Acetaminophen, Affect, and Risk:

An Analysis of Psychological and Neurochemical Mechanisms

THESIS

Presented in Partial Fulfillment of the Requirements for the Degree Master of Arts in the Graduate School of The Ohio State University

By

Alexis A. Keaveney

Graduate Program in Psychology

The Ohio State University

2016

Master's Examination Committee:

Dr. Baldwin M. Way, Advisor

Dr. Jennifer Crocker

Dr. Ellen Peters

Abstract

Recent research has demonstrated that acetaminophen reduces affective reactivity. Because affect is a critical determinant of risk perception and risk-taking, this drug taken by 23% of Americans each week could potentially impact these important judgments and decisions. To test this hypothesis, we examined the effects of acetaminophen on well-validated risk perception and risk-taking tasks. In Study 1 (N = 142) and Study 2 (N = 189), we demonstrated that acute doses of acetaminophen increase risk-taking behavior. This increase in risk-taking emerged on post-loss trials, not on the first trial, suggesting acetaminophen may be affecting how individuals respond to experiences of loss. However, acetaminophen did not affect self-reports of reactivity to loss events, motivation to avoid loss, focus on gains or losses, or perceived probability of a loss. In Study 2, but not Study 1, we also found evidence that acetaminophen reduced the negative correlation between perceived risk and benefit in some risk perception domains, suggesting less reliance on the "affect heuristic." To examine the neurochemical mechanism underlying this effect, Study 3 tested whether the increase in risk-taking extends to the non-steroidal anti-inflammatory drug ibuprofen. We did not find an effect of ibuprofen on risk-taking overall, but did see a significant increase in risk-taking among those who reported higher recent illness and who received ibuprofen. Taken together, the results suggest acetaminophen, an over-the-counter drug, can impact critically important risk judgment and risk-taking behavior.

Acknowledgements

First, I would like to thank my adviser, Baldwin Way, for his time, support, and mentorship over the last two years. His thoughtful feedback and encouragement have been invaluable to me.

Additionally, I owe a great deal of thanks to my collaborator and committee member Ellen Peters. Her expertise in the judgment and decision making domain and her enthusiastic willingness to contribute to this project have served as vital resources.

I would also like to thank my secondary adviser and committee member Jenny Crocker, both for her willingness to serve on my committee and for her advisement and collaboration on our other projects.

Thanks also go to my wonderful lab members, Ian Roberts and Geoff Durso, for their suggestions and support of this project. Their insights are greatly appreciated.

Finally, I would like to thank my parents Tina and Steve Keaveney, sister Stephanie Keaveney and partner Ian Breitz. I could not do this without their emotional support and continued belief in my potential.

Vita

2009……Elmira High School, Elmira, OR

2013……B.S. Psychology, Oregon State University

2014-2015……Graduate Fellow, Department of Psychology, The Ohio State University

2015-present……Graduate Teaching Associate, Department of Psychology, The Ohio State University

Fields of Study

Major Field: Psychology

Table of Contents

List of Tables

List of Figures

Chapter 1: Introduction

Acetaminophen, the active ingredient in Tylenol, is an over-the-counter pain reliever that an estimated 23% of the U.S. population takes each week (Kaufman, Kelly, Rosenberg, Anderson, & Mitchell, 2002). Researchers have long theorized about a potential behavioral and neural overlap between experiences of pain that are physical in origin and experiences of pain that are psychological in origin (Panksepp, Herman, Conner, Bishop, & Scott, 1978). Recently, this led to the hypothesis that over-the-counter physical pain relievers may also alleviate experiences of psychological discomfort or pain (DeWall et al., 2011). This hypothesis was supported in a study by DeWall and colleagues (2011) which demonstrated that daily acetaminophen use reduced hurt feelings over the course of three weeks and reduced neural responses to social rejection in the dorsal anterior cingulate cortex and anterior insula, areas previously associated with experiences of pain.

Following this initial study, researchers began exploring other effects of acetaminophen on psychological experiences that could be described as uncomfortable. For instance, an acute dose of acetaminophen was shown to reduce the compensatory affirmations typically seen following meaning threats, including writing about one's own mortality and viewing a surrealist film clip (Randles, Heine, & Santos, 2013). Additionally, acetaminophen has been shown to reduce empathic concern and personal distress when reading scenarios about others experiencing pain (Mischkowski, Crocker,

& Way, 2016). Acetaminophen also reduces affective reactivity to viewing negatively-valenced disgusting or scary images (Durso, Luttrell, & Way, 2015). Interestingly, this study also showed blunting of affective reactivity to positively-valenced images, suggesting acetaminophen may reduce affective reactivity more generally, rather than have actions specific to negative experiences of discomfort. Finally, acetaminophen has also been shown to reduce what DeWall, Chester, and White (2015) called "the pain of decision-making." Here, they showed acetaminophen reduced the post-decision spreading of alternatives that can accompany experiences of cognitive dissonance and reduced selling prices set for a gift participants had been given, attenuating what is often described as the endowment effect.

Each of these studies suggests acetaminophen can reduce affective reactivity and therefore have downstream consequences on processes that rely on affective experiences. However, the effects of acetaminophen on risk judgment and risk-taking, processes that rely on affect, have not yet been explored. This is the aim of the present research.

Affect and Decision Making

Researchers have provided a compelling case that affect, or feeling states that distinguish positive from negative, play a critical role in the judgment and decision making process. Loewenstein and colleagues (2001) proposed a central role for affect in choice under risk and uncertainty with his *risk as feelings* hypothesis. He suggested that anticipatory affect, or the affect experienced when considering a possible choice, is an essential input into the decision-making process that drives choice and behavior (Loewenstein, Weber, Hsee, & Welch, 2001). To support this hypothesis, Loewenstein

and colleagues (2001) reviewed a large literature suggesting that affective experiences during the consideration of decisions often direct choice and indeed may exert a stronger influence than cognitive considerations. This work suggests that manipulation of the affect experienced during considerations of judgment and risk-taking should lead to downstream consequences on judgment and choices made.

Along these lines, work on the "affect heuristic," or the reliance on affect as a decision-making shortcut, has also demonstrated a key role for affect in risk judgment and choice (Finucane, Alhakami, Slovic, & Johnson, 2000). Slovic, Finucane, Peters, and MacGregor (2004) have argued for a dual-system model of information processing, suggesting that people can process information both through an "analytic system" and through an "experiential system." In the analytic system, individuals carefully deliberate and cognitively process information to come to decisions. This system does not provide a direct role for affective reactions. In the experiential system, individuals rely on the affect that is salient in the moment to guide their judgment and behavior, allowing for quicker, more efficient processing. This affect may be integral in nature, meaning it results from reactions to the stimulus itself, or incidental, meaning it is not tied to the stimulus itself, though it may be misattributed as such and may similarly affect judgment. Clearly, manipulations of affect, either integral or incidental, should be able to affect judgments and decisions made through the experiential system.

If acetaminophen does indeed reduce affective reactivity, as a growing body of work suggests, then the above theoretical approaches which posit a central role for affect in experiential judgment and decision making suggest a clear hypothesis: acetaminophen

should have effects on judgment and choice. A prudent approach to studying the effects of acetaminophen on risk judgment and risk behavior is to examine the effects of the drug on tasks that are sensitive to affective processing. For this, we first turn to a risk judgment task and then to a risk-taking behavior task, both of which have been shown to involve affective processing in the choices made by participants, and so likely rely on use of the affect heuristic and are processed through the experiential system.

Affect Heuristic and Risk Judgment

The use of the affect heuristic has been explored in the context of risk and benefit judgments. While 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 (Fischoff, Slovic, Lichtenstein, Read, & Combs, 1978). It has since been demonstrated that the strength of affective reactions to the judged object predicts the inverse relationship between perceived risk and perceived benefit (Alhakami & Slovic, 1994). If perceiving some object, for instance alcoholic beverages, elicits positive affect, that object is likely to be judged as having high benefits and low risks. If an object, say nuclear power, elicits negative affect, that object is likely to be judged as low in benefit and high in risk. Follow up work suggested that placing people under time pressure increases the reliance on the affect heuristic, resulting in stronger negative correlations between perceived risk and perceived benefit (Finucane et al., 2000). They also showed that providing information that should only affect either risk or benefit perception affected perception of both risk and benefit. This suggests that rather than separately

processing the perceived benefits and perceived risks, people rely on a single affective response, which contributes to both their risk and their benefit judgment.

Because acetaminophen appears to reduce the extremity of affective reactions to stimuli, it may therefore reduce perceived risk and perceived benefit of a behavior or policy. Additionally, people may rely less on the affective heuristic if the affective signal is weaker, and therefore show weaker negative correlations between the two judgments. This would demonstrate a way in which acetaminophen could alter judgements through blunting the anticipatory affect experienced when encountering a stimulus prior to making a risk and benefit judgment about it. This leads to our first hypothesis: acetaminophen will reduce use of the affective heuristic when making judgments of risk and benefit, leading to weaker negative correlations between the two.

Affect Heuristic and Risk-Taking Behavior

Affect has also been studied in the context of risk-taking behavior. When deciding how much risk-taking to engage in, individuals can use the affect heuristic to guide their decision. This is especially likely to be true for risk-taking tasks that are affectively-stimulating and experientially engaging. One task that is particularly well-suited for studying the use of the affect heuristic in risk-taking is the Balloon Analogue Risk Task (BART; Lejuez et al., 2002). The BART is a computerized task where participants inflate a balloon, earning $0.05 per pump, and can make the choice at any time to end the trial and transfer the money earned to their permanent bank. However, the balloon can pop at any time, and if the pop occurs before the individual ends the trial and transfers the money to their permanent bank, no money is earned. This experiential

risk-taking task involves visual depictions of the risk-taking, salient loss events that provide direct feedback to the participant, and does not provide explicit information about the probability of loss events, making it a strong candidate for a task in which participants' choices are likely to involve use of the affect heuristic.

Involvement of affect in the BART has primarily been studied through the measurement of individual differences in affective reactivity or through the manipulation of incidental affect prior to the task. For example, individuals who tend to experience more negative anticipatory affect, like those high in dispositional anxiety, show reduced risk-taking on the BART (Maner et al., 2007).

In terms of incidental affect, individuals who watched a sad movie clip compared to a happy one also exhibited less risk-taking behavior (Yuen & Lee, 2003). Additionally, experiences of incidental negative affect that accompany receiving disappointing exam results reduce risk-taking on the BART (Heilman, Crisan, Houser, Miclea, & Miu, 2010). Interestingly, this effect was attenuated when individuals engaged in cognitive reappraisal but not expressive suppression emotion regulation strategies, suggesting the impact of negative affective experiences on risk-taking can be reduced if the negative event is reappraised less negatively. Cognitive reappraisal effectively reduces the intensity of negative emotion experienced, whereas expressive suppression only reduces the behavioral expression, not intensity of experience of an emotion (for a review see Gross, 2002).

In what might be considered a manipulation of anticipatory affect that is more integral to the stimulus being considered, researchers have shown that having individuals

play the BART while watching another's face grow more anxious as the balloon size increases also reduces risk-taking (Parkinson, Phiri, & Simons, 2012). Here, seeing an anxious face may increase one's negative affect toward the balloon size increasing, which may in turn lead to reduced risk-taking.

This research suggests that negative affect experienced during the BART signals one to engage in less risk-taking behavior. Because the negative loss events are more visually and auditorily salient in the BART than the win events, and because traditionally participants have been more risk-averse than would maximize profit in this task, it seems likely that negative affect toward potential or experienced losses rather than positive affect toward potential or experienced gains may exert a stronger influence on decision making in the BART. Therefore, acetaminophen's blunting of negative affect may lead to a reduction in this negative affect signal and an increase in risk-taking behavior. This negative affect guiding choice in the BART may be particularly strong following the experience of loss events, and thus we may see stronger effects of acetaminophen on post-burst trials than trials that occur before a negative, affect-stimulating loss has occurred. These considerations lead to our second hypothesis: Acetaminophen will increase risk-taking on the BART. Moreover, this difference may be especially strong on trials that occur right after a negative, affect-stimulating loss event.

The Neurochemical Mechanism underlying Acetaminophen's Effect on Risk-Taking

While acetaminophen has been shown to reduce affect intensity in a number of studies, the neurochemical pathway through which these effects occur remains unknown. There is some evidence to suggest it acts through an anti-inflammatory pathway by inhibiting the synthesis of prostaglandins, which are molecules that produce the pain, swelling, and fever associated with inflammation (Aronoff, Oates, Boutaud, 2006). There is also some evidence to suggest it acts through the serotonin system, as serotonin receptor antagonists inhibit acetaminophen's analgesic effects (Pickering et al., 2006).

There is reason to believe that the reduction of inflammation could account for acetaminophen's effects on affect. A recent meta-analysis has suggested non-steroidal anti-inflammatory drugs (NSAIDs) can reduce depression (Kohler et al., 2014). Additionally, chronic inflammatory disorders have been associated with increased experiences of negative affect, including depressed feelings (sadness, hopelessness) and anxiety, with the degree of affect dysregulation associated with the degree of inflammation (Fassbender et al., 1998). Experimentally induced inflammation has also been shown to increase negative affective reactions toward strangers (Eisenberger, Inagaki, Mashall, & Irwin, 2010) and increase positive affective reactions toward support figures (Inagaki et al., 2015), suggesting inflammation can increase both negative and positive affect reactivity depending on the context in which the inflammation is induced.

To provide convergent validity for the hypothesis that acetaminophen increases risk taking via the inhibition of prostaglandin production, we propose to study the effects of ibuprofen on risk-taking. Ibuprofen, along with aspirin, are the prototypical drug in the non-steroidal anti-inflammatory drug (NSAID) class (Vane & Botting, 1998). These

drugs inhibit prostaglandin synthesis in the body as well as in the brain, whereas acetaminophen only inhibits prostaglandin synthesis in the brain (Graham, Davies, Day, Mohamudally, & Scott, 2013). Both ibuprofen and acetaminophen act on several other neurochemical pathways as well, but share effects on prostaglandin synthesis in the brain. If acetaminophen and ibuprofen have similar effects on psychological processes, this would be suggestive evidence that acetaminophen is acting through an anti-inflammatory pathway (e.g. reducing prostaglandin synthesis). This leads to our third hypothesis: Ibuprofen will increase risk-taking on the BART.

Overview of Present Research

To address our three hypotheses, we designed three pharmacological studies. Each used a double-blind, placebo-controlled, parallel arm design. In the first study, participants consumed acetaminophen or placebo and then completed a risk and benefit judgment task as well as a behavioral measure of risk-taking. Study 2 built upon Study 1 first by determining whether or not the main findings on risk-taking from Study 1 replicated, then by adding in measures to assess individual's affective reactions to components of the BART in order to assess the underlying psychological processes occurring. In Study 3, ibuprofen was used rather than acetaminophen to examine risk-taking on the same behavioral measure used in Study 1 and Study 2 in order to explore the physiological processes through which acetaminophen may be exerting its effects.

Chapter 2: Study 1

Overview

Study 1 aimed to examine acetaminophen's effect on risk and benefit perception and the correlation between the two. Next, we assessed whether acetaminophen increased risk-taking behavior, and whether these effects were particularly pronounced on post-loss trials.

Methods

Participants. Participants were 142 undergraduates at The Ohio State University who voluntarily participated in exchange for course credit in their introductory psychology course. The sample consisted of 76 men and 64 women (2 participants did not answer) with a mean age of 19.36 years (SD = 1.68).

Acetaminophen. A double-blind, placebo-controlled study design was used. Participants were randomly assigned to drug condition using a random number generator (69 in placebo, 73 in acetaminophen). Participants were given 1000mg of acetaminophen, the recommended dosage for a headache and the dosage commonly used in studies of acetaminophen's psychological effects (e.g. Durso et al., 2015), or were given a placebo. 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) dissolved in Ora-Plus suspension liquid and flavored with Ora-Sweet Syrup. The placebo solution consisted of Avicel

Microcrystalline powder (100 mg/ml) dissolved in the same vehicle. After consuming the drug solution, participants were given a small glass of water to wash down the drug.

Risk and benefit perception. To assess acetaminophen's effect on use of the affect heuristic, participants completed the risk and benefit perception tasks used by Finucane, Alhakami, Slovic, and Johnson (2000; Appendix A). Participants were asked to make risk and benefit judgments of various activities and technologies for U.S. 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 use of the affect heuristic, participants were put under time pressure with a countdown clock on the screen while they made each judgment, allowing 5.2 seconds for each item (as in Finucane et al., 2000). The scale consisted of 23 items, presented one at a time on the screen. Items were presented in a 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.

Risk-Taking. To measure risk-taking behavior, the BART was used (Lejuez, et al., 2002). This risk-taking measure predicts drug and alcohol use, delinquent behavior, and risky sexual behavior (e.g. Aklin, Lejuez, Zvolsenky, Kahler, & Gwadz, 2005; Lejuez et al., 2007; Leju e, Simmons, Aklin, Daughters, & Dvir, 2004). Participants completed 30 trials. Each trial began with a small, uninflated balloon on a computer screen. Participants were allowed to 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 on the task. Participants were allowed to collect their earnings for each trial and move them to a permanent bank at any point by pressing a button saying "Collect $$$". However, participants were also told the balloon can explode at any point. If the balloon bursted prior to the participants pressing the "Collect $$$" button, they lost any money they had earned thus far on that trial, and moved on to the next trial having added no money to their permanent bank.

A balloon burst could occur at any point from the first pump to the maximum 128th pump. For each balloon, the first pump had a 1/128 probability of bursting, the second pump 1/127, and so on until on the 128th pump there was a 1/1 probability of bursting. The gain amount remained constant across pumps at $0.05, meaning the gain was 100% on the second pump (i.e. from 5 cents to 10 cents), 50% on the third pump (i.e. from 10 cents to 15 cents) and so on. Thus, with each additional pump, the probability of a loss increased and the relative gain decreased.

Participants were not told about the maximum number of pumps nor the likelihood of bursts. They were told that the balloon could burst as early as the first trial and as late as when the balloon fills the entire computer screen. Bursts were accompanied by a bursting sound and popping animation.

Procedure. Upon arrival at the lab and after providing informed consent, 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 minutes to begin the main tasks of the study. During drug uptake, participants completed a number of background personality and health measures. At 45 minutes, participants began

completing decision-making tasks. At approximately 50 minutes after drug consumption, participants completed the risk and benefit perception task using the online survey program Qualtrics (Qualtrics, Provo, UT). Immediately following this and approximately 60 minutes after drug consumption, participants completed the BART task, implemented using the Psychology Experiment Building Language package and pre-packaged BART script (PEBL; Mueller & 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 and benefit perception. To assess risk perception, average ratings were computed across the 23 items. The same process was used for benefit perception. There was homogeneity of variances as assessed by Levene's test for both average risk and average benefit perception (*p's* >.05). A t-test for average risk perception revealed no significant difference between drug conditions, $t(140) = 1.48$, $p = .14$. Descriptively, those on placebo perceived more risk ($M = 3.93$, $SD = 0.62$) than those on acetaminophen ($M = 3.78$, $SD = 0.56$). A t-test for average benefit perception also revealed no significant difference between drug conditions, $t(140) = 0.74$, $p = .46$. Descriptively, those on placebo perceived more benefit ($M = 4.58$, $SD = 0.61$) than those on acetaminophen ($M = 4.50$, $SD = 0.62$).

Risk and benefit correlation. As in Finucance 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

Finucance study. The correlations between risk and benefit perception for each item, separated by drug condition, can be found in Table 1 (Appendix B). 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. This suggests that the predictive relationship 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 ($p > .05$), 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, there was not strong support for the hypothesis that acetaminophen would dampen the inverse relationship between risk and benefit perception.

Risk-taking main effect. To analyze the BART data, participants' adjusted average number of pumps across the 30 trials were computed. To compute this, any trial on which a balloon burst occurred was excluded, as the number of pumps completed on this trial reflects where the balloon bursts rather than the desired amount of risk-taking a

participant would have engaged in had a burst not occurred (Lejuez et al., 2002). After those trials were excluded, averages across the remaining trials were computed.

There was homogeneity of variances as assessed by Levene's test (p = .42). A t-test revealed a significant difference in risk-taking between those on acetaminophen and those on placebo, $t(140) = -2.29$, p = .02. Those in the placebo condition engaged in significantly less risk-taking as indexed by adjusted average number of pumps (M = 33.10, SD = 15.75) than those on acetaminophen (M = 38.98, SD = 14.80). For an illustration, see Figure 1 (Appendix C).

Risk-taking trial type interaction. Next, to assess whether this drug effect on risk-taking was particularly strong for trials that occurred right after a negative, affectively-stimulating loss event, we compared first-trial risk-taking to post-burst risk-taking. First, number of pumps on the first trial was assessed, and those who had a burst on the first trial were eliminated as their pumps do not necessarily reflect their desired amount of risk-taking. First trial risk-taking indexes the amount of risk individuals are willing to engage in prior to experiencing any loss events. Next, trials that occurred right after a burst were isolated. Then, any of those post-burst trials that had a burst occur were eliminated, leaving only trials that occurred after a burst and on which a burst did not occur. Values on these trials were then average together to create an index of post-burst risk-taking. This left us with an effective sample size of 76 individuals who had both a non-burst first trial and at least one valid (non-burst) post-burst trial.

A two-way mixed analysis of variance (ANOVA) was used to assess whether acetaminophen's effects on risk-taking were stronger post-burst than on the first trial.

Acetaminophen condition (placebo versus acetaminophen) was used as the between-subjects factor and trial type (first versus post-burst) as the within-subjects factor. An examination of the studentized residuals revealed no values greater than +/- 3, suggesting no outliers. Levene's test revealed homogeneity of variances ($p > .05$) and Box's test revealed homogeneity of covariances ($p = .67$).

There was no significant interaction between drug condition and trial type on risk-taking, $F(1,74) = 1.96$, $p = .17$, partial $\eta^2 = .03$. While the interaction was not significant, the means were descriptively consistent with the hypothesis. While on the first trial, those on placebo ($M = 33.95$, $SD = 26.60$) and those on acetaminophen ($M = 34.78$, $SD = 21.90$) engaged in fairly similar amounts of risk-taking, a larger difference between the placebo group ($M = 29.57$, $SD = 15.09$) and the acetaminophen group ($M = 36.46$, $SD = 14.97$) is seen on trials occurring right after a burst. This suggests that acetaminophen's effects on risk-taking are particularly potent right after a negatively-valenced loss occurs, providing some insight into the process by which acetaminophen is increasing risk-taking. For a graph of this data, see Figure 2 (Appendix C).

Study 1 Summary

Study 1 revealed very little evidence for the hypothesis that acetaminophen would attenuate the inverse relationship between risk and benefit perception. It is possible that the participants in our sample found these items to be less affectively stimulating than those in the original Finucane, Alhakami, Slovic, and Johnson (2000) affect heuristic study done 16 years ago. Indeed, among the placebo group, the negative correlations between risk and benefit perceptions were obtained, but were much weaker than those of

the previous study. While Finucane et al. found an average correlation of -.80 across the 23 items, we found only -.03. If participants were relying on affect to a lesser extent in our study, acetaminophen may not have exerted an effect on this judgment. Therefore, Study 2 uses a scale with different items that may be more affectively-stimulating than those of Study 1 to test this hypothesis again.

Study 1 did provide initial evidence that acetaminophen increases risk-taking behavior on the BART. Those on acetaminophen engaged in significantly more risk-taking than those on placebo. While the interaction between trial type (first versus post-burst) and drug condition was not significant, the pattern of means was in the hypothesized direction, suggesting that the drug effect on risk-taking may be particularly potent right after a loss event has occurred. As this initial test was potentially underpowered to detect the interaction effect, a larger sample may be necessary to determine if this pattern is reliable and can provide insight into the psychological pathway through which acetaminophen increases risk-taking behavior via altering affective reactions to loss events. Study 2 provides an opportunity to test this interaction with a larger sample and combine data from Studies 1 and 2 to increase power to detect this effect. Moreover, in Study 2 we added additional self-report items to assess participants' psychological experience with the loss events in the BART, to begin to get a more fine-grained assessment of how acetaminophen increases risk-taking in the BART.

Chapter 3: Study 2

Overview

In Study 2, we used a different scale of risk and benefit perception to again test whether acetaminophen would reduce the inverse correlation between the two. Additionally, we aimed to replicate the increase in risk-taking on acetaminophen observed in Study 1, again assess the trial-type interaction, and assess a number of self-report items following the BART to examine participants' responses to loss events in the task. We derived these self-report items from an examination of the literature on how affect can alter judgments and decisions.

Affect and Risk-Taking Behavior: Psychological Mechanisms

Because the BART, like most risk-taking tasks, involves multiple components including both anticipation and experience of loss and reward as well as a potential for learning over the course of the task, it is possible that affect could be involved in individuals choices in multiple ways, and therefore acetaminophen could exerts its effects in multiple ways. Four hypothesized mechanisms are proposed below.

First, the pattern of means from Study 1 suggested acetaminophen's effects on risk-taking may be particularly potent on post-burst trials. Indeed, it may be that acetaminophen reduces affective reactivity to the loss events during the BART, reducing both how negative and how emotionally-evocative the bursts are perceived as. We can use participant's self-reported affective reactions to balloon bursts to assess this.

Therefore, the hypothesized mechanism 1 is: acetaminophen will reduce the recalled negativity of a balloon burst. If the loss events elicit less negative affect when participants are taking acetaminophen, this could have a number of consequences on perception of or reaction to the task, which are discussed next.

For instance, we know that affective reactions can guide perception of the probability of a loss event occurring. Indeed, manipulations of negative affect have been shown to increase perceived likelihood of negative outcomes of risky events (Johnson & Tversky, 1983). In the BART, individuals may experience negative affect in response to a loss event, and this in turn may increase the perceived likelihood of a loss on the next trial, triggering reductions in risk-taking. Acetaminophen may interfere with this process, and so hypothesized mechanism 2 is: those on acetaminophen may perceive balloon bursts as less likely and therefore engage in greater risk-taking.

It has also been argued that affect can act as a spotlight, directing our attention toward certain aspects of our environment, increasing processing of some components and decreasing processing of others (Peters, 2006). This may be exemplified in the work by Alhakami and Slovic (1994), where positive affective reactions to stimuli may increase focus on and processing of benefits while negative affective reactions may increase focus on and processing of risks. In the BART, negative affect experienced in response to a loss event may direct individuals to pay attention more to avoiding future losses and less to seeking gains. Acetaminophen may interfere with this processes, and therefore hypothesized mechanism 3 is that those on acetaminophen will focus less on avoiding losses, more on seeking gains, and therefore exhibit greater risk-taking.

Another key function of affect is to act as a motivator (Peters, 2006). As early as 1890, William James described pain and pleasure as the "springs of action," calling pain a "tremendous inhibitor" and pleasure a "tremendous reinforcer." Elliot (2006) proposed classification of stimuli as positive or negative in valence as the "core evaluative dimension of approach-avoidance motivation," suggesting we seek to approach positive stimuli and maintain positive states and avoid negative stimuli and get rid of negative states. In experimental work, Chen and Bargh (1999) have shown stimuli classified as good tend to promote approach, while stimuli classified as bad promote avoidance. Here, we hypothesize that (mechanism 4) those on placebo will respond to loss events with negative affect and that this negative affect will motivate them to avoid future balloon bursts. Alternatively, those on acetaminophen will be less reactive to the bursts, less motivated to avoid them, and therefore engage in greater risk-taking.

Each of these are potential ways in which acetaminophen, through its action on affect, could affect risk-taking behavior. With the use of self-report questions following the BART, we probe each of these hypothesized processes, assessing whether acetaminophen reduces affective reactivity to bursts, decreases perceived probability of a burst, reduces focus on avoiding losses, and reduces motivation to avoid losses. We can then examine whether the effect of acetaminophen on risk-taking is mediated through any of these psychological mechanisms.

Methods

Participants. One-hundred eighty-nine undergraduates at The Ohio State University voluntarily participated in exchange for course credit in their introductory

psychology course. The sample was comprised of 109 men and 79 women (1 participant did not answer) with a mean age of 19.35 years (*SD* = 2.83). We aimed for a sample of 200 participants based on a power analysis of Study 1, and were able to collect 188 prior to the end of the semester.

Acetaminophen. Just as in Study 1, we used a double-blind, placebo-controlled design. Participants were randomly assigned to consume 1000mg of acetaminophen or placebo (94 in placebo, 95 in acetaminophen).

Risk and benefit perception. To examine acetaminophen's effect on risk and benefit perception and the inverse relationship between the two, we used the revised Domain Specific Risk-Taking Scale (DOSPERT; Blais & Weber, 2006; Appendix A). This 30-item scale provides behavioral scenarios and asks participants for their gut-level perception of the riskiness of the behaviors as well as the expected benefits that would be obtained from enacting those behaviors on a 7-point scale ranging from *not at all risky (no benefits at all)* to *extremely risky (great benefits)*. We hypothesized that this scale may be more affectively-stimulating than the items from Study 1 as they are more experientially descriptive and participants are asked to judge risk and benefit personally rather than for society as a whole.

The DOSPERT scale can be analyzed both for general risk and benefit perception 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 ("piloting a small plane") and social ("moving to a city far away from your extended family") domains. Blais and Weber

(2006) have argued that some domains may be more affectively-stimulating than others. As such, we analyze the data both examining average risk/benefit overall and within each of the five specific domains separately.

BART. The same behavioral measure of risk-taking, the BART, was again 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 (Appendix A). The questions focused on the 4 hypothesized mechanisms: affective reactions to bursts, perceived likelihood of bursts, focus on losses and wins during the task, and motivation to avoid bursts. Participants rated the valence of a burst on an 11-point scale ranging from *extremely negative* to *extremely positive*. They also rated their emotional reaction to a burst on an 11-point scale from *little to no emotion* to *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 *not at all* to *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 *not at all likely* to *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 *not at all* to *very much so*. We used these items to explore the psychological processes acetaminophen may be acting on and to determine if acetaminophen's effect on any of these items explained the drug's effect on risk-taking.

Procedure. The procedure for Study 2 was nearly identical to Study 1 and used the same software. Participants gave informed consent, consumed drug or placebo, and

waited 45 minutes while completing background measures. Approximately 50 minutes after drug administration, participants completed the DOSPERT. Following this and approximately 60 minutes after drug administration, participants completed the BART, followed by the self-report BART items.

Results

Risk and benefit perception. First, we used t-tests to compare placebo and acetaminophen groups' summed risk and summed benefit perception across all 30 items of the DOSPERT, as is typically done when analyzing the DOSPERT scale. A t-test revealed a significant difference in risk perception between conditions, $t(187) = 2.72$, $p = .007$. Those on acetaminophen ($M = 133.89$, $SD = 18.03$) perceived significantly less risk than those on placebo ($M = 140.96$, $SD = 17.71$). When analyzed by each domain separately, this effect held for risk perception in the social ($p = .005$) and recreational ($p = .03$) domains, was marginally significant in the financial ($p = .07$) domain, and was non-significant but in the hypothesized direction in the health ($p = .12$) and ethical ($p = .70$) domains.

For benefit perception, a t-test revealed no significant difference in summed benefit perception between conditions, $t(187) = 0.10$, $p = .92$, and this remained true for each of the five domains when analyzed separately.

Risk and benefit correlation. We next 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) to test this. This revealed a trend toward the hypothesized interaction, $b = 0.22$,

$t(185) = 1.52$, $p = .13$. While 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 can be seen in Table 2 (Appendix B), negative correlations between risk and benefit perception were reduced in all domains for participants on acetaminophen. There was a significant interaction between risk perception and drug condition predicting benefit perception in the health domain, $b = 0.23$, $t(185) = 2.11$, $p = .04$, such that there was a stronger negative association between risk and benefit perception for those on placebo ($b = -0.42$, $t(92) = -4.25$, $p < .001$) than those on acetaminophen ($b = -0.19$, $t(93) = -2.59$, $p = .01$). There was also a marginally significant interaction between risk perception and drug condition predicting benefit perception in the ethical domain, $b = 0.20$, $t(185) = 1.90$, $p = .06$, such that there was a stronger negative association between risk and benefit perception for those on placebo ($b = -0.46$, $t(92) = -4.25$, $p < .001$) than those on acetaminophen ($b = -0.17$, $t(93) = -1.65$, $p = .10$). 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: $r = -.45$).

Risk-taking main effect. As in Study 1, we computed participants' adjusted average number of pumps across the 30 trials. Levene's test revealed homogeneity of variances (p = .09). A t-test revealed a significant difference in risk-taking between those on placebo and those on acetaminophen, $t(187) = -2.14$, $p = 0.03$. Those on acetaminophen (M = 36.38, SD = 14.79) engaged in significantly more risk-taking than those on placebo (M = 32.15, SD = 12.14). This replicates the effect seen in Study 1. For an illustration, see Figure 3 (Appendix C).

Risk-taking trial type interaction. Next, we computed the adjusted first-trial pumps and adjusted post-burst pumps as in Study 1. This left us with an effective sample size of 118 participants that had both non-burst first trials and at least one valid (non-burst) post-burst trial. A two-way mixed ANOVA was again used to assess whether drug effects on risk-taking depended on trial type. All studentized residuals were less than +/-3, suggesting no outliers. Levene's test revealed homogeneity of variances ($p > .05$), and Box's test revealed homogeneity of covariances (p = .13). There was a significant interaction between drug condition and trial type on risk-taking, $F(1, 116) = 6.94$, p = .01, $\eta^2 = 0.06$. There was a marginally significant difference in risk-taking between drug conditions on the first trial, $F(1,117) = 3.30$, $p = 0.07$, $\eta^2 = 0.03$. Those on acetaminophen (M = 25.85, SD = 18.76) engaged in marginally significantly less risk-taking on the first trial than those on placebo (M = 32.42, SD = 22.32). There was a significant difference in risk-taking between drug conditions on post-burst trials, $F(1,186) = 4.21$, $p = 0.04$, $\eta^2 = 0.02$, with those on acetaminophen (M = 33.07, SD = 14.83) engaging in significantly more risk-taking on post-burst trials than those on placebo (M = 29.74, SD = 13.35).

There was no statistically significant effect of trial type on risk-taking for those on placebo, $F(1,65) = 1.25$, $p = .27$, $\eta^2 = 0.02$. However, the means were in the hypothesized direction, with those on placebo engaging in more risk-taking on the first trial compared to post-burst trials. There was a significant effect of trial type on risk-taking for those on acetaminophen, $F(1,51) = 5.98$, $p = 0.02$, $\eta^2 = 0.11$. Those on acetaminophen engaged in significantly less risk-taking on the first trials compared to post-burst trials. This is graphed in Figure 4 (Appendix C).

Combining BART data from Study 1 and Study 2. Because the interaction patterns were somewhat inconsistent between Study 1 and Study 2 and because the procedures were very similar in design, we combined the BART data from both studies to look at the pattern overall. A t-test on the combined data revealed acetaminophen significantly increased risk-taking on the BART, $t(329) = -3.15$, $p = 0.002$. This is depicted in graphical from in Figure 5 (Appendix C).

A two-way mixed model ANOVA examined drug effects on the first-trial versus post-burst risk-taking. No studentized residuals were greater than +/- 3, suggesting no outliers. Levene's test revealed homogeneity of variances ($p > .05$), and Box's test revealed homogeneity of covariances ($p = .15$). There was a significant interaction between drug condition and trial type on risk-taking, $F(1, 192) = 8.38$, $p = .004$, $\eta^2 = 0.04$. There was no significant effect of acetaminophen on first-trial risk-taking across the two studies, $F(1,195) = 1.00$, $p = .32$, $\eta^2 = .01$. Those on placebo ($M = 32.49$, $SD = 23.93$) and those on acetaminophen ($M = 29.28$, $SD = 20.55$) did not engage in significantly different amounts of risk-taking on the first trial. There was a significant

effect of acetaminophen on post-burst risk-taking across the two studies, $F(1,326) = 8.87$, $p = .003$, $\eta^2 = .03$. Those on placebo ($M = 30.97$, $SD = 13.99$) engaged in significantly less risk-taking than those on acetaminophen ($M = 35.89$, $SD = 15.85$) on post-burst trials. Across studies, those on placebo engaged in marginally significantly less risk-taking on post-burst trials than on the first trial, $F(1,104) = 3.00$, $p = .09$, $\eta^2 = .03$. Those on acetaminophen engaged in significantly more risk-taking on post-burst trials than on the first trial, $F(1,88) = 5.45$, $p = .02$, $\eta^2 = .06$ (Fig 6, Appendix C).

BART self-reports. Means and standard deviations for all post-BART self-reports can be found in Table 3 (Appendix B). T-tests were used to determine whether acetaminophen significantly affected any of the self-report items that followed the BART in Study 2. There were no significant differences 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 the effects of acetaminophen on risk-taking.

Study 2 Summary

Study 2's findings diverge from Study 1 in that we found stronger evidence that acetaminophen affected use of the affect heuristic on the DOSPERT, but not the scale used by Finucane and colleagues (2000) that was used in Study 1. The negative correlations between risk and benefit perception were substantially stronger in Study 2, and acetaminophen's attenuation effects were found in the domains with larger risk/benefit correlations in the placebo group. This suggests that Study 1 may not have

found an effect due to the items used being somewhat less affectively-stimulating than those in Study 2, leading to less reliance on the affect heuristic.

Additionally, Study 2 provided a replication and attempted extension of Study 1's risk-taking finding. Here, we found acetaminophen again increased risk-taking, and this difference appeared on post-burst trials rather than first trials. When combining data from Study 1 and Study 2 we found strong support for our hypothesis that acetaminophen increased risk-taking.

In terms of mechanism, the interaction analysis on the BART data revealed that those on acetaminophen did not respond to balloon bursts like those on placebo, and the effect of acetaminophen increasing risk-taking is seen only on post-burst trials, not on the first trial before any loss event has been experienced. Interestingly, we did not find any significant drug effects on any of the self-reported items following the BART, suggesting that while acetaminophen does increase risk-taking, it does not appear to affect participant's subjective recalled experiences with the balloon bursts. Unfortunately, this left us without evidence of the potential mediating pathways involving affective reactions to bursts through which acetaminophen leads to increased risk-taking.

Chapter 4: Study 3

Overview

In Study 3, we began to explore the neurochemical mechanisms through which acetaminophen is exerting its risk-taking effects. Here, we explored the effect of another analgesic drug with shared action on the inhibition of prostaglandin synthesis, ibuprofen, on risk-taking behavior. If ibuprofen caused a similar increase in risk-taking behavior, this would suggest acetaminophen may be exerting its effect on risk-taking through action on this immune system pathway.

A second way to examine whether the effects of these drugs on risk-taking occurs through action on an anti-inflammatory pathway is to determine whether the effects of the drug depend on the current state of inflammation in the body. If the effects of acetaminophen or ibuprofen depend on current inflammation, this may suggest that the drugs are interacting with the immune system to produce changes in psychology. We can use self-reported recent illness as a proxy to assess current inflammation in the body. Therefore, we first tested whether ibuprofen significantly increased risk-taking and then tested whether the effects of either acetaminophen (Study 1 and Study 2) or ibuprofen (Study 3) on risk-taking depended on recent illness. The results of these interaction analyses in Study 1 and 2 are reported here as they are more conceptually related to the

research question Study 3 is attempting to address about the physiological mechanism of acetaminophen.

Method

Participants. Participants were 164 undergraduates in an introductory psychology course at The Ohio State University. They voluntarily participated in exchange for course credit. The mean age of participants was 19.25 years (*SD* = 1.42). All participants in this study were male, as ibuprofen is contraindicated for pregnancy and it was not feasible to pregnancy test all of our participants during the study's time frame. There were no interactive effects of acetaminophen and participant sex on any of the dependent variables assessed in Study 1 and Study 2.

Ibuprofen. This study used a double-blind, placebo-controlled design. Participants were randomly assigned to either 400mg of ibuprofen or placebo (81 in placebo and 83 in ibuprofen). This is the manufacturer's recommended dose for reducing the pain of experiences such as a headache. After drug consumption, participants consumed water.

Recent illness. Because ibuprofen inhibits the effects of inflammation in the brain, an indirect assessment of current inflammation was made, as it was hypothesized that the effects of ibuprofen may depend on current inflammatory state. To indirectly assess this, participants reported the extent to which they agreed with the statement "I have felt ill within the past week" on a 5-point scale from *strongly disagree* to *strongly agree.* This same item was included in Studies 1 and 2.

BART. Due to time constraints, participants completed a shortened 20-trial version of the BART. Participants were given the same instructions as in the previous studies.

Procedure. After providing informed consent, participants were randomly assigned to either the ibuprofen or placebo condition. To allow sufficient time for drug uptake, participants completed background measures for the next 45 minutes. At 45 minutes, participants completed three other social cognitive tasks, including an empathy task, a trust game, and responding to affective images. These tasks are in collaboration with other researchers and will not be discussed in this thesis. Approximately 65 minutes after drug administration, participants completed the BART task. To allow for ease of transition between tasks, this task was implemented using the software Inquisit and Inquisit's pre-packaged BART script (Inquisit, Seattle, WA), rather than the PEBL version used in Studies 1 and 2.

Results

Risk-taking main effect. Levene's test revealed homogeneity of variances ($p > .05$). A t-test was used to determine whether the placebo and ibuprofen groups differed on adjusted average number of pumps on the BART. This revealed no significant difference between conditions, $t(160) = -0.26$, $p = .80$. Those on placebo ($M = 28.67$, $SD = 13.98$) and those on ibuprofen ($M = 29.22$, $SD = 13.16$) did not engage in significantly different amounts of risk-taking.

Ibuprofen interaction with recent illness. Self-reported recent illness trended toward predicting risk-taking on the BART, $b = -1.20$, $t(160) = -1.44$, $p = .15$, such that

higher recent illness was associated with lower risk-taking. This may suggest that illness triggers withdrawal or self-protective behaviors, consistent with animal models of sickness behavior being a motivated state (Dantzer, O'Connor, Freund, Johnson, & Kelley (2008).

Next, we tested whether the effect of ibuprofen depended on an individual's inflammatory state, as measured by proxy with self-reported recent illness. To do this, we used PROCESS Model 1 (Hayes, 2012). This revealed a significant interaction between condition and recent illness, $b = 4.29$, $t(158) = 2.49$, $p = .01$. The 95% confidence interval based on 10,000 bootstrap samples did not include zero: [0.89, 7.70]. Probing this interaction using a pick-a-point approach revealed no significant effect of ibuprofen at low levels of recent illness, $p = .28$, or average levels of recent illness, $p = .51$, but ibuprofen significantly increased risk-taking for those at higher levels of recent illness, $p = .03$. Probing this interaction using the Johnson-Neyman technique revealed the point of recent illness at which ibuprofen's effects became significant at the $\alpha = .05$ level was a score of 2.92 on the 5-point recent illness scale. Approximately 29.01% of the sample scored above 2.92.

Acetaminophen interaction with recent illness. To continue to test whether acetaminophen exerted effects on risk-taking through an anti-inflammatory pathway, we returned to the data from Study 1 and Study 2 and tested whether acetaminophen interacted with recent illness to predict risk-taking, using the same statistical models described above. This revealed no significant interaction between acetaminophen condition and recent illness predicting risk-taking on the BART in Study 1, $b = 3.19$,

$t(133) = 1.53$, $p = .13$, and in Study 2, $b = -1.18$, $t(184) = -0.76$, $p = .45$. So while the effects of ibuprofen on risk-taking do seem to depend on recent illness, the effects of acetaminophen do not.

Study 3 Summary

Study 3 builds upon Study 1 and Study 2 by examining whether the effects of acetaminophen on risk-taking generalize to another analgesic. This study did not support our hypothesis. Ibuprofen did not significantly increase risk-taking overall, suggesting acetaminophen's effect on risk-taking may be occurring through a separate neurochemical pathway.

One limitation to this study is that the tasks prior to the BART were quite different. Rather than having people complete decision making, risk perception and benefit perception tasks, participants completed a number of affectively-intense and monetarily rewarding tasks. Perhaps one reason for a lack of effect of ibuprofen on risk-taking is that the BART may have been less affectively-stimulating in comparison to the prior tasks in the ibuprofen study, but not in the acetaminophen studies. Additionally, we used a 20-trial version of the BART in a different computer program. It was discovered after a large number of participants had already completed the study that the balloons in this version of the BART inflate at a faster rate in the program used in Study 3 than the program used in Studies 1 and 2, which may explain why the adjusted average number of pumps was noticeably lower in this study compared to the other two. Finally, we also only had male participants in this study. While there were no significant interactions between acetaminophen and gender predicting risk-taking in Studies 1 and 2, the effect of

ibuprofen may still be different for men versus women, as the single previous study on ibuprofen's social psychological effects suggested (Vangelisti, Pennebaker, Brody, & Guinn, 2014).

Interestingly, we found a significant interaction between ibuprofen and recent illness on risk-taking, such that ibuprofen increased risk-taking for those relatively higher in recent illness. This suggests that inflammation may indeed be involved in risk-taking and ibuprofen may attenuate the sickness-induced withdrawal and inhibition that may decrease risk-taking in those who are ill. The lack of a main effect of ibuprofen on risk-taking in this study and the lack of an interaction of illness symptoms with acetaminophen in Study 1 or Study 2 suggests that there are differences in biological mechanisms between ibuprofen and acetaminophen. However, the significant effect of ibuprofen increasing risk-taking for those with higher recent illness does suggest a potential role for inflammation in risk taking.

Chapter 5: General Discussion

This package of three studies examined the effects of analgesic drugs on risk perception and risk-taking behavior. Overall, the results revealed mixed support for the hypothesis that acetaminophen would reduce the inverse relation between perceived risk and benefit, strong support for the hypothesis that acetaminophen would increase risk-taking and that this would be particularly apparent on post-burst trials, and no support for the hypothesis that the risk-taking effect would extend to another NSAID analgesic, ibuprofen.

While we did not see a reduced correlation between risk and benefit perception for the items tested in Study 1, we did find some evidence for attenuation of reliance on the affect heuristic in Study 2. For domains in which the placebo group exhibited stronger negative correlations between perceived risk and benefit, the acetaminophen group showed significant attenuation of this inverse relationship. This provides some evidence that acetaminophen can affect judgments of risk and benefit, and seems to do so for stimuli that are particularly affectively-stimulating. Interestingly, acetaminophen significantly reduced perceived risk but did not reduce perceived benefit in Study 2. This effect may be due to the construction of the task and will be discussed in the limitations and future directions sections below.

In both Study 1 and Study 2, acetaminophen significantly increased risk-taking on the BART. When decomposed by trial type, acetaminophen did not significantly increase risk-taking on the first trial, but did significantly increase risk-taking on post-burst trials. This provides some insight into how acetaminophen may increase risk-taking by altering the ways in which individuals respond to loss events. Post-burst trials occur right after a strong, negative stimulus, and those on placebo and those on acetaminophen seem to respond to this stimulus in divergent ways. To further probe this potential mechanism, we examined participants self-reports about the loss events experienced during the BART. This, however, did not provide definitiveinsight into the psychological mechanisms through which acetaminophen increases risk-taking, as there was no effect of drug on these items.

Finally, Study 3 revealed no significant effect of ibuprofen on risk-taking overall, though we did find significantly greater risk-taking for those on ibuprofen who reported higher recent illness, an interaction that was not present in the acetaminophen data. This null effect poses some interpretational challenges. Though acetaminophen and ibuprofen do not seem to have exactly the same effects, they do both increase risk-taking, but the effects of ibuprofen are limited to those who are more ill. Perhaps acetaminophen is acting through a different, non-inflammatory mechanism to affect risk perception and risk-taking and ibuprofen is acting through an immune pathway, and both lead to similar results. Or, perhaps ibuprofen's effects are somewhat weaker and were only evident in those who were ill, who may also be those who are more affectively reactive to potential

risks. Further exploration of this effect is necessary to continue to explore the neurochemical underpinnings of acetaminophen's effects.

Limitations

One limitation of Study 2 in particular is the reliance on self-report items to assess the psychological mechanisms through which acetaminophen is increasing risk-taking. The items, which were created for this study, may not have been ideally worded to assess affective reactions, and may have instead elicited more cognitive evaluations. Moreover, these items were assessed only once at the end of the task, rather than during the task, which means individuals had to recall how they felt right after a burst, potentially weakening the effects.

With respect to the lack of an effect of acetaminophen on the benefits items on the DOSPERT, the way the benefit ratings in the DOSPERT were worded may have elicited more cognitive evaluation, while the risk questions may have been more affectively stimulating. This may account for the reduction in perceived risk among participants taking acetaminophen in Study 2, but the lack of an effect on perceived benefits on the DOSPERT.

A limitation for Study 3 in particular is the difficult to interpret nature of null effects. For instance, we cannot assess whether or not a sufficient amount of ibuprofen was acting in the brain during the tasks performed. While we know that acetaminophen exerts effects as early as 45 minutes after drug administration, the formulation of ibuprofen we used may have been absorbed more slowly, and thus require a longer time to exert stronger effects. A measure of physical pain at 45 minutes after administration

would help clarify whether ibuprofen is sufficiently absorbed such that it could affect psychological processes. Moreover, the tasks leading up to the BART in Study 3 were potentially quite different, experientially, than those in Study 1 and Study 2, and the BART itself was run through a different program and with only 20 trials. Because of several potential differences that may have influenced the use of affect in the task, it is difficult to interpret the null results for ibuprofen. Another study should be completed that more closely matches the design of Studies 1 and 2.

One major question concerning the result of all three studies is the degree to which they are generalizable. These participants were not in pain. While we would like to understand the effects acetaminophen may be having on behavior outside the lab, at this point it is not possible to generalize beyond our healthy college student sample. If we want to make claims about the effects of acetaminophen societally, this is something that must be addressed.

Future Directions

There are many opportunities for future work stemming from these initial studies which will further clarify how acetaminophen influences judgment and decision making. First, repeating the DOSPERT task with a few manipulations could elucidate the pattern of results obtained in Study 2. If the lack of effect on perceived benefit was indeed due to the way the question was worded, we should be able to manipulate whether there is an acetaminophen effect on both perceived risk and perceived benefit by framing the question more as a cognitive evaluation or an affective assessment. This would help clarify acetaminophen's effects on risk and benefit perception and determine whether the

effects are only present when affect, rather than cognitive evaluation, is the guiding input. Moreover, we should also assess affective reactions to each item on the risk and benefit perception scales used in Study 1 and Study 2 to examine whether acetaminophen's reduction in risk-benefit correlation occurs through action on affective reactions and to clarify whether Study 1's risk and benefit items are indeed less affectively stimulating than Study 2's.

Additionally, while it seems clear acetaminophen can increase risk-taking, the process through which this occurs is still an open question. While we focused on affect in response to the loss events occurring, it is also possible that affect could be experienced from other stimuli in the task. One mechanism we have not directly explored yet is anticipatory anxiety. As the balloon increases in size, those on placebo may feel increasing amounts of anxiety about a potential burst. When the anxiety reaches a certain threshold, they choose to end the trial. Acetaminophen may be reducing this anxiety, and thus leading to a later escape point and therefore greater risk-taking. There are a few ways we can assess this. One is through adding self-report questions about how anxious individuals felt as the balloon increased in size. Another is through manipulating anxiety during the task itself. Recent research suggests that reducing the ambiguity of when a balloon will burst in the BART by adding a visual depiction of the balloon burst probability attenuates anxiety's effect on risk-inhibition (Smith, Ebert, Broman-Fulks, 2016). Therefore, if acetaminophen is acting through reduced anxiety, it should only increase risk-taking in the original, ambiguous version of the BART which triggers anxiety and not in the new, unambiguous one.

Finally, there are many potentially interesting ways to examine the impact of risk-taking on tasks that involve stronger positive affect. Although we focused more on negative affect in these studies, acetaminophen also reduces positive affect. Risk-taking tasks that focus on the positive affect associated with gains may actually show reverse effects of acetaminophen. For instance, if we manipulated the BART to make the gain events more salient (adding sounds and visuals) or more intense (larger payoffs), we should see acetaminophen actually decrease risk-taking in this case.

Potential Implications

As mentioned before, acetaminophen is a drug taken by an estimated 23% of the U.S. population each week. While the effects of acetaminophen on physical pain have been known since its therapeutic efficacy was demonstrated in the 1940's (Flinn & Brodie, 1948), very little consideration has been given to the effects of this over-the-counter medication on psychological processes.

As we have demonstrated, acetaminophen can influence people's perception of risk and their risk-taking behavior. This is unlikely to be a consideration someone has before they take a few Tylenol with their morning coffee; and yet, this drug potentially impacts judgment and decision-making processes. Now certainly, acetaminophen may not always have negative impacts on judgments. Indeed, affect may sometimes act as a nuisance signal that interferes with the ability to make sound choices. However, affect also often guides and informs decisions in very useful ways, and it may be wise to be cautious of a drug that reduces that important signal.

One domain in which acetaminophen's effects may be particularly impactful is that of the medical decisions made by those in hospital settings. Acetaminophen is the most commonly used drug ingredient, found in more medications than any other drug, according to the manufacturers of Tylenol (www.chpa.org/Acetaminophen.aspx). It is likely that many of the patients who are presented with risk information and asked to make potentially life-changing assessments of risk have acetaminophen in their systems. It is imperative that we understand what effect this may be having on choices made and risks taken.

It is clear that there are many open questions that remain and are worthy of pursuit. As has been evidenced in numerous studies now, acetaminophen has effects on psychological processes. Yet you won't find this information on the drug's warning label. Risk perception and risk-taking are judgments and decisions that can affect so many aspects of our lives, and this common, over-the-counter drug may be interfering with this critical process, unbeknownst to the millions taking the drug.

References

Aklin, W.M., Lejuez, C.W., Zvolensky, M.J., Kahler, C.W., Gwadz, M. (2005). Evaluation of behavioral measures of risk taking propensity with inner city adolescents. *Behaviour Research and Therapy*, *43*(2), 215-228.

Alhakami, A.S., & Slovic, P. (1994). A psychological study of the inverse relationship between perceived risk and perceived benefit. *Risk Analysis, 14*(6), 1085-1096.

Aronoff, D.M., Oates, J.A., & Boutaud, O. (2006). New insights into the mechanism of action of acetaminophen: Its clinical pharmacologic characteristics reflect its inhibition of the two prostaglandin H2 synthases. *Clinical Pharmacology & Therapeutics, 79*(1), 9-19.

Blais, A.R., & Weber, E.U. (2006). A Domain-Specific Risk-Taking (DOSPERT) scale for adult populations. *Judgment and Decision Making, 1*, 33-47.

Chen, M., & Bargh, J. A. (1999). Consequences of automatic evaluation: Immediate behavioral predispositions to approach or avoid the stimulus. *Personality & Social Psychology Bulletin, 25*(2), 215-224.

Dantzer, R., O'Connor, J. C., Freund, G. G., Johnson, R. W., & Kelley, K. W. (2008). From inflammation to sickness and depression: when the immune system subjugates the brain. *Nature Reviews Neuroscience, 9*(1), 46–56.

DeWall, C.N., Chester, D.S., & White, D.S. (2015). Can acetaminophen reduce the pain of decision-making? *Journal of Experimental Social Psychology, 56*, 117-120.

DeWall, C.N., MacDonald, G., Webster, G.D., Masten, C.L., Baumeister, R.F., Powell, C., Combs, D., Schurtz, D.R., Stillman, T.F., Tice, D.M., & Eisenberger, N.I.

(2011). Acetaminophen reduces social pain: Behavioral and neural evidence. *Psychological Science, 21*(7), 931-937.

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*(6), 750-758.

Eisenberger, N.I., Inagaki, T.K., Mashal, N.M., Irwin, M.R. (2010). Inflammation and social experience: An inflammatory challenge induces feelings of social disconnection in addition to depressed mood. *Brain, Behavior, and Immunity, 24*(4), 558-563.

Elliot, A.J. (2006). The hierarchical model of approach-avoidance motivation. *Motivation and Emotion, 30*, 111-116.

Fassbender, K., Schmidt, R., Mosner, R., Kischka, U., Kuhnen, J., Schwartz, A., & Hennerici, M. (1998). Mood disorders and dysfunction of the hypothalamic-pituitary-adrenal axis in Multiple Sclerosis: Association with cerebral inflammation. *Archives of Neurlogy, 55*, 66-72.

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

Fischoff, B., Slovic, P., Lichenstein, S., Read, S., & Combs, B. (1978). How safe is safe enough? A psychometric study of attitudes toward technological risks and benefits. *Policy Sciences, 9*, 127-152.

Flinn, F.B., & Brodie, B.B. (1948). The effect on the pain threshold of n-acetyl p-aminophenol, a product derived in the body from acetanilide. *The Journal of Pharmacology And Experimental Therapeutics, 94*(1), 76-77.

Graham, G. G., Davies, M. J., Day, R. O., Mohamudally, A., & Scott, K. F. (2013). The modern pharmacology of paracetamol: therapeutic actions, mechanism of action, metabolism, toxicity and recent pharmacological findings. *Inflammopharmacology, 21*(3), 201–232.

Gross, J.J. (2002). Emotion regulation: Affective, cognitive, and social consequences.

Psychophysiology, *39*(3), 281-291.

Hayes, A.F. (2012). PROCESS: A versatile computational tool for observed variable mediation, moderation, and conditional process modeling [White paper]. Retrieved from http://www.afhayes.com/public/process2012.pdf

Heilman, R.M., Crisan, L.G., Houser, D., Miclea, M., & Miu, A.C. (2010). Emotion regulation and decision making under risk and uncertainty. *Emotion, 10*(2), 257-265.

Inagaki, T.K., Muscatell, K.A., Irwin, M.R., Moieni, M., Dutcher, J.M., Jevtic, I., Breen, E.C., & Eisenberger, N.I. (2015). The role of ventral striatum in inflammatory-induced approach toward support figures. *Brain, Behavior, and Immunity, 44*, 247-252.

James, W. (1890). *The principles of psychology* (vol. 2). NY: Henry Holt & Co.

Johnson, E.J., & Tversky, A. (1983). Affect, generalization, and the perception of risk. *Journal of Personality and Social Psychology, 45*(1), 20-31.

Kaufman, D.W., Kelly, J.P, Rosenberg, L., Anderson, T.E., & Mitchell, A.A. (2002). Recent patterns of mediation use in the ambulatory adult population of the United State: The Slone survey. *Journal of the American Medical Association, 287,* 337-344.

Kohler, O., Benros, M.E., Nordentoft, M., Farkouh, M.E., Iyengar, R.L., Mors, O., & Krogh, J. (2014). Effect of anti-inflammatory treatment on depression, depressive symptoms, and adverse effects: A systematic review and meta-analysis of randomized clinical trials. *JAMA Psychiatry, 71*(12), 1381-1391.

Lejuez, C.W., Aklin, W., Daughters, S., Zvolensky, M., Kahler, C., Gwadz, M. (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 & Adolescent Psychology, 36*(1), 106-111.

Lejuez, C.W., Read, J.P., Kahler, C.W., Richards, J.B., Ramsey, S.E., Stuart, G.L., Strong, D.R., & Brown, R.A. (2002). Evaluation of a behavioral measure of risk-taking: The Balloon Analogue Risk Task (BART). *Journal of Experimental*

Psychology: Applied, 8(2), 75-84.

Lejuez, C.W., Simmons, B.L., Aklin, W.M., Daughters, S.B., & Dvir, S. (2004). Risk-taking propensity and risky sexual behavior of individuals in residential substance use treatment. *Addictive Behaviors, 29*(8), 1643-1647.

Loewenstein, G.F., Weber, E.U., Hsee, C.K., & Welch, N. (2001). Risk as feelings. *Psychological Bulletin, 127*(2), 267-286.

Maner, J.K., Richey, J.A., Cromer, K., Mallott, M., Lejuez, C.W., Joiner, T.E., & Schmidt, N.B. (2007). Dispositional anxiety and risk-avoidant decision-making. *Personality and Individual Differences, 42,* 665-675.

Mischkowski, D., Crocker, J., & Way, B.M. (2016). From painkiller to empathy killer: Acetaminophen (paracetamol) reduces empathy for pain. *Social Cognitive & Affective Neuroscience, 11*(5).

Mueller, S. T. & Piper, B. J. (2014). The Psychology Experiment Building Language (PEBL) and PEBL test battery. *Journal of Neuroscience Methods, 222*, 250-259.

Panksepp, J., Herman, B., Conner, R., Bishop, P, & Scott, J.P. (1978). The biology of social attachments: Opiates alleviate separation distress. *Biological Psychiatry,* 607-618.

Parkinson, B., Phiri, N., & Gwenda, S. (2012). Bursting with anxiety: Adult social referencing in an interpersonal Balloon Analogue Risk Task (BART). *Emotion, 12*(4), 817-826.

Peters, E. (2006). The functions of affect in the construction of preferences. In S. Lichtenstein & P. Slovic (Eds). The Construction of Preference. New York: Cambridge University Press.

Pickering, G., Loriot, M., Libert, F., Eshcaliere, A., Beaune, P., & Dubray, C. (2006). Analgesic effect of acetaminophen in humans: First evidence of a central serotonergic mechanism. *Clinical Pharmacology & Therapeutics, 79*(4), 371-378.

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*(6), 966-973.

Singla, N.K., Parulan, C., Samson, R., Hutchinson, J., Bushnell, R., Beja, E.G., Ang, R., & Royal, M.A. (2012). Plasma and cerebrospinal fluid pharmacokinetic parameters after single-dose administration of intravenous, oral, or rectal acetaminophen. *Pain Practice, 12*(7), 523-532.

Slovic, P., Finucane, M.L., Peters, E., & MacGregor, D.G. (2004). Risk as analysis and risk as feelings: Some thoughts about affect, reason, risk, and rationality. *Risk Analysis, 24*(2), 311-322.

Smith, A.R., Ebert, E.E., & Broman-Fulks, J.J. (2016). The relationship between anxiety and risk taking is moderated by ambiguity. *Personality and Individual Differences, 95,* 40-44.

Vane, J.R., & Botting, R.M. (1998). Mechanism of action of nonsteroidal anti-inflammatory drugs. *The American Journal of Medicine, 104*(3), 2S-8S.

Vangelisti, A.L., Pennebaker, J.W., Brody, N., & Guinn, T.D. (2014). Reducing social pain: Sex differences in the impact of physical pain relievers. *Personal Relationships, 21*(2), 349-363.

Yuen, K.S.L, & Lee, T.M.C. (2003). Could mood state affect risk-taking decisions? *Journal of Affective Disorders, 75*(1), 11-18.

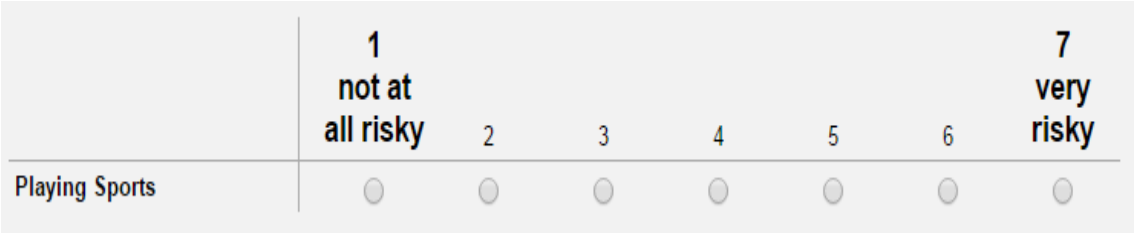
Appendix A: Scales

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.

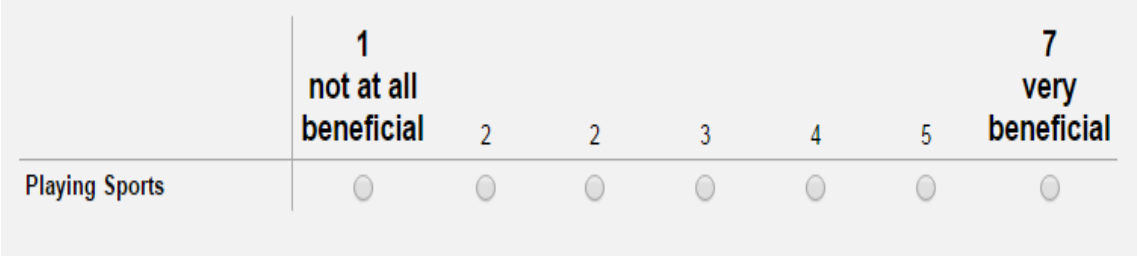


You will only have a **SHORT TIME** to make your decisions. A countdown clock will appear for 5.2 seconds and you must make your decision by the end of the countdown. Your goal is to make your judgments as quickly as you can. Each time, you will select a number on the scale and then click the arrow at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

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)

Appendix B: Tables

Table 1

Risk/Benefit Correlations by Drug Condition in Study 1

Scale Item	**Placebo**	**Acetaminophen**
Averaged All Items	-.01	-.07
Alcoholic Beverages	-.09	-.34**
Water Fluoridation	-.31*	-.60**
Chemical Plants	-.20†	-.21†
Eating Beef	-.40**	-.46**
Food Preservatives	-.28*	-.31*
Cars	-.35**	-.08
Cigarettes	-.16	-.44**
Pesticides	-.29*	-.27*
Natural Gas	-.24†	-.20†
Chemical Fertilizers	-.09	-.42**
Explosives	-.26*	-.23†
Cellular Phones	-.41**	-.29*
Food Irradiation	-.31*	-.38**
Roller Blades	-.25*	.02
Nuclear Power Plants	-.32*	-.44**
Surfing	-.09	.05
Swimming Pools	-.12	-.12
Solar Power	-.48**	-.06
Railroads	-.16	-.27*
Air Travel	-.18	-.23†
Motorcycles	-.12	-.12
Microwave Ovens	-.26*	-.29*
Bicycles	.14	-.03

Note †<.10 *<.05 **<.01

Table 2

Risk/Benefit Correlations by Drug Condition and Domain in Study 2

Domains	**Placebo**	**Acetaminophen**
Averaged All Items	-.18†	.04
Ethical	-.44**	-.16
Financial	-.174 †	-.166
Health	-.45**	-.29**
Recreational	-.34**	-.29**
Social	-.06	.09

Note †<.10 *<.05 **<.01

Table 3

Means and Standard Deviations for Post-BART Self-Reports in Study 2

Self-Report Item	**Placebo**	**Acetaminophen**
Burst Valence	3.83 (2.16)	3.99 (1.95)
Burst Emotion	4.60 (2.71)	4.42 (2.56)
Want to Avoid Future Bursts	6.62 (2.79)	6.51 (2.63)
Try Hard to Avoid Future Bursts	6.55 (2.51)	6.28 (2.60)
Perceived Probability 1	4.49 (1.80)	4.17 (1.65)
Perceived Probability 2	4.53 (1.76)	4.22 (1.61)
Focus on Avoiding Losses	4.54 (1.61)	4.27 (1.61)
Focus on Seeking Gains	5.14 (1.76)	5.18 (1.60)

Appendix C: Figures

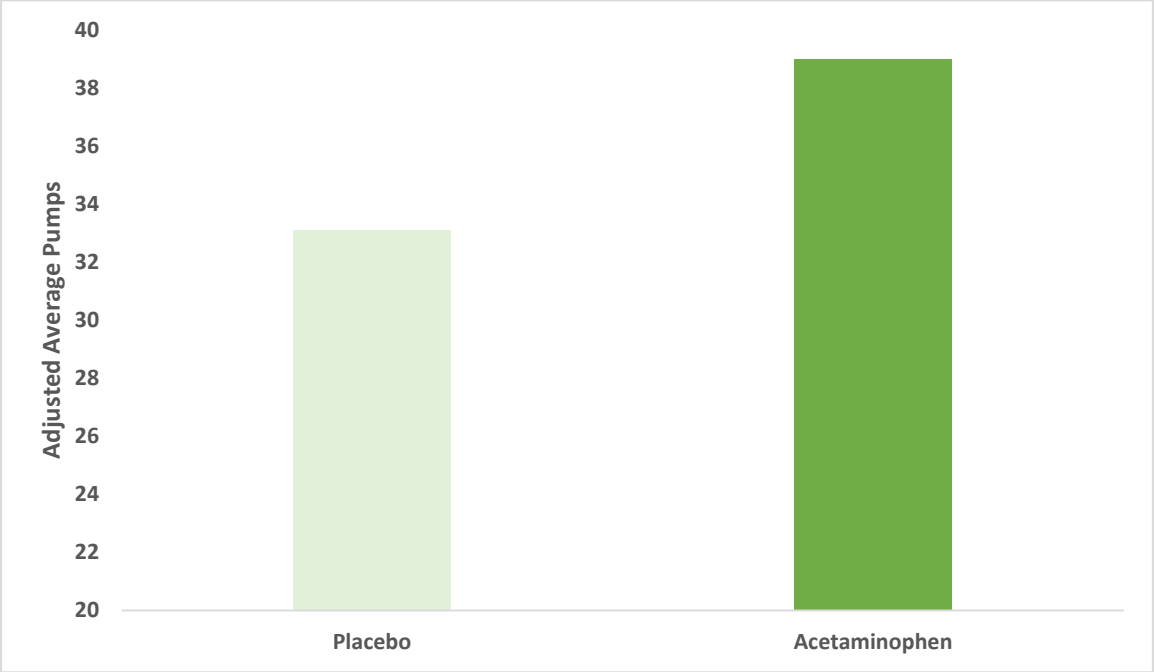


Figure 1. Study 1 main effect on risk-taking. Those on acetaminophen engaged in significantly more risk-taking than those on placebo.

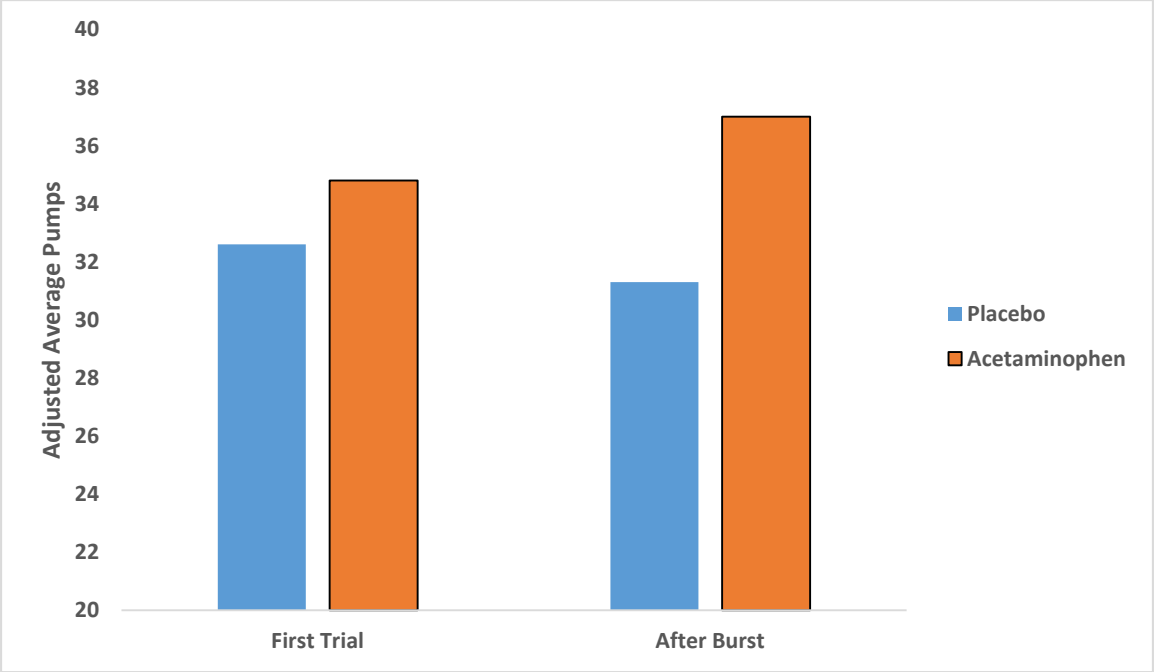


Figure 2. Study 1 risk-taking on first trial versus post-burst. Descriptively, there is a smaller difference between drug conditions on the first trial than post-burst.

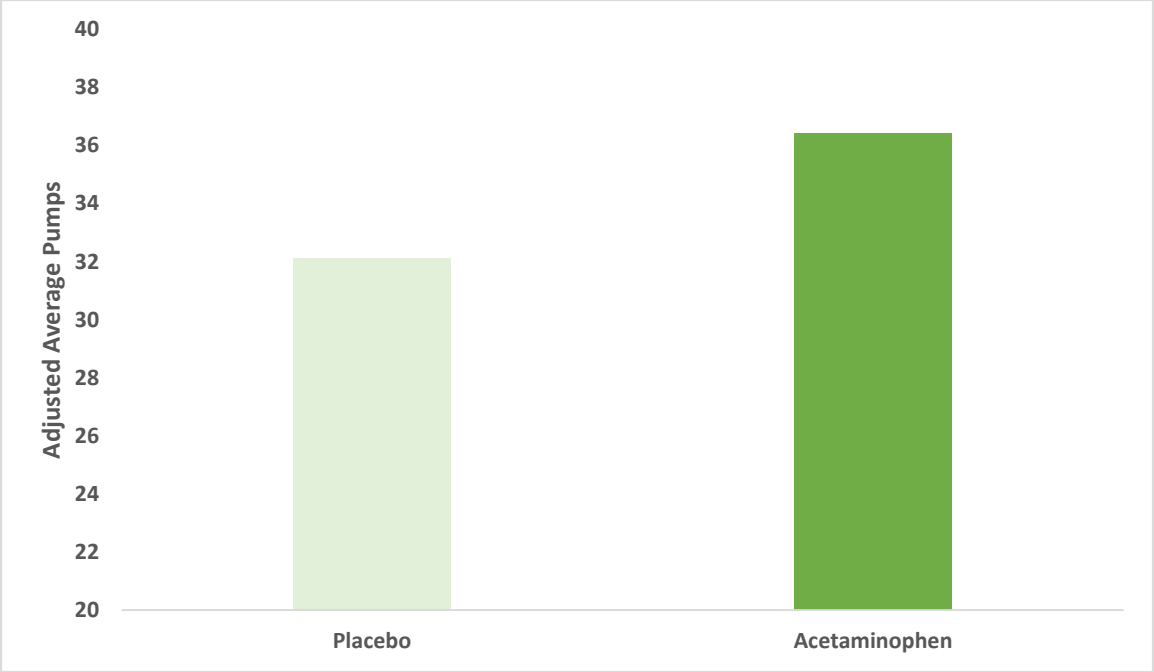


Figure 3. Study 2 main effect on risk-taking. Those on acetaminophen engaged in significantly more risk-taking than those on placebo.

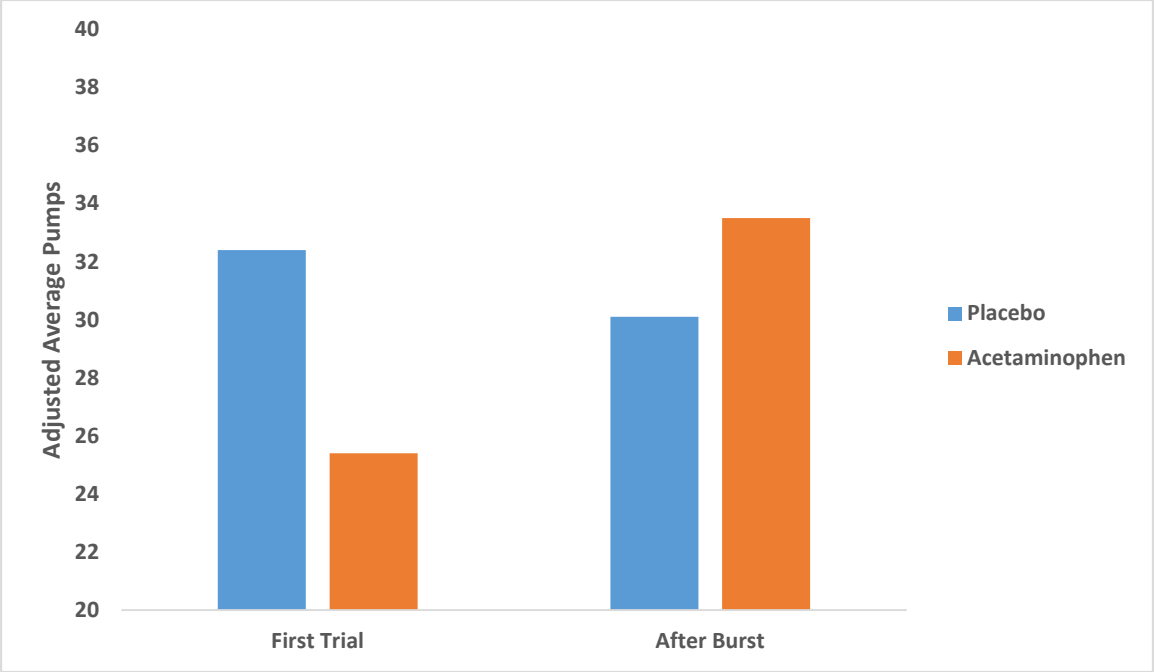


Figure 4. Study 2 risk-taking on first trial versus post-burst. While on the first trial, those on acetaminophen engage in marginally significantly less risk-taking, they engage in significantly more risk-taking on post-burst trials than those on placebo.

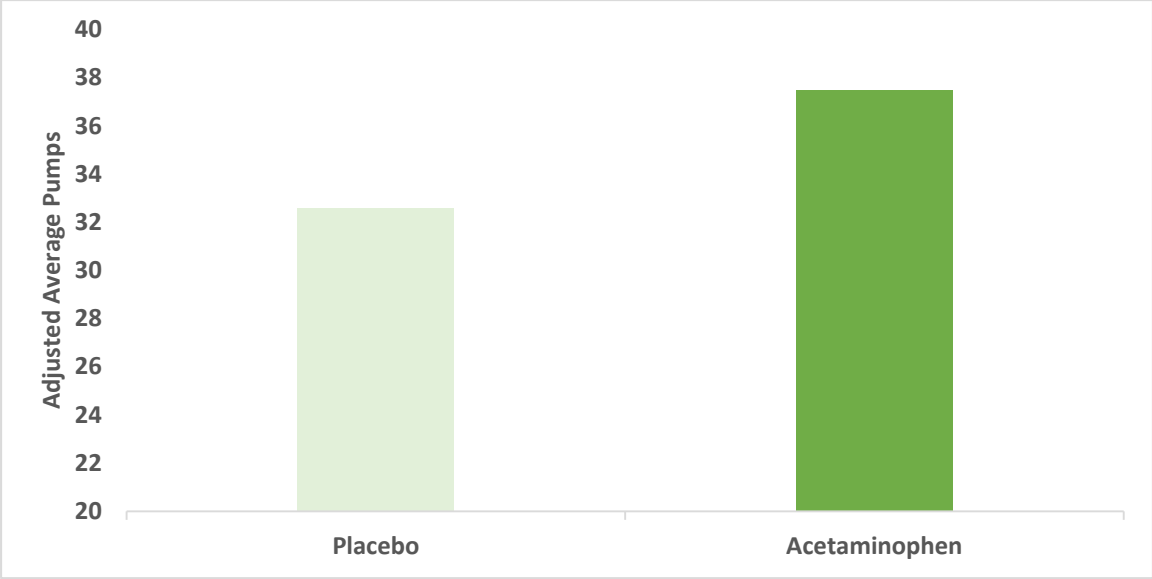


Figure 5. Study 1 and Study 2 combined main effect on risk-taking. Those on acetaminophen engaged in significantly more risk-taking than those on placebo.

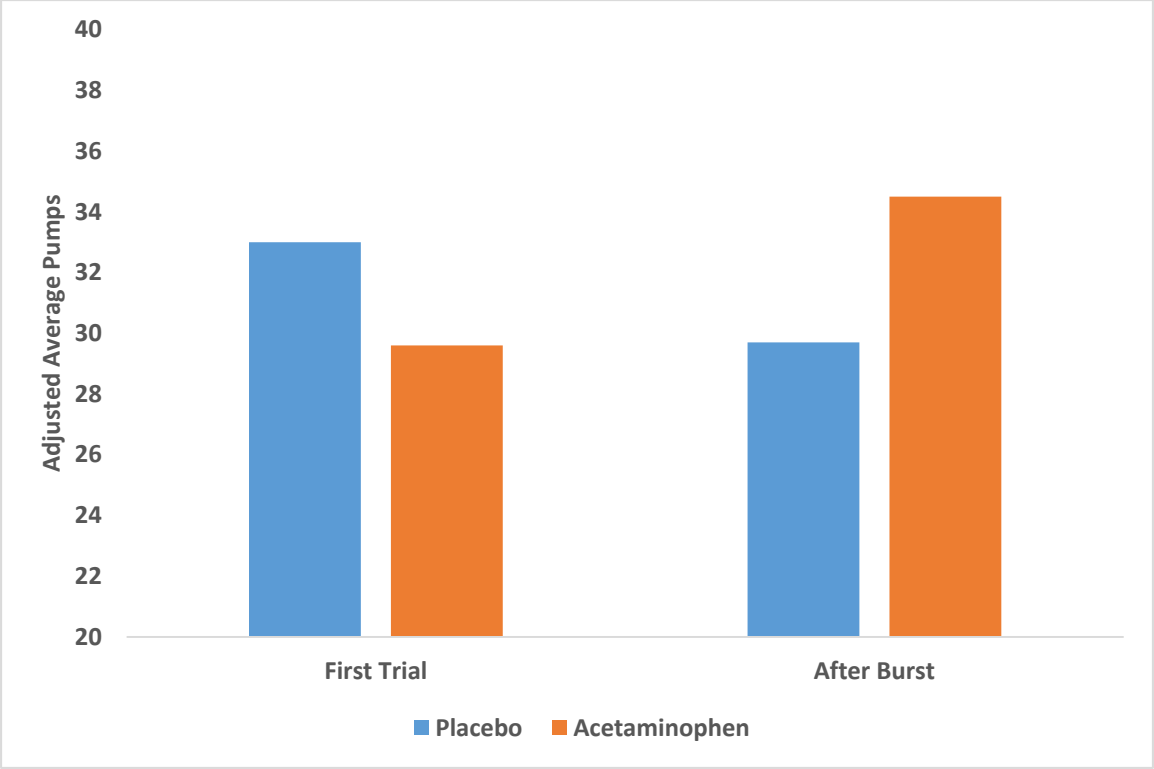


Figure 6. Study 1 and Study 2 risk-taking on first trial versus post-burst. While there is no significant difference between drug conditions on risk-taking on the first trial, those on acetaminophen engage in significantly greater risk-taking than those on placebo on post-burst trials.

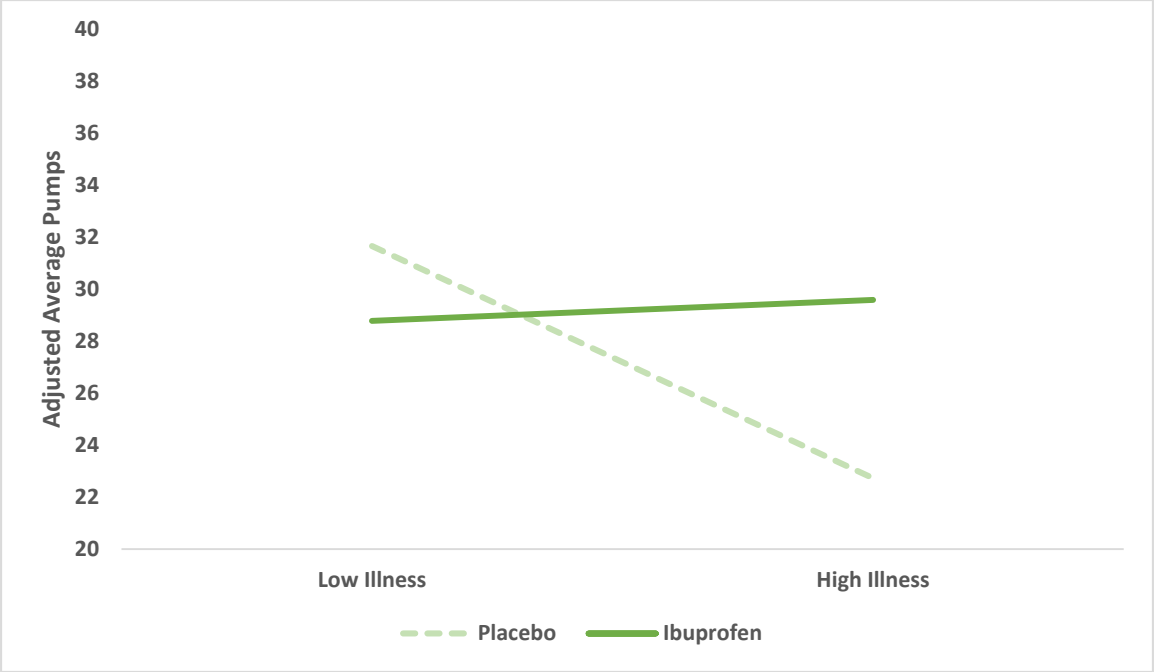


Figure 7. Study 3 ibuprofen by recent illness interaction. Ibuprofen significantly increases risk-taking for those who report higher recent illness, but has no effect for lower or average recent illness.