	Acetaminophen	Interaction P-value
Ethical	-.44**	-.16	.06
Financial	-.17 †	-.17	.79
Health	-.45**	-.29**	.04
Recreational	-.34**	-.29**	.95
Social	-.06	.09	.27
Average Correlation	-.29**	-.16	

The correlation between risk and benefit on the DOSPERT items (Blais & Weber, 2006) in Study 2. Pearson's r values reported for the acetaminophen condition (n = 95) and placebo condition (n = 94); †, p <.10; *, p<.05; **, p<.01.

Multilevel Modeling Analyses of the Balloon Analogue Risk Task (BART)

We conducted exploratory modeling analyses of the BART data in Study 1 and Study 2 to probe for evidence of the underlying psychological mechanisms. For instance, we thought the effects of acetaminophen may be most pronounced on trials following a negative-affect-stimulating loss trial.

Study 1 Multilevel Mixed-effect Modeling (MLM) analysis. To probe our prediction that acetaminophen's effect on risk taking may be particularly pronounced on post-loss trials, we used multilevel mixed-effect modeling. With this approach, we can model group differences in risk taking, allowing the consideration of both standard fixed effects and covariates bound to items (e.g. risk taking after a burst) and bound to participants (e.g., drug condition). We based our modeling approach on a prior model of the BART (Mata *et al.*, 2012).

We modeled pumping behavior as a function of the intercept, trial number (1 to 30), trial type (0 = no burst, 1 = burst), previous trial type (0= no burst, 1 = burst), and drug condition (0 = placebo, 1 = acetaminophen). In this model, trial type (b = -11.89, p <.001) and drug condition (b = 5.73, p<.001) were significant predictors of risk taking (thus, again supporting our first hypothesis that acetaminophen would increase BART risk taking), while trial number and previous trial type were not. We then examined our prediction that acetaminophen would reduce the influence of a previous burst on next-trial risk taking, as indexed by an interaction between drug condition and previous trial type predicting risk taking. This interaction was not significant, p = .45. Similarly, there was no significant three-way interaction between drug condition, trial, and previous burst (p = .44), or between drug condition, previous burst, and burst size, p = .93.

Study 2 MLM analysis. As in study 1, we again modeled pumping behavior as a function of the intercept, trial number (1 to 30), trial type (0 = no burst, 1 = burst), previous trial type (0= no burst, 1 = burst), and drug condition (0 = placebo, 1 = acetaminophen). In this model, trial number (b = 0.11, p = .03), trial type (b = -9.89, p <.001), and drug condition (b = 5.73, p<.001) were significant predictors of risk taking, while previous trial type was not. Next, we again probed for interactions. No significant interactions existed between drug condition and previous

trial type, $p = .09$, between drug condition, trial, and previous burst ($p = .83$), or between drug condition, previous burst, and burst size, $p = .88$.

Study 2 Self-Reported Experience during the Balloon Analogue Risk Task

For Study 2, we added self-report items at the conclusion of the BART to assess participants' psychological experience. Like most risk-taking tasks, the BART involves the anticipation and experience of loss and reward and the potential for learning throughout the task. We attempted to measure each of these multiple components to identify potential mediating pathways by which acetaminophen exerts its effect.

The questions focused on four hypothesized mechanisms: affective reactions to bursts, motivation to avoid bursts, perceived likelihood of bursts, and focus on losses and wins during the task. The specific text of the questions is at the conclusion of the supplementary material. Participants rated the valence of a burst on an 11-point scale ranging from 1=*extremely negative* to 11=*extremely positive*. They also rated their emotional reaction to a burst on an 11-point scale from 1=*little to no emotion* to 11=*an extreme amount of emotion*. Next, they were asked how much they wanted and how hard they would try to avoid future bursts if they played the game again, each on 11-point scales ranging from 1=*not at all* to 11=*very much so*. Then they rated how likely they perceived a burst to be, both when they first started playing and on the last trial they played, each on 7-point scales ranging from 1=*not at all likely* to 7=*very likely*. Finally, participants rated how much they were focused on avoiding bursts and on gaining money during the task, each on a 7-point scale ranging from 1=*not at all* to 7=*very much so*. We used these items to explore the psychological processes upon which acetaminophen acts and to determine if acetaminophen's effect on any of these items explained the drug's effect on risk taking.

Means and standard deviations for all post-BART self-reports can be found in Supplementary Table 4. T-tests were used to determine whether acetaminophen significantly affected any of the self-report items that followed the BART in Study 2. No significant differences existed between the acetaminophen and placebo groups on any of the self-report items assessing affective reactions to bursts, motivation to avoid future bursts, perceived likelihood of bursts, and loss and gain focus during the task (*all p's* >.05). Thus, none of these potential mediators explained acetaminophen's effects on risk taking.

Supplementary Table 4.

Self-Report Item	Placebo	Acetaminophen	p-value
Burst Valence	3.83 (2.16)	3.99 (1.95)	.59
Burst Emotion	4.60 (2.71)	4.42 (2.56)	.65
Want to Avoid Future Bursts	6.62 (2.79)	6.51 (2.63)	.78
Try Hard to Avoid Future Bursts	6.55 (2.51)	6.28 (2.60)	.46
Perceived Probability 1st set	4.49 (1.80)	4.17 (1.65)	.20
Perceived Probability 2nd set	4.53 (1.76)	4.22 (1.61)	.21
Focus on Avoiding Losses	4.54 (1.61)	4.27 (1.61)	.25
Focus on Seeking Gains	5.14 (1.76)	5.18 (1.60)	.87

Means (Standard Deviations) for Post-BART Self-Reports in Study 2 with p values from independent samples t-test (acetaminophen group n = 95; placebo group n = 94).

Although acetaminophen increases risk taking, it may not influence subjective recalled experiences concerning balloon bursts.

Several limitations of these self-report items for assessing the psychological mechanisms through which acetaminophen increases risk taking may explain the lack of significant effects. First, the items, which were created for this study, may not have been ideally phrased to assess affective reactions, and may have instead elicited more cognitive evaluations. Second, these items were assessed only once at the end of the task, rather than multiple times during the task

and participants had to recall how they felt post-burst, potentially weakening any effects. For example, self-report of affective experience after the Trier Social Stress Test is not reliably correlated with cortisol increases, but reports of experience during the task are (Dickerson and Kemeny, 2004; Hellhammer and Schubert, 2012). A similar process could have occurred here.

Study 3 Self-Reported Experience during the Balloon Analogue Risk Task

In Study 3, participants provided their self-reported experience after the first 15 balloons as well as at the end of the second block of 15 balloons. As summarized in Supplementary Table 5, there were no significant differences between the acetaminophen or placebo conditions according to independent sample t-tests.

Supplementary Table 5.

Self-Report Item	Placebo	Acetaminophen	p-value
Burst Valence (1st block of 15 balloons)	3.84 (2.69)	3.89 (2.33)	0.88
Burst Emotion (1st block of 15 balloons)	5.63 (2.84)	5.62 (2.82)	0.99
Want to Avoid Future Bursts (1st block of 15 balloons)	8.65 (2.18)	8.39 (2.37)	0.41
Try Hard to Avoid Future Bursts (1st block of 15 balloons)	8.08 (2.39)	7.67 (2.56)	0.23
Focus on Avoiding Losses (1st block of 15 balloons)	5.28 (1.58)	5.33 (1.52)	0.80
Focus on Seeking Gains (1st block of 15 balloons)	4.87 (1.86)	5.07 (1.83)	0.42
Burst Valence (2nd block of 15 balloons)	4.10 (2.52)	4.04 (2.31)	0.84
Burst Emotion (2nd block of 15 balloons)	5.48 (3.06)	5.51 (3.00)	0.94
Want to Avoid Future Bursts (2nd block of 15 balloons)	8.06 (2.81)	7.91 (2.77)	0.70
Try Hard to Avoid Future Bursts (2nd block of 15 balloons)	7.89 (2.78)	7.75 (2.84)	0.72
Perceived Probability when first started game	4.17 (1.78)	3.97 (1.69)	0.41
Perceived Probability of burst when ended game	3.72 (1.64)	3.56 (1.59)	0.46
Focus on Avoiding Losses (2nd block of 15 balloons)	5.19 (1.59)	4.92 (1.69)	0.23
Focus on Seeking Gains (2nd block of 15 balloons)	5.30 (1.87)	5.13 (1.86)	0.53

Means (Standard Deviations) for Self-Reports in Study 3 with p values from independent samples t-test (acetaminophen group n = 109; placebo group n = 106).

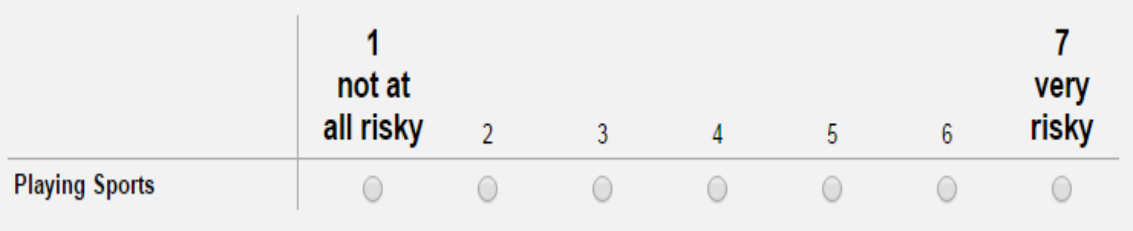
Materials

Risk/Benefit Perception Scale used in Study 1

Risk Perception

You will be making judgments about the **RISK** of various activities and technologies for the U.S. society as a whole. You will be asked to use a scale ranging from not at all risky to very risky for a number of different items.

Read the word on the left and then click a number on the scale. You can look at the scale below for an example of what the questions will look like.



You will only have a **SHORT TIME** to make your decisions. A countdown clock will appear for 5.2 seconds and you must make your decision by the end of the countdown. Your goal is to make your judgments as quickly as you can. Each time, you will select a number on the scale and then click the arrow at the bottom of the screen.

Benefit Perception

You will be making judgments about the **BENEFIT** of various activities and technologies for the U.S. society as a whole. You will be asked to use a scale ranging from not at all beneficial to very beneficial for a number of different items.

Read the word on the left and then click a number on the scale. You can look at the scale below for an example of what the questions will look like.

You will only have a **SHORT TIME** to make your decisions. A countdown clock will appear and you must make your decision by the end of the countdown. Your goal is to make your judgments as quickly as you can. Select a number on the scale and then click the arrow at the bottom of the screen.

Items

1. Alcoholic Beverages
2. Water Fluoridation
3. Chemical Plants
4. Eating Beef
5. Food Preservatives
6. Cars
7. Cigarettes
8. Pesticides
9. Natural Gas
10. Chemical Fertilizers
11. Explosives
12. Cellular Phones
13. Food Irradiation
14. Roller Blades
15. Nuclear Power Plants
16. Surfing
17. Swimming Pools
18. Solar Power
19. Railroads
20. Air Travel
21. Motorcycles
22. Microwave Ovens
23. Bicycles

DOSPERT (used in Study 2)

Risk Perception

People often see some risk in situations that contain uncertainty about what the outcome or consequences will be and for which there is the possibility of negative consequences. However, riskiness is a very personal and intuitive notion, and we are interested in **your gut level assessment of how risky** each situation or behavior is.

For each of the following statements, please indicate **how risky you perceive** each situation. Provide a rating from *Not at all Risky* to *Extremely Risky*, using the following scale:

1	2	3	4	5	6	7
Not at all Risky	Slightly Risky	Somewhat Risky	Moderately Risky	Risky	Very Risky	Extremely Risky

Expected Benefits

For each of the following statements, please indicate **the benefits** you would obtain from each situation. Provide a rating from **1 to 7**, using the following scale:

1	2	3	4	5	6	7
No benefits At all			Moderate Benefits			Great Benefits

Items

1. Admitting that your tastes are different from those of a friend. (S)
2. Going camping in the wilderness. (R)
3. Betting a day's income at the horse races. (F/G)
4. Investing 10% of your annual income in a moderate growth diversified fund. (F/I)
5. Drinking heavily at a social function. (H/S)
6. Taking some questionable deductions on your income tax return. (E)
7. Disagreeing with an authority figure on a major issue. (S)
8. Betting a day's income at a high-stake poker game. (F/G)
9. Having an affair with a married man/woman. (E)
10. Passing off somebody else's work as your own. (E)
11. Going down a ski run that is beyond your ability. (R)
12. Investing 5% of your annual income in a very speculative stock. (F/I)
13. Going whitewater rafting at high water in the spring. (R)
14. Betting a day's income on the outcome of a sporting event (F/G)
15. Engaging in unprotected sex. (H/S)
16. Revealing a friend's secret to someone else. (E)
17. Driving a car without wearing a seat belt. (H/S)
18. Investing 10% of your annual income in a new business venture. (F/I)
19. Taking a skydiving class. (R)
20. Riding a motorcycle without a helmet. (H/S)
21. Choosing a career that you truly enjoy over a more secure one. (S)
22. Speaking your mind about an unpopular issue in a meeting at work. (S)
23. Sunbathing without sunscreen. (H/S)
24. Bungee jumping off a tall bridge. (R)
25. Piloting a small plane. (R)
26. Walking home alone at night in an unsafe area of town. (H/S)
27. Moving to a city far away from your extended family. (S)
28. Starting a new career in your mid-thirties. (S)
29. Leaving your young children alone at home while running an errand. (E)
30. Not returning a wallet you found that contains $200. (E)

Note. E = Ethical, F = Financial, H/S = Health/Safety, R = Recreational, and S = Social.

Self-Report Items used in the BART (Studies 2 and 3)

1. To what extent was a balloon bursting positive or negative?

   (-5 Extremely Negative – +5 Extremely Positive)

2. To what extent did a balloon bursting make you feel an emotional reaction?

   (0 Little to No Emotion – 10 An Extreme Amount of Emotion)

3. If you played the game again, how much would you want to avoid a balloon bursting in future trials?

   (0 Not At All – 10 Very Much So)

4. If you played the game again, how hard would you try to avoid future balloons bursting?

   (0 Not At All – 10 Very Much So)

5. How likely did you think a balloon burst was when you first started playing the game?

   (1 Not At All Likely – 7 Very Likely)

6. How likely did you think a balloon burst was during the last round you played?

   (1 Not At All Likely – 7 Very Likely)

7. How much were you focused on avoiding a balloon burst during the game?

   (1 Not At All – 7 Very Much So)

8. How much were you focused on gaining as much money as possible during the game?

   (1 Not At All – Very Much So)

Online Supplement References

Alhakami, A.S., Slovic, P. (1994). A psychological study of the inverse relationship between perceived risk and perceived benefit. *Risk analysis*, **14**, 1085–96

Blais, A.-R., Weber, E.U. (2006). A domain-specific risk-taking (DOSPERT) scale for adult populations. *Judgment and Decision Making*, **1**, 33–47

Dickerson, S.S., Kemeny, M.E. (2004). Acute stressors and cortisol responses: a theoretical integration and synthesis of laboratory research. *Psychological Bulletin*, **130**, 355–91

Durso, G.R.O., Luttrell, A., Way, B.M. (2015). Over-the-Counter Relief From Pains and Pleasures Alike: Acetaminophen Blunts Evaluation Sensitivity to Both Negative and Positive Stimuli. *Psychological Science*, **26**, 750–58

Finucane, M.L., Alhakami, A., Slovic, P., et al. (2000). The affect heuristic in judgments of risks and benefits. *Journal of behavioral decision making*, **13**, 1–17

Fischhoff, B., Slovic, P., Lichtenstein, S., et al. (1978). How safe is safe enough? A psychometric study of attitudes towards technological risks and benefits. *Policy sciences*, **9**, 127–52

Hayes, A.F. (2012). *PROCESS: A versatile computational tool for observed variable mediation, moderation, and conditional process modeling*. University of Kansas, KS.

Hellhammer, J., Schubert, M. (2012). The physiological response to Trier Social Stress Test relates to subjective measures of stress during but not before or after the test. *Psychoneuroendocrinology*, **37**, 119–24

Mata, R., Hau, R., Papassotiropoulos, A., et al. (2012). DAT1 polymorphism is associated with risk taking in the Balloon Analogue Risk Task (BART). *PloS one*, **7**, e39135

Rosenthal, R. (1979). The file drawer problem and tolerance for null results. *Psychological bulletin*, **86**, 638