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Neurophysiological Contributors to Advantageous Risk-Taking:

An Experimental Psychopharmacological Investigation

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Abstract

The ability to learn from experience is critical for determining when to take risks and when to play it safe. However, we know little about how within-person state changes, such as an individual's degree of neurophysiological arousal, may impact the ability to learn which risks are most likely to fail vs. succeed. To test this, we used a randomized, double-blind, placebo-controlled design to pharmacologically manipulate neurophysiological arousal and assess its causal impact on risk-related learning and performance. Eighty-seven adults (45% female, M_{age}= 20.1 ± 1.46 years) took either propranolol (*n*= 42), a beta-adrenergic receptor blocker that attenuates sympathetic nervous system-related signaling, or a placebo (*n*= 45). Participants then completed the Balloon Emotional Learning Task, a risk-taking task wherein experiential learning is necessary for task success. We found that individuals on propranolol, relative to placebo, earned fewer points on the task, suggesting that they were less effective risk-takers. This effect was mediated by the fact that those on propranolol made less optimal decisions in the final phase of the task on trials with the greatest opportunity for advantageous risk-taking. These findings highlight how neurophysiological arousal supports risk-related learning and, in turn, more advantageous decision-making and optimal behavior under conditions of risk.

Keywords: Beta-Adrenergic Blockade; Propranolol; Learning; Risk-Taking; Arousal

Everyday life is filled with situations in which we must decide whether to take a risk or play it safe. Should we ask that attractive stranger for their number, try out that new restaurant, risk not getting a health concern examined? Effective risky decision-making does not just involve estimations of chance, but also requires learning from prior information and experience in order to predict the likelihood of positive or negative outcomes (Ben-Elia, Erev, & Shiftan, 2008; Denrell, 2007). One classic illustration of learning-informed risk-taking is how drivers learn over time which roads have the least risk of traffic given the time of day, weather conditions, etc. For example, during rush-hour, a driver might risk using a short-cut but discover that this risky choice proved worse than their typical route, reducing their likelihood to risk similar short-cuts in the future during comparable traffic conditions.

Ultimately, what factors contribute to people's ability to learn from experience in order to optimize when to play it safe vs. take a risk? Most prior literature investigates the role of trait-based factors such as impulsivity or sensation-seeking in predicting risk-taking (e.g., Khurana, Romer, Betancourt, & Hurt, 2018; Nigg, 2017). This focus on trait-based predictors means we still know little about how *state* factors within the individual impact risk-taking, especially in contexts where experiential learning is critical to success. One longstanding state factor of interest has been *arousal*, with prior theory suggesting that some arousal is beneficial or facilitative for decision-making, especially when decisions are more intuitive, uncertain, ambiguous, or risky (e.g., Bechara, Damasio, & Damasio, 2000; Storbeck & Clore, 2008). Furthermore, a certain degree of arousal can support effective learning, as arousal helps sustain the attention needed for noticing and encoding information while also potentially promoting the acquisition of feedback for learning via exploration and experimentation (e.g., Aston-Jones & Cohen, 2005; Eldar, Cohen, & Niv, 2013; Yerkes & Dodson, 1908). Arousal can be operationalized in several ways—subjectively (e.g., self-report), behaviorally (e.g., pupil dilation), or neurophysiologically (e.g., sympathetic nervous system or SNS signaling). Herein, we manipulated SNS-related neurophysiological arousal using the beta-blocker drug *propranolol* and investigated subsequent effects on risk-taking behavior in a task that requires learning from experience, with the key prediction that propranolol would ultimately impair advantageous risk-taking.

Advantageous Risk-Taking Involves Learning from Experience

Building more accurate predictions from past experience (i.e., learning) is key for guiding advantageous risk decisions in real life outside the laboratory (Ben-Elia et al., 2008; Denrell, 2007; Lo & Repin, 2002). However, most prior lab research examines risk-taking in the context of gambling-based chance games wherein there is little opportunity for learning (FeldmanHall, Glimcher, Baker, & Phelps, 2016; Lejuez et al., 2002; Rogers, Lancaster, Wakeley, & Bhagwagar, 2004). When learning-guided risk-taking is studied in the lab, the Iowa Gambling Task (Bechara et al., 1994) is often used. In this task, participants choose cards from four decks with different—initially unknown—average reward and punishment contingencies. As an implicit learning task, participants must learn from successive trials which decks produce advantageous versus disadvantageous outcomes. Although the Iowa Gambling Task allows for a behavioral test following implicit learning, the choices are forced choice (i.e., participants must choose a card) and categorical, resulting in fewer opportunities to learn and explore within each trial.

To address the need for a more dimensional, learning-driven risk-taking task, Humphreys and colleagues (Humphreys, Lee, & Tottenham, 2013) created the Balloon Emotional Learning Task (BELT). In the BELT, individuals have more opportunity within each trial to explore the bounds of risk-taking (e.g., via balloon pumps) while learning across multiple trials which conditions afford more advantageous vs. disadvantageous risks. The BELT thus offers an improvement over other implicit learning tasks (e.g., Iowa Gambling Task), as it captures more dimensional decision-based processes in contexts that support greater exploration within each trial rather than forced-choice decisions. Initial studies using the BELT suggested that a combination of dispositional factors are associated with maximal task performance (Humphreys et al., 2013). However, less research has examined the intra-individual mechanisms that contribute to learning about advantageous risk-taking. As such, we know little about how within-person state fluctuations influence learning about when it is most effective to take risks.

Theoretical Role of Arousal in Risk-Taking

Both theory and empirical research identify arousal as one fundamental intra-individual pathway that facilitates learning and effective risk-taking. Arousal supports diverse functions such as wakefulness, motivational states, attention to salient or evocative stimuli, encoding and retrieval in learning and memory, and affect-based perceptions and decisions (see discussion in Satpute, Kragel, Barrett, Wager, & Bianciardi, 2019). Arousal is derived from the integration of afferent autonomic signals from the periphery (e.g., the SNS) alongside signals from other neuro-modulating pathways such as the adrenergic/noradrenergic, serotoninergic, and dopaminergic systems (e.g., Berridge, 2008; Coull et al., 1997; Critchley et al., 2000; Kleckner et al., 2017; Robbins & Everitt, 1995; Satpute et al., 2019).

More generally, theories of arousal such as *affect-as-information theory* posit that individuals implicitly use their momentary feelings (e.g., arousal rooted in afferent physiological signals) to evaluate contextual cues and make decisions that drive behavior (Clore, Gasper, & Garvin, 2001; Schachter & Singer, 1962; Schwarz, 2010; Storbeck & Clore, 2008). Similarly, the *somatic marker hypothesis* suggests that physiological sensations during and after decisions help individuals better determine whether or not it will be advantageous to make that decision again in future (Bechara, Damasio, Damasio, & Lee, 1999; Damasio, 1994, 1999). Finally, *predictive inference models of affect* argue that the brain uses both *a priori* knowledge and ongoing afferent physiological signals (including arousal) to interpret contextual cues and inform behavior (Barrett, 2017; Barrett & Simmons, 2015; MacCormack & Lindquist, 2017). Ultimately, these theories suggest that the predictions built through experiential learning should interact with the neurobiology underpinning arousal to improve decision-making under conditions of uncertainty (e.g., risk). Risky decisions, as assessed in this study with a learning task rather than a gambling task and combined with the power of pharmacological blockade, provide a valuable model for testing these theory-driven hypotheses.

Neurobiological Evidence for Arousal in Learning and Risk-Taking

Consistent with the theoretical insights above, a long history of studies in animals and humans show that arousal and arousal-related neurobiology are key mediators of effective learning and risk-

taking. For instance, economic traders who exhibit greater autonomic responses during market trades and those who were more interoceptively aware of their physiological sensations make more advantageous decisions compared to their colleagues (Kandasamy et al., 2016; Lo & Repin, 2002). Arousal also appears to influence gamblers' ability to judge situations and risks effectively (Tranel, 2000). Conversely, blunted arousal or the impaired ability to perceive physiological signaling may hinder learning about advantageous risk-taking (Critchley, Mathias, & Dolan, 2001). For example, during the Iowa Gambling Task, individuals with medical conditions that weaken afferent peripheral signals selected riskier options and performed worse compared to healthy individuals (Busemeyer & Stout, 2002; Yechiam, Busemeyer, Stout, & Bechara, 2005). Neurophysiological arousal may be particularly important for guiding decisions in ambiguous contexts when more information is needed to perform optimally (FeldmanHall et al., 2016; Zink, Pagnoni, Martin-Skurski, Chappelow, & Berns, 2004).

Not only is there promising behavioral evidence for the role of arousal in facilitating advantageous risk-taking, but also there is compelling neurobiological evidence that the SNS and adrenergic/noradrenergic systems matter for both learning and risk-taking (Sara, 2009). The SNS is a fast-acting branch of the autonomic nervous system that helps initiate changes across the cardiovascular system and other modalities (e.g., pupil dilation, sweat) in response to environmental stimuli. As such, the SNS facilitates heightened action-readiness and vigilance to environmental cues, providing richer information when making decisions (Blascovich, Vanman, Mendes, & Dickerson, 2011; Ruffolo, 1991). SNS activation itself is largely instigated by the adrenergic/noradrenergic systems via binding of the catecholamines epinephrine and norepinephrine to beta-adrenergic receptors throughout the body and brain.

Classic rodent experiments demonstrates that knockout, lesioning, or blockade of SNS-related neurobiology reduces learning across multiple domains (e.g., motor, spatial, taste, affective), while increasing reactivity to novel stimuli and modulating arousal-driven memory consolidation and reconsolidation (Cahill, Pham, & Setlow, 2000; Clayton & Williams, 2000; Dębiec & Ledoux, 2004; Decker, Gill, & McGaugh, 1990; Gazarini, Stern, Carobrez, & Bertoglio, 2013; Giustino & Maren, 2018;

Heron, Gould, & Bickford, 1996; Miranda, Rodríguez-García, Reyes-López, Ferry, & Ferreira, 2008; Myers & Rinaman, 2002; Spreng, Cotecchia, & Schenk, 2001). SNS-related signaling further appears to regulate learning through trial-and-error (Amemiya, Kubota, Umeyama, Nishijima, & Kita, 2016), which underscores how arousal-related neurobiological systems may drive learning through the accumulation of priors. More recently, parallel evidence has been observed in humans, wherein SNS-related signaling can alter learning and memory across many domains, including in the affective contexts of reward, threat, and uncertainty (Chae et al., 2019; Coull et al., 1997; Kroes, Strange, & Dolan, 2010; Marshall et al., 2016; Mihov et al., 2010; Soeter & Kindt, 2011). For instance, recent evidence suggests that the this same neurobiology also helps regulate prediction updating in humans during learning tasks (Jepma et al., 2018).

In addition to arousal-related neurobiology supporting learning, these systems are firmly implicated in the computation of risk and resultant decisions and behaviors. Prior experiments suggest that pharmacologically attenuating SNS activation using beta-blockers such as propranolol to disrupt beta-adrenergic signaling can impair cognitive processes related to advantageous risk-taking. Yet most of this work has been conducted in the context of chance-based gambling tasks. For example, individuals randomly assigned to take propranolol were less able to discriminate large potential losses and gains from small ones, in order to guide advantageous gambling decisions (Rogers et al., 2004). Propranolol has also been shown to reduce the ability to track and refer to recent experiences (Lempert, Lackovic, Tobe, Glimcher, & Phelps, 2017), reduce aversion to monetary loss (Sokol-Hessner, Lackovic, et al., 2015), and diminish amygdala-driven modulation of memory in contexts of chance (Phelps, 2006). Despite this work suggesting that beta-adrenergic signaling causally influences decision-making during chance-based gambling, we understand little about whether this same pathway impacts risk-taking during situations in which learning from experience is crucial for success.

The Present Study

The present study thus used *propranolol*, a beta-blocker that blocks the SNS-related effects of epinephrine and norepinephrine at the sites of $\beta 1$ and $\beta 2$ adrenoceptors (Turner, Granville-Grossman, & Smart, 1965) in order to blunt neurophysiological arousal. Specifically, in a randomized, double-blind,

placebo-controlled mechanistic trial, participants took a single 40 mg dose of propranolol or a placebo and completed the BELT to examine beta-adrenergic impacts on learning and advantageous risk-taking. We hypothesized that individuals on propranolol (vs. placebo) would learn the task parameters less effectively and thus take fewer advantageous risks, due to blunted access to neurophysiological arousal.

Methods

Participants

Data presented here were collected as part of a larger project examining how beta-adrenergic receptor blockade impacts reactivity to stress (MacCormack et al., 2021; MacCormack et al., under review). None of the data herein are published elsewhere. Participants were recruited from the University of North Carolina at Chapel Hill and its surrounding community via flyers, class announcements, and email listservs and then screened for eligibility via telephone interview and an in-person visit. Individuals were excluded if they: reported prior/current use of beta-blockers, cigarettes, substances, or prescription medications; had a history of/current physical or mental illness, a pacemaker, known cardiac irregularities, BMI over 33; or if they exhibited low resting blood pressure (BP <80 Hg/ml) or heart rate (HR <60 bpm), given that low BP/HR are contraindications for propranolol. Of the 90 total participants enrolled in the study, 3 had missing BELT data due to computer error. The remaining 87 participants (45% female; M_{age}=20.1±1.46 years, 18-25 years; 56% White, 25% Asian, 9% Black, 7% bi- or multi-racial, and 2% other) are included herein, with n=42 randomly assigned to take propranolol and n=45 randomly assigned to take placebo. Drug groups were randomized such that they were matched on sex [$t(85)$=.074, p=.942] and race/ethnicity [$\chi^2(4, N=87)$= 1.25, p= .870]. See **Table 1** for full participant characteristics and the Supplementary Materials (SMs) for details on statistical power.

Procedures

Participants received either a visually-identical propranolol (40 mg) or placebo tablet, which they self-administered orally under supervision. A single propranolol dose of 40 mg was chosen given that higher doses may have lowered HR/BP to the point of causing fainting in our healthy, young adult sample, and given that 40 mg is a common clinical dosage administered for one-time performance anxiety

situations (e.g., Alexander, Hillier, Smith, Tivarus, & Beversdorf, 2007; Currie, Lewis, McDevitt, Nicholson, & Wright, 1988; Ernst, Lago, Davis, & Grillon, 2016). Given that this was part of a larger study examining stress (see OSF), all participants in both conditions first completed a standard laboratory paradigm designed to elicit social stress (Kirschbaum, Pirke, & Hellhammer, 1993), reported their affective responses, and provided biological samples. Two hours after completing the stressor and 3.5 hours after ingesting the propranolol or placebo, participants completed the BELT. Given that the half-life of propranolol is 5 hours after oral administration (Paterson, Conolly, Dollery, Hayes, & Cooper, 1970; Williams, Leeser, & Rawlins, 1986), propranolol was still in effect during this task. Participants were compensated $100 USD and discharged after confirming that their HR and BP had returned to baseline levels. Procedures were approved by the University of North Carolina at Chapel Hill's Human Subjects Protection Committee (IRB #16-2498).

Measures

Balloon Emotional Learning Task (BELT). To measure risk-taking and learning, participants completed the BELT, a computer task in which participants make decisions about how much to pump up three different colored balloons in order to obtain the highest score. Participants were told that the more points they earned in the game, the more money they would receive as an extra reward.

Participants pumped three different types of balloons which differed by color (blue, pink, orange). Each successful pump was worth one point regardless of balloon color, but each balloon color exploded after a different number of pumps. Specifically, *certain-long* balloons always exploded at 20 pumps, *certain-short* balloons always exploded at 8 pumps, and *uncertain* balloons were unpredictable, exploding at 8, 14, or 20 pumps, depending on the trial. Participants were not told that balloon colors signified different explosion points, but they were explicitly told that not all balloons explode at the same point. Thus, to perform well on the task, participants needed to learn the strength of each balloon type (i.e., color). To make the most advantageous decisions on when to continue vs. stop pumping, participants had to learn that *certain-long* balloons could be pumped the most and would yield the greatest number of points, *certain-short* balloons could only be pumped a few times and yielded fewer points but were still

predictable, whereas *uncertain* balloons could sometimes be pumped many times and thus yield many points but were risky because they would sometimes explode quickly.

To track learning effects, the BELT is divided into three separate task phases (Humphreys et al., 2013). Participants first complete an *early phase* (first 1/3 of trials) wherein they know little about which balloons are the least vs. most risky. This is when we would expect participants to experiment and learn through trial-and-error. The second or *mid-phase* allows individuals to continue learning and fine-tuning their risk predictions based on the early phase. Finally, the third or *late phase* is where individuals can most fully apply whatever information they gained from the prior phases (if they learned effectively) in order to make the most advantageous risk decisions. Ultimately, we expected that if individuals are effectively learning about risk throughout the task, then by the late phase, they should be at their most effective in judging when to vs. not to pump up balloons further.

There were 18 trials per balloon type across the entire task (54 trials in total), and for each third of the task, there was an equal number of trials of each balloon type. This task was identical to that used in prior work (Humphreys et al., 2013), except that we doubled the number of trials, allowing us to examine learning over a longer period of time and provided more opportunities for participants to explore and learn the different balloon contingencies. Participants pressed the spacebar to "pump up" balloons. After the first pump, participants could press another button to "cash in" their pumps for points, or they could continue pumping the balloon. Points accumulated across the course of the entire task. If participants pumped beyond a balloon's limit, an explosion occurred, resulting in the loss of all points for that trial. We examined two primary outcomes from the BELT: (1) *number of points*, which served as our measure of overall task performance and (2) *number of pumps*, which served as our measure of risk-taking. Finally, as a secondary measure of risk-taking—and more specifically, untempered risk-taking, we examined (3) the *number of explosions* that an individual incurred. Given that we doubled the number of trials compared to prior work (e.g., Humphreys et al., 2013), in analyses, we first replicated prior findings with this lengthened task in the placebo group to confirm that participants effectively learned task parameters (see SMs).

Covariates. Both negative, high arousal affect post-stressor and BMI were examined as covariates, to assess whether the stressor from two-hours previously had any lingering effects on BELT performance, and whether BMI altered dosage effects of propranolol. There were no main effects or interactions of either covariate with propranolol or the BELT task parameters in predicting outcomes (see SMs for full details and results).

Data Analyses

Following prior analytical approaches with the BELT (Humphreys et al., 2013), we examined task outcomes (i.e., points, pumps, explosions) by balloon type (i.e., certain-long, certain-short, uncertain) and by task phase (i.e., early, mid, late). **Table 2** displays descriptive statistics for the BELT outcomes split by drug. We conducted three separate mixed ANOVAs (with points, pumps, and explosions as the outcome, respectively), with *balloon type* (certain-long, certain-short, uncertain) x *task phase* (early, mid, late) as within-subjects predictors, and *drug* (0=placebo, 1=propranolol) as a between-subjects predictor. Significant interactions were probed via ANOVAs within each specific task phase and balloon type, to minimize the inflation of a Type 1 error due to multiple pair-wise comparison testing (Kao & Green, 2008). Results presented herein are the main effects of drug, and interactions of drug with the within-subjects variables (e.g., task phase, balloon type). Full results are presented in the SMs.

After testing main effects of drug and interactions, we ran a mediation model used SPSS PROCESS Model 4 (Hayes, 2012), in order to model a simple, parallel mediation between *(a)* the predictor of drug (0=placebo, 1=propranolol), (*b*) the primary mediator of interest, pumps made in the late phase with the certain-long balloon, and (*c*) the primary outcome, total number of points overall achieved across the entire BELT. To assess the indirect effect (*a*b*), we used a nonparametric boot-strap procedure with replacement (*N*= 5000) with 95% bias-corrected confidence intervals (CIs). If the CIs did not include zero, the indirect effect was considered statistically significant.

Results

Beta-Adrenergic Blockade Reduces Overall Task Performance

To examine whether SNS signaling via beta-adrenergic receptors impacts the overall ability to perform well on the BELT, we assessed the effects of propranolol on the number of points earned (**Tables 3-5**). As shown in **Figure 1**, there was a main effect of *drug*, $F(1, 84)=4.86$, $p=.030$, partial $\eta^2=.055$, such that participants on propranolol ($M=337.74$, $SD=72.50$) earned fewer points overall in the task overall relative to those on placebo ($M=373.96$, $SD=82.44$). This suggests that attenuated beta-adrenergic signaling impaired overall task performance. There were no two- or three-way interactions of *task phase* or *balloon type* with *drug* on total points earned across the task (see **Table 3**).

Beta-Adrenergic Blockade Reduces Advantageous Risk-Taking

To examine how SNS signaling via beta-adrenergic receptors impacts advantageous risk-taking, we assessed effects of propranolol on the number of pumps made. There was no main effect of *drug*, though participants on propranolol on average made fewer pumps overall ($M=457.14$, $SD=116.02$) relative to those on placebo ($M=487.36$, $SD=98.93$). There was however a significant three-way interaction between *drug*, *balloon type*, and *task phase*, $F(4, 336)=3.91$, $p=.011$, partial $\eta^2=.044$ (see **Table 3**). To probe this interaction, we ran mixed ANOVAs within each *task phase* (early, mid, late) to examine the main effects and interaction of *balloon type* and *drug*. Within the late task phase (but not the early or mid-phases), we also found a significant interaction of *balloon type* x *drug*, $F(2, 168)=4.52$, $p=.027$, partial $\eta^2=.051$ (see **Table S1** in SMs).

To probe these interactions further, we conducted three separate ANOVAs within the late task phase for each balloon type (**Table 4)**. In each of these three models, *drug* was the independent variable (i.e., between-subjects factor) and pumps in the late phase was the dependent variable. As shown in **Figure 2**, the difference in pumps in the late task phase between drug groups was only significant for the certain-long balloon (i.e., the balloon type with the greatest opportunity for advantageous risk-taking), $F(1, 84)=4.39$, $p=.039$, $\eta^2=.050$. Specifically, individuals on propranolol pumped the certain-long balloon

less (*M*=66.29, *SD*=29.72) than those on placebo (*M*=79.13, *SD*=29.93) in the late task phase. This effect of drug in the late task phase was not observed for the certain-short nor uncertain balloons.

As a secondary measure of risk-taking—and more specifically, untempered risk-taking, we examined the number of explosions. Although the propranolol group exploded more balloons on average (*M*=13.07, *SD*=6.32) than those on placebo (*M*=12.38, *SD*=5.82), there was no main effect of *drug*, nor any two-way or three-way interactions between *drug*, *balloon type*, and *task phase* (**Table 3)**. These findings suggest that people in both the propranolol and placebo conditions exploded balloons at a similar rate.

Mediation Linking Propranolol with Reduced Task Performance

Finally, in a mediation model, we examined if decreased pumping of the certain-long balloon during the final phase explained why individuals on propranolol scored fewer points overall relative to those on placebo. As shown in **Figure 3**, all paths were significant (*ps*<.00-.03), with a significant total effect (*c*= -37.40, *SE*= 16.95, *p*= .028). The indirect (a*b) effect was also significant, 95% CIs [-61.78, -2.17], demonstrating mediation. This suggests that blunted neurophysiological arousal (i.e., via SNS-related beta-adrenergic signaling) among those on propranolol disrupted optimal performance in part because it decreased effective learning about which risks were advantageous, particularly in the task condition with the most opportunity for risk-taking.

Discussion

The goal of this study was to examine how in-the-moment neurophysiological arousal impacts learning which risks are likely to be rewarded vs. detrimental. In a sample of healthy young adults, we pharmacologically manipulated SNS-related beta-adrenergic signaling, a key contributor to neurophysiological arousal, and examined consequent effects on risk-taking during a task in which learning from experience is critical for success. We found that individuals randomly assigned to take propranolol earned fewer points in the task than those on placebo, suggesting that blockade of beta-adrenergic signaling impaired performance. Moreover, mediation analysis suggested that attenuated beta-adrenergic signaling impaired performance in part because it reduced learning about which risks (i.e.,

balloon pumps) were advantageous. Together, these results suggest that a certain amount of neurophysiological arousal can help individuals more effectively learn over time which risks are advantageous, ultimately optimizing decision-making performance.

Specifically, we found that individuals with full access to their neurophysiological signals (i.e., those on a placebo) took more risks compared to those with attenuated neurophysiological arousal (i.e., those on propranolol), but only in the task condition that allowed the most risk-related exploration (i.e., the balloon that exploded the slowest), and only toward the end of the task (i.e., in the last phase of the trials). Indeed, mediation analysis showed that the placebo group's greater pumping during this condition partially explained their greater overall task performance. We take these findings as evidence that SNS-related beta-adrenergic signaling helped facilitate more effective information gathering and risk-related learning, leading those on placebo to ultimately take more advantageous risks. In contrast, we there were no arousal effects on BELT performance in the early phase, as presumably both groups (regardless of whether they were on placebo vs. propranolol) were gathering information about the risky nature of each balloon type. Likewise, there were no effects of propranolol in the mid-phase of the task, suggesting that beta-adrenergic facilitation of risk-related learning may take time to unfold. Beta-adrenergic signaling also did not impact risk-taking behavior within the certain-short balloon type (i.e., balloons that quickly exploded consistently). Indeed, it appears that all participants quickly mastered the meaning of certain-short balloons, perhaps because quickly exploding balloons may be more surprising or easy to detect. Similarly, beta-adrenergic signaling did not impact risk-taking in the uncertain condition, in which balloons exploded seemingly at random, consistent with the notion that arousal could not facilitate effective learning when there were no predictable rules or parameters that could be inferred from the context.

Collectively, these findings are consistent with classic work wherein an optimal amount of arousal can be facilitative for performance (Yerkes & Dodson, 1908) whereas too little arousal (e.g., when blunted by beta-blockade) can impair performance. We did not test what might happen when there is a high degree of neurophysiological arousal (e.g., upon administration of epinephrine or

norepinephrine), but it is likely that this would likewise impair performance on the BELT, given that high arousal states and related neurophysiology can impair several domains of performance, memory, and cognition (e.g., Maran et al., 2017; Marko & Riečanský, 2018; Wichary, Mata, & Rieskamp, 2016).

One possible psychological mechanism underlying these findings is that optimal neurophysiological arousal heightens attention and salience of low-level perceptual cues that augment performance. Supporting this interpretation, affect-as-information theory and related work posit that arousal provides valuable insight in part by heightening attention to important environmental stimuli (Critchley & Garfinkel, 2018; Storbeck & Clore, 2008). Indeed, SNS-derived physiological activation is known to amplify the sensitivity of sensory modalities associated with vigilance, such as pupil dilation (Bradley, Miccoli, Escrig, & Lang, 2008; Lempert et al., 2017). Supporting this, a recent study found that propranolol led individuals to commit to an early decision in an information sampling task, rather than continue to gather more information (Hauser, Moutoussis, Purg, Dayan, & Dolan, 2018). Moreover, there is emerging evidence that visceral afferent signals and interoceptive awareness thereof can more broadly enhance evaluations of risk and learning more generally (Kandasamy et al., 2016; Pfeifer et al., 2017; Sokol-Hessner et al., 2009, 2015). Given that neurophysiological arousal facilitates the saliency of and attention to low-level perceptual cues in the environment, an optimal amount of arousal could, as part of learning, increase attention to the success vs. failure of past and ongoing risky decisions, thus guiding effective decision-making.

A second possible psychological mechanism is that individuals on propranolol may have been less cognitively alert compared to those on placebo, which may have reduced their capacity to learn from task feedback (e.g., explosions or tracking of point gains). As propranolol lowers heart rate and blood pressure and can contribute to feelings of lethargy (Ko, 2002), individuals on propranolol may have exerted less effort in the task. In future studies, one way to assess this "effort" hypothesis would be to collect trial-by-trial reaction times, as these could provide implicit measures of participant effort and risky decision deliberation. Unfortunately, we did not collect reaction time data during the BELT, and

thus can only speculate that propranolol-induced lethargy and/or a lack of alertness could be one pathway contributing to these effects.

This study had limitations. Although propranolol's bioavailability peaks one hour after ingestion, we did not administer the BELT until 3.5 hours after participants took the medication. Although this is within the 5-hour half-life of propranolol (Paterson et al., 1970; Williams et al., 1986), our effects may have differed or been stronger if the BELT was completed when effects of propranolol were at their peak. Further, we did not collect physiological measures proximal to BELT completion, which would have provided further confirmation that propranolol was still active. It is also possible that the stress task completed as part of the larger study influenced the present results, although we controlled for post-stressor negative, high arousal affect in analyses to reduce this possibility. Future replications and extensions wherein the BELT is completed at the peak of propranolol bioavailability and without preceding tasks would provide a more precise estimate of the effect of propranolol on advantageous risk-taking. In addition, future research should clarify the extent to which laboratory-based tasks such as the BELT generalize to real-world contexts wherein optimal performance is contingent upon higher-stakes learning, such as in classroom, health, and personal finance settings.

In sum, the present study adds to growing literature on the role of arousal and SNS-related beta-adrenergic signaling as a key neurophysiological pathway subserving successful risk-taking and learning. These findings are important given that real-world risk-taking is often predicated upon experiential, adaptive learning processes (e.g., using predictions gained through trial-and-error) that support optimal risk-related decisions (Denrell, 2007; Pleskac, 2008). To our knowledge, this constitutes the first known causal evidence in humans that neurophysiological arousal instantiated by beta-adrenergic signaling contributes to our ability to learn when to take advantageous risks that lead to desired outcomes. More generally, these findings contribute to growing understanding that physiology influences cognitive and behavioral processes (e.g., Critchley & Garfinkel, 2018; Eisenberger, Moieni, Inagaki, Muscatell, & Irwin, 2017; MacCormack & Lindquist, 2018) and extends this work by

suggesting that neurophysiological arousal can enhance the learning of risky, yet advantageous, behavioral strategies.

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Table 1. Participant characteristics.

Demographics	Placebo	Propranolol	Total
N Sex: Female	20 (23.0%)	19 (21.8%)	39 (44.8%)
N Sex: Male	25 (28.7%)	23 (26.4%)	48 (55.2%)
N Race: Asian descent	11 (12.6%)	11 (12.6%)	22 (25.3%)
N Race: African descent	5 (5.7%)	3 (3.4%)	8 (9.2%)
N Race: European descent	26 (30.0%)	23 (26.4%)	49 (56.3%)
N Race: Bi- or multi-racial	2 (2.3%)	4 (4.6%)	6 (6.9%)
N Race: Other	1 (1.1%)	1 (1.1%)	2 (2.3%)
Mean Age	20.49 ± 1.59	20.07 ± 1.30	20.28 ± 1.45
Mean BMI	22.96 ± 2.38	22.47 ± 2.52	22.72 ± 2.45
Mean Obj SES	16.48 ± 1.95	16.24 ± 1.88	16.36 ± 1.92

Note: Frequency counts show percentages of total sample. Objective SES was operationalized as the mean years of education that both parents completed. There were no significant differences between drug groups (as tested by Person's chi-square and independent samples t-tests) on sex, race, age, BMI, or objective SES (all *ps*> .10).

Table 2. Mean points, pumps, and explosions by balloon condition, drug, and task phase.

Outcome	Balloon	Drug	Task Phase					
			Early Phase		Mid-Phase		Late Phase	
			M	*SD*	*M*	*SD*	*M*	*SD*
Points [a]	**Certain-long**	Placebo	55.02	18.34	66.98	23.53	73.69	27.54
		Propranolol	49.38	15.07	60.83	25.37	59.95	23.53
	Certain-short	Placebo	16.31	8.86	24.18	11.02	26.07	11.21
		Propranolol	16.14	6.57	19.57	9.81	22.14	11.63
	Uncertain	Placebo	37.07	13.35	35.40	13.17	39.29	11.25
		Propranolol	26.69	10.26	34.10	13.61	29.02	13.21
Pumps [b]	**Certain-long**	Placebo	59.60	21.94	71.44	27.49	79.13	29.93
		Propranolol	55.69	23.22	64.26	28.99	66.29	29.72
	Certain-short	Placebo	42.31	4.96	41.82	4.34	40.73	4.86
		Propranolol	40.19	7.03	40.52	7.25	39.90	7.25
	Uncertain	Placebo	48.53	12.02	48.53	12.03	49.89	10.34
		Propranolol	50.45	15.26	49.79	13.56	51.05	16.06
Explosions [b]	**Certain-long**	Placebo	0.33	0.56	0.38	0.65	0.42	0.69
		Propranolol	0.41	0.73	0.24	0.43	0.52	0.77
	Certain-short	Placebo	3.38	1.50	2.24	1.69	1.96	1.68
		Propranolol	3.07	1.40	2.69	1.81	2.38	1.96
	Uncertain	Placebo	1.67	1.07	1.56	1.39	1.20	1.31
		Propranolol	1.38	1.08	1.83	1.53	1.31	1.28

Note. Points represent performance on the BELT, pumps represent risk-taking, and explosions represent untempered risk-taking. The total task contained 54 trials, with 18 trials (6 of each balloon type) in each phase of the task. [a] In each task phase, participants could earn a maximum of 114 points from the *certain-long* balloons, 42 points from the *certain-short* balloons, and variable number of points from the *uncertain* balloons. [b] In each task phase, the *certain-long* balloon exploded on the 20th pump (with a maximum number of 114 possible safe pumps and up to 6 explosions), the *certain-short* balloons exploded on the 8th pump (with a maximum number of 42 possible safe pumps and up to 6 explosions), and *uncertain* balloons exploded on the 8th, 14th, or 20th pumps (with a variable number of maximum possible safe pumps and up to 6 explosions). For any trial where a balloon exploded, all points on that trial were lost.

Table 3. Mixed effects ANOVAs assessing overall effects of propranolol, balloon type, and BELT task phase on BELT points earned, pumps made, and explosions, controlling for negative, high arousal affect.

		Points Model			**Pumps Model**			**Explosions Model**		
Predictors	***df***	***F***	***p***	***partial η^2***	***F***	***p***	***partial η^2***	***F***	***p***	***partial η^2***
Between-subject effects										
Intercept	1	**224.34**	**.000**	**.728**	**192.41**	**.000**	**.699**	**56.63**	**.000**	**.403**
Drug	1	**4.86**	**.030**	**.055**	1.90	.172	.022	0.16	.688	.002
Affect	1	0.22	.641	.003	0.55	.463	.007	0.56	.456	.007
Error	84									
Within-subject effects										
Balloon	2	**35.26**	**.000**	**.296**	**11.94**	**.000**	**.124**	**20.43**	**.000**	**.196**
Balloon x Drug	2	2.65	.092	.031	2.22	.135	.026	0.23	.728	.003
Balloon x Affect	2	0.38	.613	.004	0.19	.713	.002	0.14	.808	.002
Balloon (Error)	168									
Task phase	2	3.08	.051	.035	2.36	.115	.027	0.70	.491	.008
Task phase x Drug	2	1.57	.213	.018	0.38	.616	.004	2.43	.094	.028
Task phase x Affect	2	0.01	.984	.000	0.40	.599	.005	0.88	.412	.010
Task phase (Error)	168									
Balloon x Task	4	**2.72**	**.034**	**.031**	**6.53**	**.000**	**.072**	**2.86**	**.031**	**.033**
Balloon x Task x Drug	4	1.32	.264	.015	**3.91**	**.011**	**.044**	1.52	.203	.018
Balloon x Task x Affect	4	0.70	.584	.008	0.78	.500	.009	1.40	.239	.016
Balloon x Task (Error)	336									

Note: *Drug* was coded 0=Placebo, 1=Propranolol. *Affect* refers to post-stressor mean negative, high arousal affect. *Balloon* included three types: certain-long, certain-short, and uncertain. *Task* included three phases or averaged timepoints: the early task phase, mid-task phase, and the late task phase. Given that the repeated measures of *balloon type* and *task phase* were significant in Mauchly's test of sphericity (*ps*<.000), model p-values reported use the Greenhouse-Geisser correction. Significant effects are bolded.

Table 4. Univariate ANOVAs probing overall effects of propranolol on BELT pumps in the late task phase split by balloon type, controlling for negative, high arousal affect.

		Long-Certain Balloon Model			**Short-Certain Balloon Model**			**Uncertain Balloon Model**		
Predictors	***df***	***F***	***p***	η^2	***F***	***p***	η^2	***F***	***p***	η^2
Between-subject effects										
Intercept	1	**72.19**	**.000**	**.462**	**479.18**	**.000**	**.851**	**153.86**	**.000**	**.647**
Drug	1	**4.39**	**.039**	**.050**	0.58	.448	.007	0.11	.744	.001
Affect	1	0.61	.438	.007	0.92	.339	.011	0.22	.639	.003
Error	84									

Note: *Drug* was coded 0=Placebo, 1=Propranolol. *Affect* refers to post-stressor mean negative, high arousal affect. Significant effects are bolded.

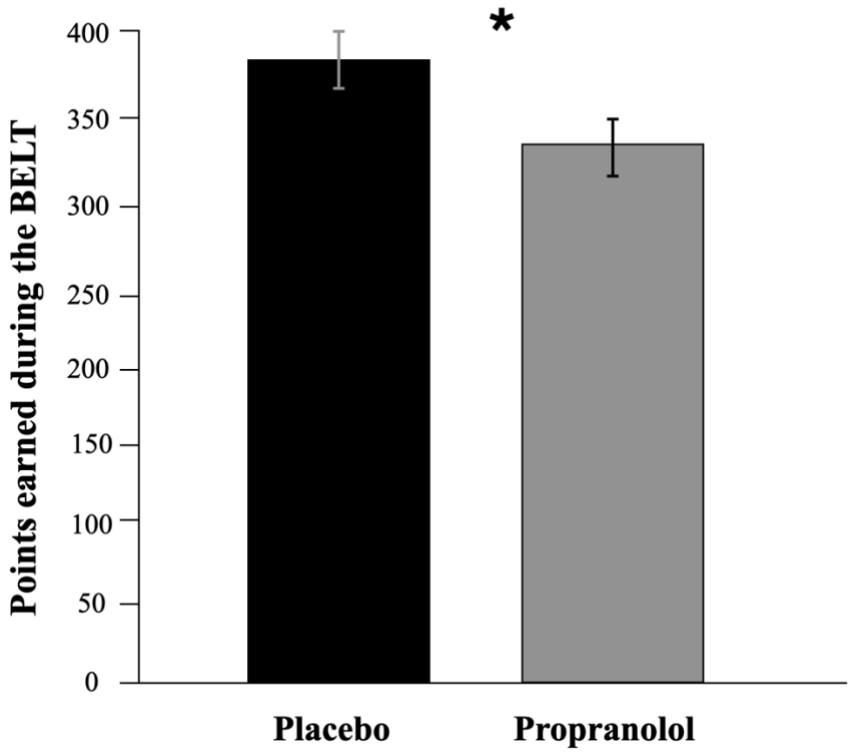

Figure 1. Points earned by placebo and propranolol groups in across the task. There was a main effect of drug, $F(1, 84)=4.85$, $p=.030$, partial $\eta^2=.055$, such that participants on propranolol ($M=337.74$, $SD=72.50$) earned fewer points across the task than those on placebo ($M=373.96$, $SD=82.44$). Error bars are standard errors.

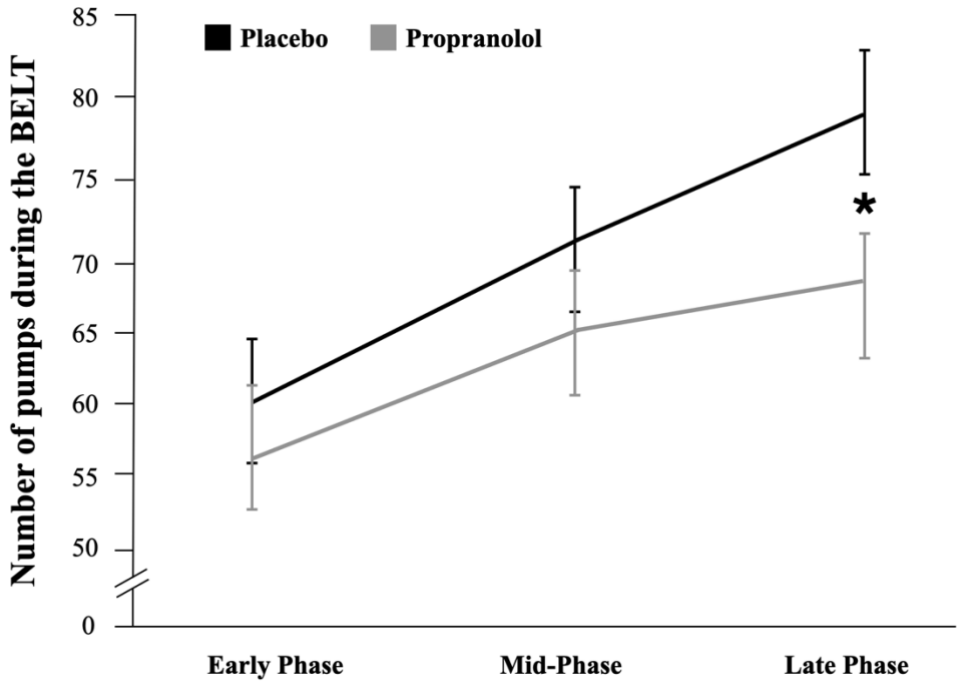

Figure 2. Pumps across task phases split by drug within the certain-long balloon type. The difference in pumps between drug groups was only significant for the certain-long balloon in the final phase of the task, $F(1, 84)=4.39$, $p=.039$, $\eta 2=.050$, and not the first two task phases ($ps>.05$), such that the propranolol group ($M=66.29$, $SD=29.72$) pumped less in the final third of the task than did the placebo group ($M=79.13$, $SD=29.93$). Error bars are standard errors.

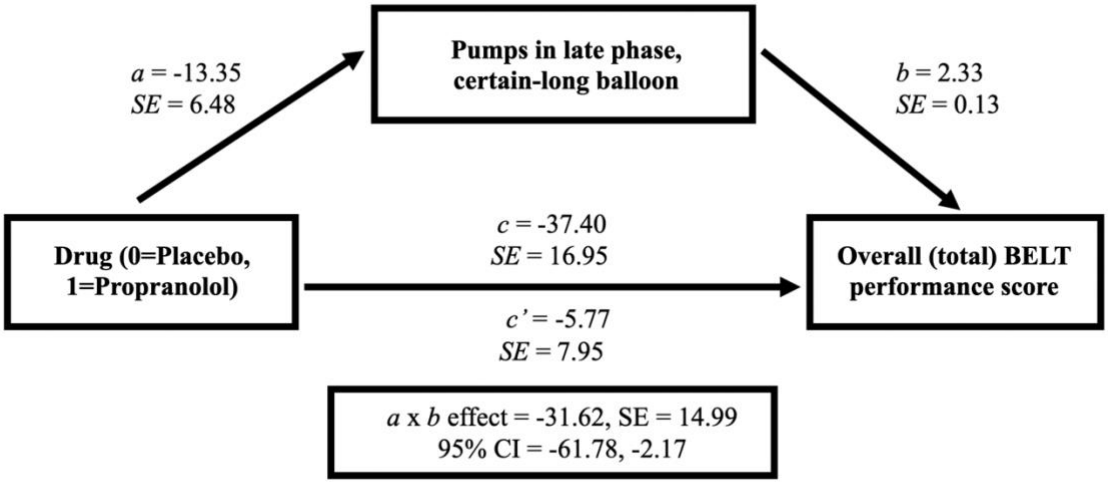

Figure 3. Mediation model. The link between drug condition and higher overall BELT performance scores (total accumulated points across the entire task) was mediated via a significant indirect (a*b) effect of pumps made in the late phase with the certain-long balloon, estimated between 95% CIs [-61.78, -2.17]. Because zero was not within the 95% CI, the indirect effect was significantly different from zero at $p<.05$. Note all paths are significant but see Results for specific details.

Supplementary Materials for: "Neurophysiological Contributors to Advantageous Risk-Taking: An Experimental Psychopharmacological Investigation" in *Social Cognitive & Affective Neuroscience*

Supplementary Methods

Power Estimates

A priori power analyses were conducted to determine sample size with respect to the study's primary goal of investigating the effects of beta-blockade with propranolol on stress reactivity, but not with respect to secondary measures such as the BELT. However, there are two prior studies which similarly investigated the effects of propranolol on decision-making and risk-taking: Sokol-Hessner, Lackovic et al. (2015) with a final overall N=47 and Lempert et al. (2017) with a final N=37. Our sample of N=87 roughly doubles that of prior studies, increasing the power to detect a between-subjects effect of propranolol. Finally, the BELT task is a within-subjects, repeated-measures design with numerous trials for each balloon type and task phase, affording greater power to detect significant effects.

Covariates

One of the primary questions of interest in the broader study was propranolol's effect on participants' emotional responses to an acute psychological stressor, which was operationalized as a mean score of self-reported negative, high arousal affect after the stress task. Negative, high arousal affect was assessed with the expanded Positive and Negative Affect Schedule (e.g., endorsement of emotions such as anxious, embarrassed, stressed; Watson, Clark, & Tellegen, 1988) after the stressor. Participants in the propranolol condition reported somewhat lower negative, high arousal affect after the stressor (M=1.63, SD=.67) relative to those in the placebo condition (M=1.82, SD=.61), although this was not significant: $t(85)=1.36$, $p=.179$. The BELT task was administered two hours after the termination of the stressor, which should have provided ample time for recovery. Nonetheless, as one could argue that there may be lingering stressor effects on BELT performance, we included negative, high arousal affect as a covariate in the present statistical models (though there was never a significant effect of this variable in any model).

Finally, some prior relevant work with propranolol and risk-taking has found that BMI can moderate propranolol's effects (e.g., Sokol-Hessner, Lackovic et al., 2015 and Lempert et al., 2017), especially in samples with a wide range in participant BMI. In our study, we specifically excluded individuals with high BMI (i.e., greater than 33), resulting in a restricted BMI range (BMI=18-28) and no significant *drug condition* differences by BMI. Nonetheless, to support completeness in the literature, we report exploratory analyses controlling for BMI in addition to negative, high arousal affect. No BMI effects were observed (see below).

While our primary analyses control for negative, high arousal affect and/or BMI, we also report the results from unadjusted analyses with no covariates included in models in Tables S4-S5, for the sake of future meta analyses.

Supplementary Results

Assessing Potential Participant Unblinding

We assessed whether participants were able to correctly guess whether they were on placebo or propranolol using a Pearson χ^2 test. Within the placebo group (n=45), 43 participants (95.6% on placebo) correctly guessed they were on placebo, with only 2 participants (4.4% on placebo) incorrectly guessing they might be on propranolol. Within the propranolol group (n=42), 14 participants (36.8% on propranolol) correctly guessed they were on propranolol, 24 participants (63.2%) incorrectly thought they were on placebo, with responses missing from 4 participants on propranolol. The overall χ^2 test was significant: $\chi^2(1, N=87)= 13.90$, $p<.001$, largely driven by placebo participants correctly guessing they were on placebo. Notably, when examining within-guess type effects, there were no significant differences between groups in terms of guessing they were on placebo nor guessing they were on propranolol ($ps<.05$). Altogether, this suggests that by the end of the study session when we asked participants to guess their condition, individuals on placebo were likely unblinded, but individuals on propranolol largely remained blinded to their condition (i.e., unable to guess greater than chance within the condition). The potential unblinding in the placebo condition could be explained by participants' lack of noticeable side effects, consistent with other work noting this as common in placebo groups (Kolahi,

Bang, & Park, 2009; Park, Bang, & Cañette, 2008; Schulz, Chalmers, & Altman, 2002). The fact that most individuals on propranolol also thought they were on placebo further suggests that propranolol at 40mg has a subtle (i.e., less noticeable) dampening beta-adrenergic cardiovascular effect, which is ideal for drug effect studies where it is better for drug effects to be unobtrusive.

Replication of BELT Performance in the Placebo Condition Only

Our first goal was to test for replication of findings from the BELT (Humphreys et al., 2013) with our lengthened design. In order to do so, we first examined outcomes of interest (i.e., points, pumps) first among the placebo group only (n=45) and then in the full sample (n=87). We ran two separate repeated-measures ANOVAs (one with *points* as outcome, one with *pumps* as outcome), with *balloon type* (certain-short, uncertain, certain-long) and *task phase* (early, mid, late) as within-subject factors, within the placebo group only. We also controlled for negative, high arousal affect measured after the stress task.

Points Earned. For our measure of performance, points earned, there was a main effect of *balloon type*, $F(2, 84)=15.12$, $p<.001$ partial $\eta^2=.261$, such that the most points were earned in the certain-long condition (M=195.69, SD=63.61), followed by the uncertain condition (M=111.76, SD=14.65), and then the certain-short condition (M=66.56, SD=26.91). Post-hoc analyses revealed that the difference in points earned between each of the balloon types were all significant from one another ($p<.01$). There was also a main effect of *task phase*, $F(2, 84)=3.85$, $p=0.25$, partial $\eta^2=.82$, such that number of points earned in each phase increased linearly across the task, with the greatest number of points earned in the late phase (i.e., last third of trials) of the task (M=139.04, SD=34.71), followed by mid-phase (M=126.56, SD=35.30) and then the early phase (M=108.40, SD=26.42). The differences between each of these task phases was also significant, $p<.01$. These results indicate an improvement in performance (i.e., number of points earned) with greater task experience (i.e., each subsequent phase of the task), and replicate prior work by Humphreys et al. (2013).

Pumps Made. For our measure of risk-taking, pumps, there was a main effect of *balloon type*, $F(2, 84)=4.30$, $p=.017$, partial $\eta^2=.09$, such that there were the greatest number of pumps on the certain-

long balloons (*M*=210.18, *SD*=72.28), followed by uncertain balloons (*M*=152.31, *SD*=32.20), and then certain-short balloons (*M*=124.87, *SD*=11.03). Only the difference between pumps in the certain-long balloon and pumps in the certain-short balloon was significant, $p<.05$. A marginal main effect was also found for *task phase*, $F(2, 84)=2.54$, $p=.085$, partial $\eta^2=.06$, such that pumps increased in the late phase of the task, with more pumps in the late phase (*M*=169.76, *SD*=35.18), compared to the mid-phase (*M*=161.80, *SD*=36.83) or the early phase (*M*=155.80, *SD*=38.10), $p<.05$. The difference between pumps in the early and mid- phases of the task was not significant ($p=.18$). There was also a significant *balloon type x task phase* interaction, $F(4, 168)=3.90$, $p<.005$, partial $\eta^2=.08$. To further examine this interaction, we conducted three additional ANOVAs within each task phase with pumps in each balloon type included as a within-subject factor (repeated measures). The difference between *balloon types* was only significant in the final phase of the task, $F(2,84)=6.00$, $p=.004$, partial $\eta^2=.12$, although it was also marginal for the mid-phase of the task, $F(2,84)=4.30$, $p=.017$, partial $\eta^2=.091$. This indicates that pumping differences between the balloon types were most prominent in the last phase of the task, when participants had learned task parameters.

Explosions. For our measure of un-tempered risk-taking, explosions, there was a main effect of *balloon type*, $F(2, 84)=13.08$, $p<.001$ partial $\eta^2=.23$, such that the most explosions occurred in the certain-short balloons (*M*=7.31, *SD*=4.11), followed by uncertain balloons (*M*=4.22, *SD*=2.30), and then certain-long balloons (*M*=0.84, *SD*=1.04). These were all significantly different from each other, $p<.001$. There was also a marginal main effect of *task phase*, $F(2, 84)=2.61$, $p=.08$ partial $\eta^2=.06$, such that there were significantly more explosions in the early phase of the task (*M*=5.12, *SD*=2.12), compared to the mid-phase (*M*=3.91, *SD*=2.76) and compared to the late phase (*M*=3.33, *SD*=2.18), and a trend toward more explosions in the mid-phase compared to the late phase ($p=.09$). These results indicate a general pattern of reduction in explosions with greater task experience and mirror prior work by Humphreys et al. (2013).

Taken together, analyses examining the effect of *balloon type* and *task phase* on points and pumps suggest that participants within the placebo condition were able to learn the basic task parameters

across the testing session, and that we replicate the results of Humphreys et al. (2013) in this doubled version of the original BELT task, as examined within the placebo group.

BELT Main Effects and Interactions between Balloon Type and Task Phase

As the main goal of the present study was to examine the effects of beta-adrenergic blockade on advantageous risk-taking and risk-related learning, results presented in the main text focus on the main effects of *drug condition* and interactions between *drug condition*, *balloon type*, and *task phase* on points, pumps, and explosions. Primary results control for the between-subject covariates of post-stressor negative, high arousal affect)—see **Table S1**. Exploratory results additionally controlling for BMI are presented in **Tables S2-S3**.

Points Earned. For our measure of performance, points, there was a main effect of *balloon type*, $F(2, 168)=35.26$, $p<.0001$, partial $\eta^2=.30$, such that participants scored the most points with the certain-long balloon ($M=183.36$, $SD=61.98$), followed by the uncertain balloon ($M=110.82$, SD=17.20), and then the certain-short balloon ($M=62.36$, $SD=24.61$). The differences between points earned across balloon types were all significantly different from each other, as revealed by post-hoc pairwise comparisons: long-certain vs. short-certain balloon, $M_{diff}= 40.23$, $SE=2.21$, $p<.0001$, long-certain vs. uncertain balloon, $M_{diff}= 24.04$, $SE=1.97$, $p<.0001$, and short-certain vs. uncertain balloon, $M_{diff}= -16.19$, $SE=1.13$, $p<.0001$.

There was also a marginal effect of task phase, $F(2, 168)=3.08$, $p=.051$, partial $\eta^2=.04$, such that points somewhat increased linearly across the task, with the greatest number of points in the late phase of the task ($M=130.38$, $SD=35.34$), followed by mid-phase ($M=120.74$, $SD=34.59$) and then the early phase ($M=105.41$, $SD=23.87$). The differences between each of these task phases were significant: early vs. mid-task, $M_{diff}= -5.07$, $SE=1.09$, $p<.0001$, early vs. late task, $M_{diff}= -8.26$, $SE=1.18$, $p<.0001$, and mid- vs. late task $M_{diff}= -3.18$, $SE=.97$, $p=.002$. There was also a significant *balloon type x task phase* interaction for points, $F(4, 336)=2.72$, $p=.034$, partial $\eta^2=.03$.

To further examine this *balloon type x task phase* interaction, we conducted additional ANOVAs separately for each *task phase*, with *balloon type* as a repeated-measures factor. In the early phase of the

task, there was a significant effect of *balloon type*, $F(2,168)=24.99$, $p<.0001$, partial $\eta^2=.23$. Post-hoc pair-wise comparisons showed that, in the early phase, participants scored the most points in the long condition, followed by the uncertain condition, and then the short condition, which were all significantly different from each other: long-certain vs. short-certain balloon, $M_{diff}= 35.97$, $SE=2.08$, $p<.0001$, long-certain vs. uncertain balloon, $M_{diff}= 15.32$, $SE=1.79$, $p<.0001$, and short-certain vs. uncertain balloon, $M_{diff}= -20.65$, $SE=1.70$, $p<.0001$. In the mid-phase of the task, there was a similar significant effect of balloon typ,e $F(2,168)=24.67$, $p<.0001$, partial $\eta^2=.23$, with the same pattern of participant scoring: long-certain vs. short-certain balloon, $M_{diff}= 42.02$, $SE=2.74$, $p<.0001$, long-certain vs. uncertain balloon, $M_{diff}= 29.14$, $SE=2.53$, $p<.0001$, and short-certain vs. uncertain balloon, $M_{diff}= -12.88$, $SE=1.80$, $p<.0001$. Finally, there was the same effect of balloon type in the last phase of the task as well, $F(2,168)=22.25$, $p<.0001$, partial $\eta^2=.21$, with the same pattern of participant scoring: long-certain vs. short-certain balloon, $M_{diff}= 42.69$, $SE=2.67$, $p<.0001$, long-certain vs. uncertain balloon, $M_{diff}= 27.65$, $SE=2.90$, $p<.0001$, and short-certain vs. uncertain balloon, $M_{diff}= -15.04$, $SE=1.85$, $p<.0001$.

Pumps Made. For our measure of risk-taking, pumps, we broadly replicated our main findings from the placebo group analysis. There was again a main effect of *balloon type*, $F(2, 168)=11.94$, $p<.0001$, partial $\eta^2=.12$, such that there were the greatest number of pumps on the certain-long balloons ($M=198.62$, $SD=74.92$), followed by uncertain balloons ($M=151.80$, $SD=34.50$) and then certain-short balloons ($M=122.82$, $SD=16.39$). The differences between pumps made across balloon types were all significantly different from each other, as revealed by post-hoc pairwise comparisons: long-certain vs. short-certain balloon, $M_{diff}= 25.15$, $SE=2.57$, $p<.0001$, long-certain vs. uncertain balloon, $M_{diff}= 15.47$, $SE=2.14$, $p<.0001$, and short-certain vs. uncertain balloon $M_{diff}= -9.68$, $SE=1.00$, $p<.0001$. There was no main effect of *task phase*, $F(2, 168)=2.36$, $p=.115$, partial $\eta^2=.03$. There was however, as above with points, a significant *balloon type x task phase* interaction for pumps, $F(4, 336)=6.53$, $p<.0001$, partial $\eta^2=.07$.

To further examine this interaction, we conducted additional ANOVAs separately for each *task phase*, with *balloon type* as a repeated-measures factor. Post-hoc pairwise comparisons revealed that the interaction was driven by a strong increase in pumps made across the certain-long balloon type compared to stable pumps during the certain-short condition and the uncertain balloon type. Specifically, in the early phase, there was a significant effect of balloon type, $F(2,168)=5.82$, $p=.009$, partial $\eta^2=.07$. Post-hoc pairwise comparisons revealed that participants pumped more in the long condition, followed by the uncertain condition, and then the short condition, which were all significantly different from each other: long-certain vs. short-certain balloon, $M_{diff}= 16.40$, $SE=2.33$, $p<.0001$, long-certain vs. uncertain balloon, $M_{diff}= 20.77$, $SE=2.35$, $p<.0001$, and short-certain vs. uncertain balloon, $M_{diff}= 4.37$, $SE=1.23$, $p=.001$. In the mid-phase of the task, there was a similar significant effect of balloon type, $F(2,168)=18.30$, $p<.0001$, partial $\eta^2=.18$, with the same pattern of pumps: long-certain vs. short-certain balloon, $M_{diff}= 26.70$, $SE=2.89$, $p<.0001$, long-certain vs. uncertain balloon, $M_{diff}= 33.09$, $SE=2.88$, $p<.0001$, and short-certain vs. uncertain balloon, $M_{diff}= 6.42$, $SE=1.55$, $p<.0001$. Finally, there was the same effect of balloon type in the last phase of the task as well, $F(2,168)=13.09$, $p<.0001$, partial $\eta^2=.14$, with a similar pattern of pumps as above: long-certain vs. short-certain balloon, $M_{diff}= 32.38$, $SE=3.22$, $p<.0001$, long-certain vs. uncertain balloon, $M_{diff}= 22.23$, $SE=2.83$, $p<.0001$, and short-certain vs. uncertain balloon, $M_{diff}= -10.15$, $SE=1.35$, $p<.0001$.

Explosions. For explosions, there was a main effect of *balloon type*, $F(2, 168)=20.43$, $p<.0001$, partial $\eta^2=.20$, such that the most explosions occurred in the certain-short balloons ($M=7.59$, $SD=4.17$), followed by uncertain balloons ($M=4.28$, $SD=2.51$), and then certain-long balloons ($M=0.85$, $SD=1.13$), $p=.001$. The differences between pumps made across balloon types were all significantly different from each other, as revealed by post-hoc pairwise comparisons: long-certain vs. short-certain balloon, $M_{diff}= -2.24$, $SE=.16$, $p<.0001$, long-certain vs. uncertain balloon $M_{diff}= -1.11$, $SE=.09$, $p<.0001$, and short-certain vs. uncertain balloon, $M_{diff}= 1.13$, $SE=.14$, $p<.0001$. However, there was no effect of *task phase*, $F(2,$

168)=.70, p=.491, partial η^2=.01. Finally, as in the other two models, there was a significant *balloon type x task phase* interaction, $F(4, 336)=2.86$, p=.031 partial η^2=.03.

To further examine this interaction, we conducted additional ANOVAs to examine explosions in *balloon type* included as factors (repeated measures) within each task phase. Specifically, in the early phase, there was a significant effect of balloon type on explosions: $F(2,168)=24.84$, $p<.0001$, partial η^2=.23. Post-hoc pairwise comparisons revealed that participants exploded balloons the least in the long condition, followed by the uncertain condition, and then the short condition, which were all significantly different from each other: long-certain vs. short-certain balloon, M_{diff}= -2.86, SE=.16, $p<.0001$, long-certain vs. uncertain balloon, M_{diff}= -1.16, SE=.11, $p<.0001$, and short-certain vs. uncertain balloon M_{diff}= 1.70, SE=.17, $p<.0001$. In the mid-phase of the task, there was a similar significant effect of balloon type $F(2,168)=9.64$, $p<.0001$, partial η^2=.10, with the same pattern of explosions as above: long-certain vs. short-certain balloon, M_{diff}= -2.16, SE=.19, $p<.0001$, long-certain vs. uncertain balloon, M_{diff}= -1.39, SE=.16, $p<.0001$, and short-certain vs. uncertain balloon, M_{diff}= .77, SE=.18, $p<.0001$. Finally, there was the same effect of balloon type in the last phase of the task as well, $F(2,168)=7.46$, p=.002, partial η^2=.08, with the same pattern of explosions as above: long-certain vs. short-certain balloon, M_{diff}= -1.69, SE=.22, $p<.0001$, long-certain vs. uncertain balloon, M_{diff}= -.78, SE=.16, $p<.0001$, and short-certain vs. uncertain balloon, M_{diff}= .91, SE=.22, $p<.0001$.These results again indicate a reduction of explosions with greater task experience, particularly in the certain-short and uncertain conditions, and mirror our results in the placebo group and prior work (Humphreys et al., 2013).

Supplementary Discussion

Although not the focus of the present study, it is worth speculating about the possible neural pathways through which neurophysiological arousal may contribute to successfully learning what risks are likely to be rewarded vs. those that should be avoided. Prior research suggests that an amygdala-striatal circuit is important for guiding affect-based decision-making (van Holstein, MacLeod, & Floresco, 2020; Watanabe, Sakagami, & Haruno, 2013) and that propranolol attenuates amygdala

activity (Hurlemann et al., 2010), suggesting the possibility that propranolol may disrupt effective risk-taking in part by blunting amygdala activity and/or amygdala-striatal connectivity (Phelps, Lempert, & Sokol-Hessner, 2014). Further, the anterior insula is known to play a critical role in integrating afferent physiological information to guide effective behavior (Craig, 2004, 2009; Critchley, 2009) while also helping identify salient stimuli that can then facilitate motivated behaviors (Uddin, 2015). Thus, diminished beta-adrenergic signaling among those on propranolol could potentially lead to both blunted amygdala and anterior insula activity and a corresponding decreased ability to track and identify optimal risk-taking conditions, a hypothesis that should be more fully tested in future studies. Alternatively, given that propranolol has been shown to disrupt the acquisition of emotion-related memories (Chalkia, Weermeijer, Van Oudenhove, & Beckers, 2019; Weymar et al., 2010; see Lonergan, Olivera-Figueroa, Pitman, & Brunet, 2013 for meta-analysis), it could be the case that individuals on propranolol did not learn as effectively which task conditions were optimally "risky" in part because they did not fully encode or update this information in memory during the task due to attenuations of amygdala and/or hippocampal activation. Future neuroimaging work that examines the effects of propranolol on the neural circuitry engaged during learning and risk-taking is needed to adjudicate between these different possibilities.

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Table S1. ANOVAs probing effects of propranolol on BELT points, pumps, and explosions, split by task phase, controlling for negative, high arousal affect.

		Early Task Phase			Mid-Task Phase			Late Task Phase		
Predictors	***df***	***F***	***p***	***partial η^2***	***F***	***p***	***partial η^2***	***F***	***p***	***partial η^2***
BELT Points										
Between-subject effects										
Intercept	1	**214.73**	**.000**	**.719**	**132.31**	**.000**	**.612**	**150.82**	**.000**	**.642**
Drug	1	1.65	.203	.019	2.77	.100	.032	**5.93**	**.017**	**.066**
Affect	1	0.38	.538	.005	0.12	.729	.001	0.08	.778	.001
Error	84									
Within-subject effects										
Balloon	2	**24.99**	**.000**	**.229**	**24.67**	**.000**	**.227**	**22.25**	**.000**	**.209**
Balloon x Drug	2	1.44	.239	.017	0.71	.468	.008	**3.91**	**.030**	**.044**
Balloon x Affect	2	0.11	.884	.001	0.73	.460	.009	0.49	.578	.007
Balloon (Error)	168									
BELT Pumps										
Between-subject effects										
Intercept	1	**195.37**	**.000**	**.699**	**160.01**	**.000**	**.656**	**194.84**	**.000**	**.699**
Drug	1	0.96	.330	.011	1.60	.209	.019	2.50	.118	.029
Affect	1	0.11	.747	.001	0.19	.668	.002	0.80	.374	.009
Error	84									
Within-subject effects										
Balloon	2	**5.83**	**.009**	**.065**	**18.30**	**.000**	**.179**	**13.09**	**.000**	**.135**
Balloon x Drug	2	0.33	.642	.004	1.16	.304	.014	**4.52**	**.027**	**.051**
Balloon x Affect	2	0.04	.914	.000	0.95	.363	.011	0.34	.615	.004
Balloon (Error)	168									
BELT Explosions										
Between-subject effects										
Intercept	1	**47.66**	**.000**	**.362**	**35.72**	**.000**	**.298**	**33.75**	**.000**	**.287**
Drug	1	1.03	.314	.012	0.61	.436	.007	1.18	.280	.014
Affect	1	0.01	.919	.000	1.15	.287	.014	0.59	.443	.007
Error	84									
Within-subject effects										
Balloon	2	**24.84**	**.000**	**.228**	**9.64**	**.000**	**.103**	**7.46**	**.002**	**.082**
Balloon x Drug	2	1.06	.342	.012	1.41	.248	.016	0.26	.734	.003
Balloon x Affect	2	0.12	.855	.001	1.03	.356	.012	0.81	.429	.010
Balloon (Error)	168									

Note: *Drug* was coded 0=Placebo, 1=Propranolol. *Affect* refers to post-stressor mean negative, high arousal affect. Given that *balloon type* was significant in Mauchly's test of sphericity, model *p*-values reported use the Greenhouse-Geisser correction. Significant effects are bolded.

Table S2. Mixed effects ANOVAs assessing overall effects of propranolol, balloon type, and BELT task phase on BELT points earned, pumps made, and explosions, controlling for both affect and BMI.

		Points Model			**Pumps Model**			**Explosions Model**		
Predictors	***df***	***F***	***p***	***partial η^2***	***F***	***p***	***partial η^2***	***F***	***p***	***partial η^2***
Between-subject effects										
Intercept	1	**197.33**	**.000**	**.704**	**192.41**	**.000**	**.699**	**49.55**	**.000**	**.374**
Drug	1	**4.96**	**.029**	**.056**	1.90	.172	.022	0.15	.699	.002
Affect	1	0.16	.686	.002	0.55	.463	.007	0.51	.476	.006
BMI	1	0.79	.377	.009	0.36	.553	.004	0.18	.676	.002
Error	83									
Within-subject effects										
Balloon	2	**28.81**	**.000**	**.258**	**9.34**	**.002**	**.101**	**17.89**	**.000**	**.177**
Balloon x Drug	2	2.75	.085	.032	2.35	.123	.028	0.21	.744	.002
Balloon x Affect	2	0.29	.671	.004	0.14	.755	.002	0.13	.811	.002
Balloon x BMI	2	1.22	.289	.014	1.61	.209	.019	1.13	.312	.013
Balloon (Error)	166									
Task phase	2	2.55	.084	.030	1.07	.329	.013	0.87	.419	.010
Task phase x Drug	2	1.57	.212	.019	0.40	.603	.005	2.33	.104	.027
Task phase x Affect	2	0.02	.979	.000	0.28	.683	.003	0.71	.488	.008
Task phase x BMI	2	0.10	.899	.001	2.68	.090	.031	2.44	.093	.029
Task phase (Error)	166									
Balloon x Task	4	1.85	.126	.022	**4.47**	**.005**	**.051**	2.18	.081	.026
Balloon x Task x Drug	4	1.32	.263	.016	**4.10**	**.009**	**.047**	1.51	.207	.018
Balloon x Task x Affect	4	0.59	.654	.007	0.66	.571	.008	1.29	.277	.015
Balloon x Task x BMI	4	1.38	.244	.016	2.20	.093	.026	0.66	.597	.008
Balloon x Task (Error)	332									

Note: *Drug* was coded 0=Placebo, 1=Propranolol. *Affect* refers to post-stressor mean negative, high arousal affect. *BMI* refers to body mass index. *Balloon* included three types: certain-long, certain-short, and uncertain. *Task* included three phases or averaged timepoints: the early task phase, mid-task phase, and the last or final task phase. Given that the repeated measures of *balloon type* and *task phase* were significant in Mauchly's test of sphericity (*ps*<.000), model p-values reported use the Greenhouse-Geisser correction. Significant effects are bolded.

Table S3. ANOVAs probing effects of propranolol on BELT points, pumps, and explosions, split by task phase, controlling for both affect and BMI.

		Early Task Phase			Mid-Task Phase			Late Task Phase		
Predictors	***df***	***F***	***p***	***partial η^2***	***F***	***p***	***partial η^2***	***F***	***p***	***partial η^2***
BELT Points										
Between-subject effects										
Intercept	1	**189.10**	**.000**	**.695**	**116.47**	**.000**	**.584**	**131.57**	**.000**	**.613**
Drug	1	1.70	.195	.020	2.81	.098	.033	**6.05**	**.016**	**.068**
Affect	1	0.32	.576	.004	0.09	.760	.001	0.05	.825	.001
BMI	1	0.64	.427	.008	0.32	.575	.004	0.80	.374	.010
Error	83									
Within-subject effects										
Balloon	2	**22.35**	**.000**	**.212**	**19.51**	**.000**	**.190**	**17.37**	**.000**	**.173**
Balloon x Drug	2	1.44	.239	.017	0.77	.443	.009	**4.03**	**.028**	**.046**
Balloon x Affect	2	0.11	.888	.001	0.61	.520	.007	0.38	.642	.005
Balloon x BMI	2	0.09	.906	.001	1.55	.218	.018	1.69	.194	.020
Balloon (Error)	166									
BELT Pumps										
Between-subject effects										
Intercept	1	**175.27**	**.000**	**.679**	**139.63**	**.000**	**.627**	**170.46**	**.000**	**.673**
Drug	1	0.96	.331	.011	1.67	.199	.020	2.60	.111	.030
Affect	1	0.10	.758	.001	0.13	.715	.002	0.68	.413	.008
BMI	1	0.03	.859	.000	0.87	.354	.010	1.03	.314	.012
Error	83									
Within-subject effects										
Balloon	2	**5.54**	**.011**	**.063**	**14.10**	**.000**	**.145**	**9.33**	**.001**	**.101**
Balloon x Drug	2	0.32	.648	.004	1.24	.283	.015	**4.81**	**.022**	**.055**
Balloon x Affect	2	0.04	.922	.000	0.80	.416	.010	0.23	.694	.003
Balloon x BMI	2	0.05	.896	.001	1.46	.235	.017	2.50	.108	.029
Balloon (Error)	166									
BELT Explosions										
Between-subject effects										
Intercept	1	**47.40**	**.000**	**.364**	**29.39**	**.000**	**.262**	**28.13**	**.000**	**.253**
Drug	1	0.97	.328	.012	0.56	.455	.007	1.12	.292	.013
Affect	1	0.00	.972	.000	1.00	.320	.012	0.51	.479	.006
BMI	1	0.95	.333	.011	1.02	.315	.012	0.69	.409	.008
Error	83									
Within-subject effects										
Balloon	2	**21.52**	**.000**	**.206**	**8.49**	**.000**	**.093**	**6.16**	**.004**	**.069**
Balloon x Drug	2	1.05	.343	.013	1.37	.256	.016	0.24	.748	.003

Balloon x Affect	2	.10	.881	.001	1.05	.350	.013	0.69	.480	.008
Balloon x BMI	2	.44	.614	.005	0.11	.894	.001	1.81	.173	.021
Balloon (Error)	166									

Note: *Drug* was coded 0=Placebo, 1=Propranolol. *Affect* refers to post-stressor mean negative, high arousal affect. *BMI* refers to body mass index. Given that *balloon type* was significant in Mauchly's test of sphericity, model *p*-values reported use the Greenhouse-Geisser correction. Significant effects are bolded.

Table S4. Unadjusted (i.e., no covariates included) mixed effects ANOVAs assessing overall effects of propranolol, balloon type, and BELT task phase on BELT points earned, pumps made, and explosions, reported for future meta-analytic purposes.

		Points Model			**Pumps Model**			**Explosions Model**		
Predictors	***df***	***F***	***p***	***partial η^2***	***F***	***p***	***partial η^2***	***F***	***p***	***partial η^2***
Between-subject effects										
Intercept	1	**1818.90**	**.000**	**.955**	**1680.19**	**.000**	**.952**	**398.81**	**.000**	**.824**
Drug	1	**4.70**	**.033**	**.052**	1.60	.209	.019	0.27	.606	.003
Error	85									
Within-subject effects										
Balloon	2	**247.14**	**.000**	**.744**	**79.93**	**.000**	**.485**	**150.33**	**.000**	**.639**
Balloon x Drug	2	2.47	.106	.028	2.12	.144	.024	0.28	.688	.003
Balloon (Error)	170									
Task phase	2	**29.99**	**.000**	**.261**	**8.16**	**.002**	**.088**	**10.15**	**.000**	**.107**
Task phase x Drug	2	1.66	.193	.019	0.37	.620	.004	2.90	.058	.033
Task phase (Error)	170									
Balloon x Task	4	**10.67**	**.000**	**.112**	**27.14**	**.000**	**.242**	**10.30**	**.000**	**.108**
Balloon x Task x Drug	4	1.39	.240	.016	**3.58**	**.017**	**.040**	1.61	.182	.019
Balloon x Task (Error)	340									

Note: *Drug* was coded 0=Placebo, 1=Propranolol. *Balloon* included three types: certain-long, certain-short, and uncertain. *Task* included three phases or averaged timepoints: the early task phase, mid-task phase, and the last or final task phase. Given that the repeated measures of *balloon type* and *task phase* were significant in Mauchly's test of sphericity (*ps*<.000), model p-values reported use the Greenhouse-Geisser correction. Significant effects are bolded.

Table S5. Unadjusted (i.e., no covariates included) univariate ANOVAs probing overall effects of propranolol on BELT pumps in the late task phase split by balloon type, reported for future meta-analytic purposes.

		Long-Certain Balloon Model			**Short-Certain Balloon Model**			**Uncertain Balloon Model**		
Predictors	***df***	***F***	***p***	***η^2***	***F***	***p***	***η^2***	***F***	***p***	***η^2***
Between-subject effects										
Intercept	1	**516.30**	**.000**	**.859**	**3758.81**	**.000**	**.978**	**1231.19**	**.000**	**.935**
Drug	1	**4.03**	**.048**	**.045**	0.40	.530	.005	0.16	.688	.002
Error	85									

Note: *Drug* was coded 0=Placebo, 1=Propranolol. Significant effects are bolded.