Determinants of Propranolol's Selective Effect on Loss Aversion

Peter Sokol-Hessner[1,2], Sandra F. Lackovic[1], Russell H. Tobe[3], Colin F. Camerer[4], Bennett L. Leventhal[3,5], and Elizabeth A. Phelps[1,2,3]

[1]Department of Psychology, New York University; [2]Center for Neural Science, New York University; [3]Nathan Kline Institute, Orangeburg, New York; [4]Division of the Humanities and Social Sciences, California Institute of Technology; and [5]Department of Psychiatry, University of California, San Francisco

Abstract

Research on emotion and decision making has suggested that arousal mediates risky decisions, but several distinct and often confounded processes drive such choices. We used econometric modeling to separate and quantify the unique contributions of loss aversion, risk attitudes, and choice consistency to risky decision making. We administered the beta-blocker propranolol in a double-blind, placebo-controlled within-subjects study, targeting the neurohormonal basis of physiological arousal. Matching our intervention's pharmacological specificity with a quantitative model delineating decision-making components allowed us to identify the causal relationships between arousal and decision making that do and do not exist. Propranolol selectively reduced loss aversion in a baseline- and dose-dependent manner (i.e., as a function of initial loss aversion and body mass index), and did not affect risk attitudes or choice consistency. These findings provide evidence for a specific, modulatory, and causal relationship between precise components of emotion and risky decision making.

One of the ways emotion has been suggested to influence decision making is by modulating the evaluation of risk (Bechara, Damasio, Tranel, & Damasio, 1997), a link established by studies manipulating (Dunn et al., 2010; Lerner & Keltner, 2001; Porcelli & Delgado, 2009) or measuring (Bechara et al., 1997; Lo & Repin, 2002) components of emotion during risky-decision tasks. However, the ways in which emotion does and does not shape risky decisions remain unclear, in part because risky decision making is the result of not one but multiple distinct processes. Just as various component processes contribute to emotion (Scherer, 2005), so too does decision making result from dissociable processes. For example, you may be uninterested in playing a gamble equally likely to yield a gain or a loss because you dislike the element of chance (or risk), or you may be uninterested in this gamble because you weigh the potential loss more heavily than the potential gain. These processes are termed risk attitudes and loss aversion, respectively. They are definitionally independent, but often confounded in decision-making tasks (see Method; Phelps, Lempert, & Sokol-Hessner, 2014). Because not all decision processes may be related to a given emotional component, one must separately examine the processes underlying both decision making and emotion to identify which relationships do and do not exist.

Recent studies dissociating risky-decision-making processes found that loss aversion (and not risk attitudes or consistency) correlated both with physiological arousal responses to losses versus gains (Sokol-Hessner et al., 2009) and with the amygdala's hemodynamic responses

Corresponding Author:
Elizabeth A. Phelps, New York University–Psychology, 6 Washington Place, 8th Floor, New York, NY 10003
E-mail: liz.phelps@nyu.edu

to losses versus gains (Sokol-Hessner, Camerer, & Phelps, 2013). Loss aversion alone was also reduced in case studies of patients with amygdala damage (De Martino, Camerer, & Adolphs, 2010). The amygdala mediates the effects of arousal in other cognitive domains (Garavan, Pendergrass, Ross, Stein, & Risinger, 2001; Glascher & Adolphs, 2003), which makes these studies consistent with a selective relationship between amygdala-mediated arousal responses and loss aversion, to the exclusion of risk attitudes and consistency.

Studies from two other domains align with this hypothesized selective relationship. First, in rodents, the amygdala drives avoidance actions during fear learning, via striatal projections (LeDoux, 2000). In human decision making, loss aversion is by definition avoidant, characterizing the tendency to avoid monetary loss in choices, and loss-averse actions, in turn, have been linked to striatal activity (Sokol-Hessner et al., 2013; Tom, Fox, Trepel, & Poldrack, 2007). Second, a large body of work has shown that propranolol—a beta-blocker that crosses the blood-brain barrier and interferes with the neurohormonal basis of autonomic arousal—attenuates arousal's effect on memory systems including the striatum by diminishing the amygdala's influence (McGaugh, 2002, 2004). These findings linking arousal, the amygdala, and the striatum to loss aversion (De Martino et al., 2010; Sokol-Hessner et al., 2013; Sokol-Hessner et al., 2009), and identifying amygdala-striatal modulatory circuits as necessary for avoidance actions (LeDoux, 2000) and supported by adrenergic signaling (McGaugh, 2002, 2004), are most consistent with the hypothesis that amygdala and arousal responses drive avoidant behavior, including loss aversion, via a general modulatory relationship (Phelps et al., 2014).

Here we report a study of risky decision making in which we used propranolol to pharmacologically interfere with the hypothesized mechanism of loss aversion: the neurohormonal system underlying autonomic arousal. We combined this precise manipulation with a similarly precise monetary decision task and econometric model of value and decision processes. Together, the task and model allowed us to reliably separate and quantify three decision processes for each individual (loss aversion, risk attitudes, and choice consistency; see Method) and examine how propranolol affects each process. We predicted that if amygdala-based arousal responses causally drive loss aversion, then propranolol should selectively blunt loss aversion; because neither risk attitudes nor consistency has been linked to the hypothesized modulatory circuit, we predicted they would be unaffected by this medication. Finding such a specific effect of propranolol would also more generally provide causal evidence for a precise role of one neurohormonal system in risky decision making.

Method

Participants

Fifty participants passed the medical screening (see Methodological Details in the Supplemental Material available online), and 47 completed the study. Of the 3 participants who passed the screening but did not complete the study, 1 did not show up for the second appointment, and 2 had "adverse events": One experienced a sensation of warmth in the left leg that was accompanied by tingling (similar to the phenomenon of a limb "falling asleep"), and the other reported feeling light-headed for roughly 1 hr during the experiment (though she did not mention it until the end of the session, as she attributed it to not having had her morning coffee). Both adverse events took place during the first visit, and neither of these participants was asked to return for the second test day, as they might have thought that they had been given propranolol, and thus perceived the blind to have been broken. No side effects were reported by any of the 47 remaining participants (22 females; mean age = 26.6 years, SD = 5.1 years) who completed the double-blind, 2-test-day design (Fig. 1). The target sample size of 50 was conservatively selected on the basis of previous findings of within-subjects changes in loss aversion due to emotion regulation in samples roughly half that size (Sokol-Hessner et al., 2013; Sokol-Hessner et al., 2009).

Test days

The 2 test days were separated by an average of 7.5 days (range: 5–14 days). The procedure was identical on the 2 test days, except that all participants received an orally administered propranolol pill (80 mg) at one session and a matched placebo pill at the other, with the order counterbalanced. Participants were asked to refrain from eating for 3 hr prior to each session and for 30 min following pill administration, in an attempt to standardize the propranolol dose.

Each session began with pill administration, which was followed 30 min later by consumption of a standard meal (a granola bar), in order to increase the plasma concentration of propranolol. On average, participants were blind to the order in which they received the two treatments (when asked to guess at the end of the study, they were correct 47% of the time; chance = 50%). The task began 90 min after pill administration, and task instructions, a brief comprehension quiz, practice trials, and the gamble task itself required approximately 40 min; participants left after a total of 180 min. As part of the safety protocol, blood pressure (BP) and heart rate (HR) were assessed four times: at pill administration (0 min), before the task (90 min), after the task (~130 min),
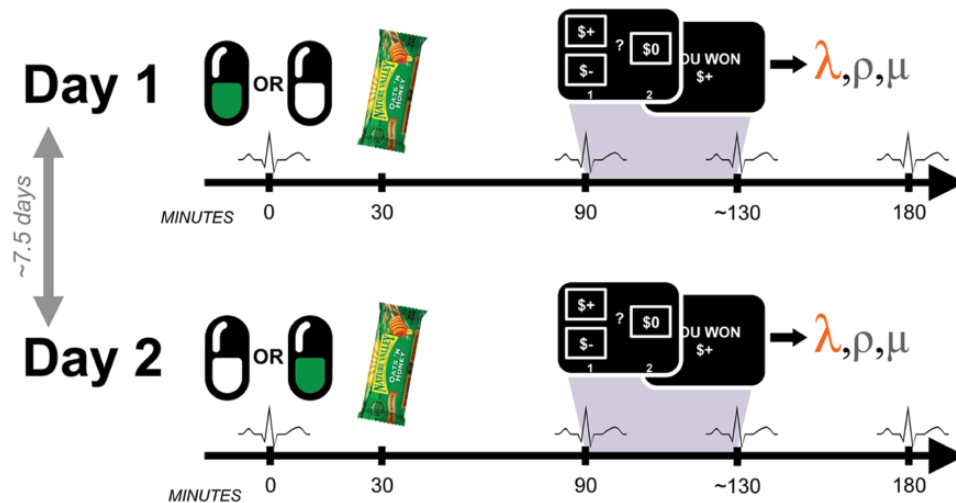
Fig. 1. Task structure. The procedure was identical on Days 1 and 2 except for the pill that was administered. Each session began with administration of one pill containing either placebo or propranolol (the actual pills were visually identical, but they are distinguished here by color). After 30 min, participants ate a granola bar, to aid propranolol absorption. Ninety minutes after pill administration, participants performed the decision-making task (see Method), from which estimates of loss aversion (λ), risk attitudes (ρ), and consistency (μ) could be calculated for each day. Blood pressure and heart rate were assessed four times each day.

and 180 min after pill administration. These measurements were either taken by a registered nurse or taken by the experimenter and checked with a nurse to ensure that participants' vital signs were within safe bounds (i.e., within the bounds that served as the criteria for inclusion in the study; see Methodological Details in the Supplemental Material). The experimenter administering the task took the BP and HR measurements only at 90 and 130 min. A nurse took the measurements at 0 and 180 min; this had the consequence of maintaining the experimenter's blind to the medication condition throughout all sessions, for all participants.

On each test day, participants made 150 choices between risky gambles and guaranteed alternatives (Sokol-Hessner et al., 2013; Sokol-Hessner, Hartley, Hamilton, & Phelps, 2015; Sokol-Hessner et al., 2009). Participants viewed the gamble in each trial for 2 s and then had up to 2 s to enter their choice. After a 1-s interstimulus interval, the outcome of the choice (one of the gamble components or the guaranteed alternative, depending on the choice) was displayed for 1 s. After an intertrial interval of 1 to 3 s, the next trial began.

At the end of each test day, participants were paid their initial endowment of $30 plus or minus the actual value of a randomly selected subset of the trials (10% of all trials, or 15 trials), plus a flat participation fee of $20 per hour. Participants' endowments increased by an average of $28.17 on the 1st day (i.e., they won $28.17 in addition to the endowment), and $26.66 on the 2nd day. The amount won did not differ significantly between the 2 days ($p = .82$). Participants were fully informed about all contingencies and probabilities in the task, and as mentioned, they were quizzed on the task to ensure that they understood it. Participants' ratings of task difficulty at the end of Day 1 (scale from 1, *very easy*, to 7, *very difficult*) indicated that they found the task to be easy ($M = 1.8$, $SE = 0.14$), a fact reflected in the number of trials on which they did not enter a response in time (Day 1: $M = 0.9$, $SD = 1.4$; Day 2: $M = 0.6$, $SD = 1.0$). The gamble amounts were identical to those specified in a previous report (Sokol-Hessner et al., 2013). Briefly, 120 trials were gain-loss trials, in which participants chose between (a) a gamble with positive and negative possible outcomes and (b) a guaranteed alternative of $0. On the remaining 30 gain-only trials, participants chose between (a) a gamble with positive and zero possible outcomes and (b) a positive guaranteed alternative. The probability associated with each gamble outcome was always .5.

All test sessions began during the morning, and an effort was made to schedule a given participant's sessions at the same time on both days (mean time of pill administration = 9:49 a.m. on Day 1 and 9:54 a.m. on Day 2).

Propranolol and dose dependence

Propranolol's ability to act within the central nervous system is due to its high lipophilicity (Woods & Robinson, 1981), that is, the fact that it easily dissolves through and into lipids, including the blood-brain barrier and peripheral adipose cells. Because of this property, propranolol has

dose-dependent pharmacokinetics (Borgström, Johansson, Larsson, & Lenander, 1981). Individuals with a higher body mass index (BMI; (weight in kilograms)/(height in meters)^2) experience lower peak concentrations and a greater medication *volume of distribution* (Bowman, Hudson, Simpson, Munro, & Clements, 1986), which therefore leads to a lower concentration in any one location (including the brain). In other words, propranolol's pharmacokinetics indicate that the effects of a given dose size should be stronger in smaller individuals. To address this issue, we used the median BMI in our sample (*Mdn* = 25.8; range: 16.4–39.1) to split participants into low- and high-BMI groups (an approach that does not involve likely incorrect assumptions of linearity in dose dependence) and included this grouping variable in our regressions.

Behavioral modeling

We modeled participants' behavior using maximum likelihood estimation as implemented in MATLAB (The MathWorks, Natick, MA) to fit the same prospect-theory-inspired model (Tversky & Kahneman, 1992) of choices that we have used in previous studies (Sokol-Hessner et al., 2013; Sokol-Hessner et al., 2014; Sokol-Hessner et al., 2009):

$$u\left(x^+\right) = p \times \left(x^+\right)^\rho \quad (1)$$

$$u\left(x^-\right) = -\lambda \times p \times \left(-x^-\right)^\rho \quad (2)$$

$$p\left(\text{gamble}\right) = \frac{1}{1 + e^{-\mu \times \left(u(\text{gamble}) - u(\text{guaranteed})\right)}} \quad (3)$$

Equations 1 and 2 calculate the utility (*u*) of gains and losses, respectively. These are used to compute the utilities of the gamble and the guaranteed alternative, which are then converted into the probability of choosing the gamble using the softmax in Equation 3. The model's parameters quantify loss aversion (λ, the relative multiplicative weight placed on losses compared with gains), risk attitudes (ρ, feelings about chance, or diminishing marginal sensitivity to value), and choice consistency (μ, noisiness in choices, also called the softmax temperature). All analyses of loss aversion used log(λ); the logarithm is commonly used because λ is positively skewed.

Our task enabled us to separate changes in loss aversion from those in risk attitudes because it included both gain-loss and gain-only trials. A gain-loss trial presents a gamble with positive and negative possible outcomes and a guaranteed alternative of zero. Choice in such a trial reflects both risk attitudes (because the gamble is risky) and loss aversion (because a loss is being evaluated). A gain-only trial presents a gamble with possible outcomes of a large positive amount or zero and a guaranteed alternative of a small positive amount. Choice in such a trial reflects risk attitudes (because the gamble is still risky) but not loss aversion (because there is no potential loss). When data from gain-loss and gain-only trials are fit simultaneously, the estimate of risk attitudes accounts for behavior across all trials, and loss aversion accounts for the remainder of gain-loss gambling behavior not explained by risk attitudes. In studies that include only gain-loss trials, it is impossible to identify the extent to which loss aversion or risk attitudes drive behavior because both processes are at work and they have similar gross effects on behavior (increasing or decreasing gambling). Both gain-loss and gain-only trials are necessary to separately identify risk attitudes and loss aversion.

To analyze changes in choice behavior, we first regressed the change in log(λ) across days on day (the constant), medication (order of treatment: −1 = placebo and then propranolol; +1 = propranolol and then placebo), BMI group (+1 = low-BMI group; −1 = high-BMI group), and the interaction between medication and BMI group. We also performed the same regression using risk attitudes (ρ) and choice consistency (μ), instead of log(λ), as the outcome variable. Next, to clarify the effect of the interaction, we subtracted the strong day effect from the change in log(λ), leaving the residual change in loss aversion (Δλ$_R$) due to propranolol. The resulting values were still in "day" space (i.e., reflecting changes from Day 1 to Day 2), so we flipped the sign of the values for individuals who received the placebo on Day 1 so that all values were in a "medication" space (reflecting propranolol-to-placebo changes). We call this variable Δλ$_R$, as it reflects the residual change in loss aversion due to propranolol. All subsequent analyses were performed on these residuals.

We think it likely that the relationship between BMI and a constant 80-mg dose of propranolol is more continuous than reflected by a median split. However, this relationship is certainly nonlinear, characterized by both a ceiling effect (i.e., a constant, maximal effect of 80 mg of propranolol below some BMI) and a floor effect (i.e., the absence of an observable effect of 80 mg of propranolol above a particular BMI). To avoid arbitrary assumptions of functional forms, and allow our data to shape the monotonic transformation of BMI, we used nonlinear curve-fitting procedures in MATLAB (NonLinearModel.fit) to fit a model based on the following two equations:

$$\text{tBMI} = z\left(\frac{1}{1 + e^{\alpha + \gamma \times z(\text{BMI})}}\right) \quad (4)$$

$$\log(\lambda_{\text{Day2}}) - \log(\lambda_{\text{Day1}}) = \beta_1 \times \text{Day} + \beta_2 \times \text{Medication} + \beta_3 \times \text{tBMI} + \beta_4 \times \text{Medication} \times \text{tBMI} \quad (5)$$

a

b
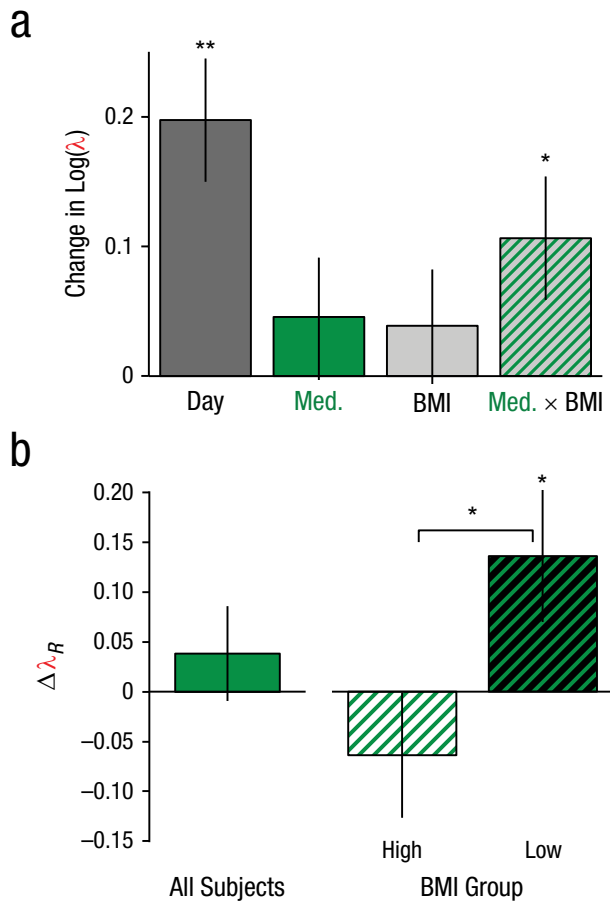
Fig. 2. The effect of propranolol on loss aversion. The graph in (a) presents the regression coefficients for the change in loss aversion, $\log(\lambda_{\text{Day 2}}) - \log(\lambda_{\text{Day 1}})$, due to day, medication ("Med"), body mass index (BMI) group, and the interaction of medication and BMI group. The graph in (b) presents the residual change in loss aversion due to propranolol, $\Delta\lambda_R$, for the sample overall and for the low- and high-BMI groups separately. Error bars indicate ±1 *SEM*, and asterisks indicate significant differences from zero or between the two BMI groups (as determined by *t* tests; *p < .05, **p < .001).

Note that $z()$ indicates the use of z scoring. This regression is identical to the one described in the previous paragraph except that instead of using a median split on BMI, we allowed the modified softmax function (Equation 4, parameterized by α and γ) to transform BMI into tBMI as best fit the change in loss aversion. This transformation function avoids arbitrary assumptions, as it can approximate a wide variety of possible monotonic relationships, including linear, sigmoidal, curvilinear, and step functions, and is thus capable of modeling both ceiling and floor effects. For analyses using BMI as a strictly linear covariate, see Additional Analyses in the Supplemental Material (though note our caveats regarding linearity earlier in this section).

Results

We fit a prospect-theory-inspired (Tversky & Kahneman, 1992) model to each participant's choices on each day. This model quantified three distinct processes—loss aversion (λ), risk attitudes (ρ), and choice consistency (μ)—and we analyzed the change in these parameter values across days, using linear regression.

When we regressed individuals' change in log loss aversion ($\log(\lambda_{\text{Day 2}}) - \log(\lambda_{\text{Day 1}})$) on day, medication, BMI group, and the interaction between medication and BMI group (Fig. 2a), we identified a strong effect of day, $\beta = 0.20$, $p = .0002$, 95% confidence interval (CI) = [0.10, 0.29], indicating that participants were generally more loss averse on Day 2 than on Day 1. The effect of medication was in the expected direction (propranolol reduced loss aversion) but not significant on its own, $\beta = 0.05$, $p = .34$, 95% CI = [−0.05, 0.14]. BMI group was also not a significant predictor, $\beta = 0.04$, $p = .42$, 95% CI = [−0.06, 0.13]. However, as expected given the dose-dependent pharmacokinetics of propranolol (Borgström et al., 1981) and the variation in propranolol concentration as a function of BMI (Bowman et al., 1986), the interaction of BMI and medication was significant, $\beta = 0.11$, $p = .03$, 95% CI = [0.01, 0.20]. In other words, propranolol interacted with BMI to reduce loss aversion in a dose-dependent manner. Because the regression was performed on the change in $\log(\lambda)$, the effect of these coefficients on λ can be understood in terms of the percentage change in the value of λ: 22% for day, 5% for medication, 4% for BMI group, and 11% for the Medication × BMI Group interaction.

No significant effects were identified when we performed the same regression on risk attitudes (ρ)—day: $\beta = −0.06$, $p = .21$, 95% CI = [−0.14, 0.03]; medication: $\beta = −0.05$, $p = .31$, 95% CI = [−0.13, 0.04]; BMI group: $\beta = 0.06$, $p = .21$, 95% CI = [−0.03, 0.14]; Medication × BMI group: $\beta = −0.01$, $p = .74$, 95% CI = [−0.10, 0.07]. Similarly, the regression predicting choice consistency (μ), using $\log(\mu)$, revealed no significant effects—day: $\beta = 0.26$, $p = .11$, 95% CI = [−0.06, 0.59]; medication: $\beta = −0.03$, $p = .87$, 95% CI = [−0.35, 0.30]; BMI group: $\beta = −0.29$, $p = .09$, 95% CI = [−0.61, 0.04]; Medication × BMI group: $\beta = 0.12$, $p = .46$, 95% CI = [−0.20, 0.45].

To clarify the interaction, we removed the strong effect of day from the change in $\log(\lambda)$ using the estimated regression coefficients, obtaining the residual change in loss aversion ($\Delta\lambda_R$) due to propranolol. The overall average $\Delta\lambda_R$ was not significantly different from zero, $t(46) = 0.81$, $p = .42$, Cohen's $d_z = 0.11$ (Fig. 2b); this result replicated the average effect of medication in the regression. However, examining the BMI groups separately, we found no significant effect of propranolol for high-BMI participants, $t(22) = −1.09$, $p = .29$, Cohen's $d_z = 0.23$,

whereas low-BMI participants were significantly less loss averse after receiving propranolol than after receiving the placebo, $t(23) = 2.17$, $p = .04$, Cohen's $d_z = 0.44$ (Fig. 2b). All of these results were replicated with nonparametric tests, which demonstrated their robustness (Wilcoxon signed-rank tests—average $\Delta\lambda_R$ vs. 0: $z = 0.69$, $p = .49$; high-BMI $\Delta\lambda_R$ vs. 0: $z = −0.97$, $p = .33$; low-BMI $\Delta\lambda_R$ vs. 0: $z = 2.17$, $p = .03$; Wilcoxon rank-sum test—high- vs. low-BMI $\Delta\lambda_R$, $z = 2.07$, $p = .04$).

Although there may be a more continuous relationship between BMI and an 80-mg dose of propranolol than reflected in a comparison between the high- and low-BMI groups, this relationship is certainly nonlinear, characterized by lower and upper bounds. That is, whatever the effects of propranolol, they should disappear entirely at very high BMIs and be constant and maximal at very low BMIs. Therefore, to avoid arbitrarily assuming a functional form for this relationship, we used nonlinear regression to estimate the transformed BMI values (tBMI; see Equation 4) simultaneously with their interaction with medication (tBMI × Medication interaction). The transformation function we fit as part of this regression allowed BMI values to be transformed in a variety of monotonic ways (e.g., linear, curvilinear, sigmoidal, or step) and could thus capture both ceiling and floor effects. These transformed values were then used in place of the BMI-group term in the regression. The best-fitting transformation of BMI was effectively a step function ($\alpha = 155$ and $\gamma = 422$; see Additional Analyses, and especially Fig. S1, in the Supplemental Material) that split individuals into low- and high-BMI groups at an intermediate point (~25.0 kg/m^2) extremely close to the median BMI (25.8 kg/m^2) used in our initial analyses. The other estimated parameters were nearly identical to those obtained previously: We found a strong effect of day, $\beta = 0.19$, $p = .0002$, 95% CI = [0.10, 0.29]; a nonsignificant effect of medication in the expected direction, $\beta = 0.047$, $p = .32$, 95% CI = [−0.05, 0.14]; no effect of tBMI, $\beta = 0.05$, $p = .28$, 95% CI = [−0.04, 0.15]; and a significant Medication × tBMI interaction, $\beta = 0.12$, $p = .02$, 95% CI = [0.02, 0.21]. Though we believe that the relationship is ultimately more likely to be sigmoidal, these findings nevertheless empirically support the conclusion that there is a threshold BMI value, above which there is no reduction in loss aversion, and below which there is a constant effect.

Finally, we examined whether propranolol's effect was related to the initial level of loss aversion. Because the correlation of the change in loss aversion with its initial level is statistically biased (Tu, Bælum, & Gilthorpe, 2005), we used an accepted, alternative test to examine whether the variance of loss aversion after participants received propranolol was different from the variance of loss aversion after they received the placebo (Tu & Gilthorpe, 2007). If the effect of propranolol is independent of initial loss aversion, variance should not differ between the placebo and propranolol conditions, but if there is baseline dependency, the range of loss aversion should be either compressed or expanded in the propranolol condition. The test of equality of correlated variances (Tu & Gilthorpe, 2007) was significant, $t(45) = 2.50$, $p = .016$, suggesting that propranolol's effect depended on the initial level of loss aversion. The variance in $\log(\lambda)$ was lower when participants received propranolol (0.17) than when they received the placebo (0.28), which shows that higher values were reduced more than smaller values; that is, the effect of propranolol in reducing loss aversion was greater in individuals with higher initial levels of loss aversion. This is a clear case of baseline dependence and is consistent with a hypothesis that propranolol operates on a modulatory mechanism—the greater the initial modulatory signal, the more of an effect propranolol will have.

Discussion

The finding that propranolol reduces loss aversion constitutes causal evidence that adrenergic responses drive the avoidance of monetary losses in risky decision making. Though other studies have linked risky decisions to arousal (Bechara et al., 1997; Lo & Repin, 2002) and have shown effects of propranolol on risky decision making (Rogers, Lancaster, Wakeley, & Bhagwagar, 2004), they failed to differentiate the contributions of loss aversion, risk attitudes, and consistency. Because all of these processes contribute to risky choices, prior studies were limited to the broad conclusion that arousal and the adrenergic system are related to risky decision making. Here we have shown that pharmacologically manipulating the neurohormonal basis of arousal alters only loss aversion (other affective components may be related to other decision-making processes; e.g., mood changes risk attitudes by altering appraisals; Lerner & Keltner, 2001). Our study corroborates and builds on studies selectively linking loss aversion to arousal (Sokol-Hessner et al., 2009), the amygdala (De Martino et al., 2010; Sokol-Hessner et al., 2013), and noradrenergic activity as revealed by positron-emission tomography (Takahashi et al., 2013), and our findings converge with previous ones identifying an amygdala-based, adrenergically mediated system modulating avoidance actions in other domains (LeDoux, 2000; McGaugh, 2002, 2004).

Propranolol's high lipophilicity and pharmacology (Borgström et al., 1981; Bowman et al., 1986) indicate that its effects should be functionally dose dependent (i.e., greater in smaller than in larger individuals), as we found. The fact that many previous reports of studies using propranolol in humans have not discussed interactions between dose size and body mass could reflect the predominant use of smaller subject pools containing young, low-BMI participants (with little variation in BMI,

which makes it hard to observe dose dependence), or could simply indicate that these interactions were not examined at all (see Additional Analyses, and especially Table S1, in the Supplemental Material). The lack of attention to dose dependence in human research sharply contrasts with the standard approach in studies using propranolol on nonhuman animals; in that field, researchers titrate doses by body weight, implicitly anticipating and correcting for dose dependence. We hope that future studies might not only more directly test dose dependence but also go beyond other limitations of the present study by, for example, allowing risk attitudes to vary within subjects between the gain and loss domains. Most important, we hope that future research will use non-centrally acting beta-blockers or combine propranolol with neuroimaging to test whether propranolol's effect is mediated by changes in the amygdala, which would be consistent with our hypothesized mechanism underlying loss aversion.

Identifying relationships between emotions and choices begins by measuring and correlating specific processes underlying both, and separating those processes from others that may appear superficially similar, despite being fundamentally different. This important first step must be followed by direct manipulation to establish causality. In performing such a manipulation, we empirically demonstrated that precise components of emotions can have very specific, causal effects on precise components of decision making.

Author Contributions

P. Sokol-Hessner designed the study with the assistance of B. L. Leventhal and E. A. Phelps. S. F. Lackovic and R. H. Tobe collected the data, and P. Sokol-Hessner, S. F. Lackovic, and R. H. Tobe analyzed the data. All authors contributed to drafting, editing, and developing the manuscript.

Declaration of Conflicting Interests

The authors declared that they had no conflicts of interest with respect to their authorship or the publication of this article.

Funding

Supplemental Material

Additional supporting information can be found at http://pss .sagepub.com/content/by/supplemental-data

Open Practices

All the data for this experiment have been made publicly available via Open Science Framework and can be accessed at https://osf.io/i5knh/. The complete Open Practices Disclosure for this article can be found at http://pss.sagepub.com/content/by/supplemental-data. This article has received the badge for Open Data. More information about the Open Practices badges can be found at https://osf.io/tvyxz/wiki/view/ and http://pss .sagepub.com/content/25/1/3.full.

References

Bechara, A., Damasio, H., Tranel, D., & Damasio, A. R. (1997). Deciding advantageously before knowing the advantageous strategy. *Science*, *275*, 1293–1295. doi:10.1126/science.275.5304.1293

Borgström, L., Johansson, C.-G., Larsson, H., & Lenander, R. (1981). Pharmacokinetics of propranolol. *Journal of Pharmacokinetics & Biopharmaceutics*, *9*, 419–429.

Bowman, S., Hudson, S., Simpson, G., Munro, J., & Clements, J. (1986). A comparison of the pharmacokinetics of propranolol in obese and normal volunteers. *British Journal of Clinical Pharmacology*, *21*, 529–532.

De Martino, B., Camerer, C. F., & Adolphs, R. (2010). Amygdala damage eliminates monetary loss aversion. *Proceedings of the National Academy of Sciences, USA*, *107*, 3788–3792.

Dunn, B., Galton, H., Morgan, R., Evans, D., Oliver, C., Meyer, M., . . . Dalgleish, T. (2010). Listening to your heart: How interoception shapes emotion experience and intuitive decision making. *Psychological Science*, *21*, 1835–1844. doi:10.1177/0956797610389191

Garavan, H., Pendergrass, J. C., Ross, T. J., Stein, E. A., & Risinger, R. C. (2001). Amygdala response to both positively and negatively valenced stimuli. *NeuroReport*, *12*, 2779–2783.

Glascher, J., & Adolphs, R. (2003). Processing of the arousal of subliminal and supraliminal emotional stimuli by the human amygdala. *The Journal of Neuroscience*, *23*, 10274–10282.

LeDoux, J. E. (2000). Emotion circuits in the brain. *Annual Review of Neuroscience*, *23*, 155–184.

Lerner, J. S., & Keltner, D. (2001). Fear, anger, and risk. *Journal of Personality and Social Psychology*, *81*, 146–159.

Lo, A. W., & Repin, D. V. (2002). The psychophysiology of real-time financial risk processing. *Journal of Cognitive Neuroscience*, *14*, 323–339. doi:10.1162/089892902317361877

McGaugh, J. L. (2002). Amygdala modulation of memory consolidation: Interaction with other brain systems. *Neurobiology of Learning and Memory*, *78*, 539–552.

McGaugh, J. L. (2004). The amygdala modulates the consolidation of memories of emotionally arousing experiences. *Annual Review of Neuroscience*, *27*, 1–28.

Phelps, E. A., Lempert, K. M., & Sokol-Hessner, P. (2014). Emotion and decision making: Multiple modulatory neural circuits. *Annual Review of Neuroscience*, *37*, 263–287.

Porcelli, A. J., & Delgado, M. R. (2009). Acute stress modulates risk taking in financial decision making. *Psychological Science*, *20*, 278–283.

Rogers, R. D., Lancaster, M., Wakeley, J., & Bhagwagar, Z. (2004). Effects of beta-adrenoceptor blockade on components of human decision-making. *Psychopharmacology*, *172*, 157–164.

Scherer, K. R. (2005). What are emotions? And how can they be measured? *Social Science Information*, *44*, 695–729. doi:10.1177/0539018405058216

Sokol-Hessner, P., Camerer, C. F., & Phelps, E. A. (2013). Emotion regulation reduces loss aversion and decreases amygdala responses to losses. *Social Cognitive and Affective Neuroscience, 8,* 341–350. doi:10.1093/scan/nss002

Sokol-Hessner, P., Hartley, C. A., Hamilton, J. R., & Phelps, E. A. (2015). Interoceptive ability predicts aversion to losses. *Cognition & Emotion, 29,* 695–701. doi:10.1080/02699931.2014.925426

Sokol-Hessner, P., Hsu, M., Curley, N. G., Delgado, M. R., Camerer, C. F., & Phelps, E. A. (2009). Thinking like a trader selectively reduces individuals' loss aversion. *Proceedings of the National Academy of Sciences, USA, 106,* 5035–5040. doi:10.1073/pnas.0806761106

Takahashi, H., Fujie, S., Camerer, C. F., Arakawa, R., Takano, H., Kodaka, F., . . . Suhara, T. (2013). Norepinephrine in the brain is associated with aversion to financial loss. *Molecular Psychiatry, 18,* 3–4.

Tom, S. M., Fox, C. R., Trepel, C., & Poldrack, R. A. (2007). The neural basis of loss aversion in decision-making under risk. *Science, 315,* 515–518.

Tu, Y.-K., Bælum, V., & Gilthorpe, M. S. (2005). The relationship between baseline value and its change: Problems in categorization and the proposal of a new method. *European Journal of Oral Sciences, 113,* 279–288.

Tu, Y.-K., & Gilthorpe, M. S. (2007). Revisiting the relation between change and initial value: A review and evaluation. *Statistics in Medicine, 26,* 443–457.

Tversky, A., & Kahneman, D. (1992). Advances in prospect theory: Cumulative representation of uncertainty. *Journal of Risk and Uncertainty, 5,* 297–323. doi:10.1007/BF00122574

Woods, P., & Robinson, M. (1981). An investigation of the comparative liposolubilities of beta-adrenoceptor blocking agents. *Journal of Pharmacy and Pharmacology, 33,* 172–173.

Supplemental Analyses

Simple Means

Mean parameter estimates (with standard errors) on placebo were consistent with those observed elsewhere (Sokol-Hessner, Camerer, & Phelps, 2013; Sokol-Hessner, Hartley, Hamilton, & Phelps, 2014; Sokol-Hessner et al., 2009): loss aversion $\lambda = 1.54$ (0.15) (taking the mean of individuals' $\log(\lambda)$ values can reduce the biasing effect of skewness; this measure yielded a recovered group mean λ of 1.32), risk attitudes $\rho = 0.91$ (0.05), and consistency $\mu = 2.48$ (0.55).

Additional Analyses of Change in Loss Aversion

No other factors we examined (including sex, age, initial heart rate, relative change in heart rate or systolic blood pressure, or payment on Day 1) significantly interacted with propranolol to reduce loss aversion.

Examining $\Delta\lambda_R$ (the residual change in $\log(\lambda)$ after removing the effect of Day) with respect to gender showed that the effect of propranolol was not significant for men (p = 0.24) or women (p = 0.95), and that the genders were not significantly different (p = 0.51).

Performing a median split on age also yielded no significant effects on $\Delta\lambda_R$. Using one-sample t-tests to test $\Delta\lambda_R$ against zero for young and old age groups: young, p = 0.29; old, p = 0.91. Using Wilcoxon signed rank tests: young, p = 0.33; old, p = 1. Testing the young and old age groups against one another using two-sample t-tests, young vs. old $\Delta\lambda_R$, p = 0.37. Using the Wilcoxon rank sum test instead, young vs. old $\Delta\lambda_R$, p = 0.41. Performing the regression using a median split on age instead of on BMI yielded no significance for Medication, Age, or Medication x Age.

Baseline heart rate (t = 0 minutes, Day 1) was not correlated with $\Delta\lambda_R$ (r(45) = -0.17, p = 0.24), and there was no significant difference between $\Delta\lambda_R$ for high baseline vs. low baseline HR participants (median split on baseline HR; two-sample t-test, p = 0.14). $\Delta\lambda_R$ also did not correlate with the effect of propranolol relative to placebo on HR (r(45) = -0.01, p = 0.92) or systolic blood pressure (r(45) = -0.096, p = 0.52). If we performed our main regression using the change in HR on propranolol minus placebo either to do a median split or as a continuous variable, we found no significant effects of Medication, ΔHR (or ΔHR group), or Medication x ΔHR (or ΔHR group). Similarly, if we regress the change in $\log(\lambda)$ on Day and difference in HR change (the difference between the change in HR on Day 2 [from t=0 to t=90 minutes] and the change in HR on Day 1), there is a strong effect of Day (p = 0.001), but no effect of difference in HR change (p = 0.53).

If we restrict analysis to those participants who had a larger decrease in systolic blood pressure on propranolol compared to placebo (N = 35), and regress change in log(λ) on Day and Medication, we find a significant effect of Day (p = 0.002), but no significant effect of Medication (p = 0.57). Similarly, if we analyze only participants with a larger decrease in HR on propranolol compared to placebo (N = 40), we recover a significant effect of Day (p = 0.003), but not of Medication (p = 0.51). Finally, analyzing only participants with larger decreases in HR and systolic blood pressure on propranolol compared to placebo (N = 29) yields nearly identical results as above (Day, p = 0.003; Medication, p = 0.73).

Participants' weight was highly correlated with BMI (r(45) = 0.89, p = 1.5×10^{-16}). It was therefore unsurprising that we found similar patterns as those reported in the main text if we used weight instead of BMI. Using one-sample t-tests to test $\Delta\lambda_R$ against zero for low and high weight groups (median split): low, p = 0.06; high, p = 0.36. Using Wilcoxon signed rank tests: low, p = 0.056; high, p = 0.47. Testing the low and high weight groups against one another using two-sample t-tests, low vs. high weight $\Delta\lambda_R$, p = 0.04. Using the Wilcoxon rank sum test instead, low vs. high weight $\Delta\lambda_R$, p = 0.05. Performing the regression using a median split on weight instead of on BMI yielded a Medication x Weight group interaction, p = 0.05.

Analyses with BMI as a strictly linear, continuous variable produced similar results as with the median split. BMI was marginally correlated with $\Delta\lambda_R$ (r(45) = -0.28, p = 0.06), consistent with a larger effect of propranolol in low-BMI individuals. If we simply used BMI as a covariate in the regression (assuming a strictly linear relationship), the interaction between Medication and BMI was trending (p = 0.11), though this model is very implausible for reasons discussed in the main manuscript (e.g. the likely presence of floor and/or ceiling effects).

Payment on Day 1 was not significantly correlated with the change in log(λ) across days (r(45) = -0.03, p = 0.83).

The nonlinear regression performed in the text (see Equations 1 & 2) estimated values of α and γ that effectively created a step function (see Figure S1 for a graph of tBMI versus BMI) with 20 participants in the "low BMI" group (9M/11F), and 27 in the "high BMI" group (16M/11F). These values should be treated as "approximate". When a step function becomes sufficiently sharp, an infinite number of parameter values can describe that sharp step with comparable predictive accuracy and quality of fit. Re-doing the estimation three times, for example, produced α = 160.2, 150.4, 159.2, and γ = 435.2, 408.9, and 432.6, but these values do not describe appreciably different transformations. Unfortunately, such discontinuity prevents the estimation of significance values or confidence intervals.

Body Mass Index and Other Variables

BMI correlated with Age ($r(45) = 0.34$, $p = 0.02$), but as observed above, Age did not account for the change in loss aversion. The low BMI group was significantly younger than the high BMI group (24.3 vs. 28.9 years old; $p = 0.001$).

Gender was not significantly different between the BMI groups (Fisher's exact test, $p = 0.39$). Nor was BMI significantly different between those who correctly guessed which day they received propranolol ($p = 0.38$).

BMI did not significantly correlate with the effect of propranolol on systolic blood pressure ($r(45) = 0.17$, $p = 0.25$), though there was a significant correlation with propranolol's effect on the difference in heart rate ($r(45) = 0.31$, $p = 0.03$), in which low BMI participants had a marginally greater effect of the medication (-9.3 beats/min, $p = 8 \times 10^{-5}$) compared to high BMI participants (-5.0 beats/min, $p = 0.002$; low vs. high BMI groups, $p = 0.08$). BMI also correlated positively with the baseline heart rate on Day 1 ($r(45) = 0.43$, $p = 0.003$).

As noted above, none of the above-discussed variables themselves predict change in loss aversion across days or do so in interaction with medication.

One possible mediating factor between BMI and propranolol's effect on loss aversion could be insulin. Obesity has been linked to lower insulin receptor sensitivity (i.e. insulin resistance; Dallman, 2010; Kullmann et al., 2012), and that this may be related to impaired memory or attention (Cholerton, Baker, & Craft, 2013; Maayan, Hoogendoorn, Sweat, & Convit, 2011; Reger et al., 2008). Future studies should consider measuring participants' insulin sensitivity to ascertain whether it could mediate the relationship between propranolol, BMI, and behavior.

Other analyses

Propranolol did not affect the probability of taking a gamble after a win outcome (paired t-test, $p = 0.62$), loss outcome ($p = 0.62$), or guaranteed outcome ($p = 0.48$).

Physiological Responses to Propranolol

As expected, propranolol (relative to placebo) strongly reduced heart rate and systolic blood pressure from 0-90 minutes ($p = 5.1 \times 10^{-7}$; $p = 8.1 \times 10^{-7}$), but had no effect on diastolic blood pressure ($p = 0.74$). Comparing the measurements taking at t = 90m and t = 130m, there was no difference in either systolic blood pressure or heart rate on either day (all p's > 0.15). A regression on the change in systolic blood pressure from 0-90 minutes indicated no interaction with BMI group ($p = 0.39$), while the same regression on heart rate found a significant interaction ($p = 0.049$), indicating that low-BMI individuals experienced a larger effect of propranolol in decreasing their heart rate (-9.25 bmp) than high-BMI individuals (-4.96 bmp; two-sample t-test, $p = 0.08$). However, note that

regressions reported above did not find an effect of heart rate on log loss aversion.

Dose Dependence with Propranolol

It is difficult to determine whether the psychological effects of propranolol in the prior literature are in any way dose-dependent, as the vast majority of studies do not report any analyses (successful or failed) that leverage relative dose size (i.e. taking into account BMI or weight). See Table S1 for a summary of studies administering propranolol.

Two of the studies in Table S1 do, however, bring attention to this problem (Maheu, Joober, Beaulieu, & Lupien, 2004; van Stegeren, Everaerd, Cahill, McGaugh, & Gooren, 1998). Van Stegeren et al (2005) noted that "in animal research, the dosage used to test for certain effects is almost always related to the body weight of the subject animal. In human studies, on the contrary, this is hardly ever done." This observation was made in the context of an observed effect of gender that the authors thought could in reality be dose-dependence: "it might simply be so that the relative dosage of 80 mg propranolol for men was lower than for women, since their body weight was higher than that of the women."

Loss Aversion over Multiple Days

In the main text, we report a strong effect of day, in that participants are, on average, more loss averse on Day 2 than Day 1. Previous studies using this paradigm have not measured loss aversion on multiple days (Sokol-Hessner, et al., 2013; Sokol-Hessner, et al., 2014; Sokol-Hessner, et al., 2009), and so we are unable to comment on whether this is unique to this study, or a more common finding. Speculatively, we believe this increase may be related to participants acting more conservatively on the second day after winning money (on average) at the end of the first day. In other words, they took the task "more seriously" on Day 2 than Day 1 because the reality of the payouts became very concrete. Even this hypothesis, however, seems unlikely, because participants were no more consistent on Day 2 than Day 1, and Day 1 payment did not predict the change in loss aversion across days (see above).
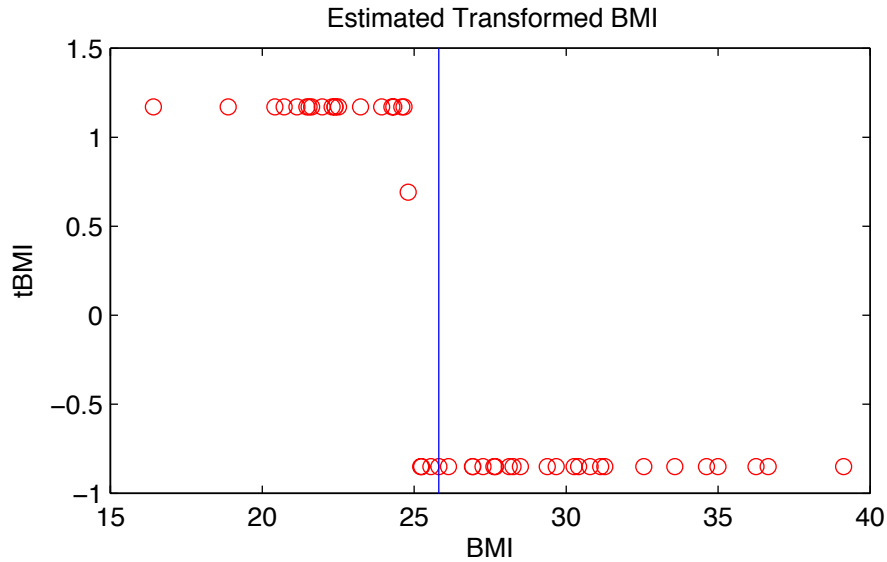
Figure S1: The best-fitting estimated transformation function. See Equation 4 in the main text. Red circles are individual participants, the blue line is the median BMI (used in the median-split). Untransformed BMIs are on the x-axis, and transformed values on the Y-axis. As can be seen, the transformation is a sharp step function that transitions between high- and low-BMI participants at nearly the same value (~25 kg/m^2) as the median BMI (25.8 kg/m^2).

Table S1 A summary of eighteen studies administering propranolol in humans.

1st Auth. & Year of Pub.	Dose	N w/ drug	N male	Mean Age	Weight/ BMI	Test for dose?	Paradigm	Rough Findings
Cahill 1994	40mg	20	~9?	27.4	-	-	Drug at encoding for later memory test of story.	Propranolol eliminated benefit to memory from emotional content.
Currie 1988	40, 80, & 160mg on sep. days	12	12	(19-29)	-	Indirectly; No effect.	Cognitive tests.	Propranolol reduced the # of photos recalled, and reduced anxiety after drug.
van Stegeren 1998	40mg	25	~8	(18-22)	-	-	Story memory paradigm.	Propranolol eliminated effect of emotion in improving recall & recognition for the emotional story only.
Harmer 2001	80mg	10	5	27.7	-	-	Emotion recognition paradigm.	Propranolol sped up reaction times to sad faces.
Reist 2001	40mg	20	20	~45	-	Directly; No effect.	Emotional story memory.	Propranolol reduced everyone's recall of emotional story, not neutral.
Pitman 2002	40mg x 4/day x 10 days	11-18	~8?	34.3	-	-	Administered to emergency department patients.	Propranolol reduced PTSD-associated symptoms.
Strange 2003	40mg	12	6	24.5	-	-	Word memory task.	Emotional words impair memory for prev. non-emotional word. Propranolol eliminates the effect, as does amygdala damage.
Vaiva 2003	40mg x 3/day x 7 days	11	7	23.9	-	-	Administered to emergency department patients.	Propranolol reduced the incidence of PTSD after a traumatic event.
Strange 2004	40mg	12	6	24.7	-	-	Memory task.	Propranolol eliminates amygdala response at encoding and later hippocampal bump at retrieval.
Rogers 2004	80mg	15	6	20.07	-	-	Decision task.	Propranolol increased gambling in one type of trial.
Maheu 2004	40mg or 80mg	25	25	(19-36)	-	Indirectly; Yes.	Emotional story; declarative memory test.	40mg didn't affect memory; 80mg impaired short & long-term memory for emotional material (but not neutral).
van Stegeren 2005	80mg	30	15	20.93	~70kg	-	Emotional image watching.	Propranolol reduced amygdala response to emotional images.
van Stegeren 2006	80mg	15	7	20.93	-	-	Emotional image watching.	Propranolol reduced salivary alpha amylase production in response to emotional images.
Brunet 2008	40mg + 60mg x 2	9	5	34.8		-	PTSD patients recalling memories, then reading script.	Propranolol reduced physiological reactions to the highly arousing reliving of their PTSD-related story
De Martino 2008	40mg	38	19	~24	-	-	Attentional blink w/ neutral and emotional items.	Propranolol reduces attentional blink effect regardless of target valence.
Zhang 2011	40mg	58-60	58-60	(20-40)	-	-	Iowa Gambling task in formerly heroin-dependent patients.	Propranolol blocked the negative effects of stress in worsening Iowa Gambling Task performance.
Schwabe 2011	40mg	34	~17?	24.3	22.8 (0.3) kg/m^2	-	Stress & choice-after-devaluation paradigm.	Stress made participants devaluation-insensitive; propranolol abolished the effect.
Terbeck 2012	40mg	18	9	22.33	-	-	IAT.	Attenuated implicit racial bias.

References

Cholerton, B., Baker, L. D., & Craft, S. (2013). Insulin, cognition, and dementia. *European Journal of Pharmacology, 719*(1-3), 170-179.

Dallman, M. F. (2010). Stress-induced obesity and the emotional nervous system. *Trends in Endocrinology and Metabolism, 21*(3), 159-165.

Kullmann, S., Heni, M., Veit, R., Ketterer, C., Schick, F., Häring, H.-U., . . . Preissl, H. (2012). The obese brain: Association of body mass index and insulin sensitivity with resting state network functional connectivity. *Human Brain Mapping, 33*, 1052-1061.

Maayan, L., Hoogendoorn, C., Sweat, V., & Convit, A. (2011). Disinhibited eating in obese adolescents is associated with orbitofrontal volume reductions and executive dysfunction. *Obesity, 19*(7), 1382-1387.

Maheu, F. S., Joober, R., Beaulieu, S., & Lupien, S. J. (2004). Differential Effects of Adrenergic and Corticosteroid Hormonal Systems on Human Short- and Long-Term Declarative Memory for Emotionally Arousing Material. *Behavioral Neuroscience, 118*(2), 420-428.

Reger, M. A., Watson, G. S., Green, P. S., Wilkinson, C. W., Baker, L. D., Cholerton, B., . . . Craft, S. (2008). Intranasal insulin improves cognition and modulates beta-amyloid in early AD. *Neurology, 70*(6), 440-448.

Sokol-Hessner, P., Camerer, C. F., & Phelps, E. A. (2013). Emotion Regulation Reduces Loss Aversion and Decreases Amygdala Responses to Losses. *Social Cognitive and Affective Neuroscience, 8*, 341-350. doi: doi:10.1093/scan/nss002

Sokol-Hessner, P., Hartley, C. A., Hamilton, J. R., & Phelps, E. A. (2014). Interoceptive ability predicts aversion to losses. *Cognition & Emotion*. doi: 10.1080/02699931.2014.925426

Sokol-Hessner, P., Hsu, M., Curley, N. G., Delgado, M. R., Camerer, C. F., & Phelps, E. A. (2009). Thinking like a trader selectively reduces individuals' loss aversion. *PNAS, 106*(13), 5035-5040. doi: 10.1073/pnas.0806761106

van Stegeren, A. H., Everaerd, W., Cahill, L., McGaugh, J. L., & Gooren, L. J. G. (1998). Memory for emotional events: differential effects of centrally versus peripherally acting beta-blocking agents. *Psychopharmacology, 138*, 305-310.

Methodological Details

Medical Screening

Screening and testing took place in the Outpatient Research Department at the Nathan Kline Institute in Orangeburg, NY. All participants provided informed consent, after which they passed a preliminary medical screening ensuring cardiovascular health, no major medication contraindications, and the absence of major psychiatric disorders. This screening included an electrocardiogram (EKG), a physical, and a review of their medical history, as performed by an MD or RN. The inclusion and exclusion criteria were as follows:

Medical Exclusion Criteria (Exclusions pertinent to medical safety):
1) History of allergic reaction to propranolol
2) History of cardiac structural disease including cardiomyopathy and valvular disease excluding instances of resolved benign cardiac murmur of childhood. A grade 1-3 cardiac murmur is permissible with documented approval from the participant's primary outpatient medical doctor.
3) History of myocardial infarction
4) History of atrial fibrillation, atrial flutter, 2nd or 3rd degree AV block. Sinus arrhythmia due to respiratory heart rate variability in an otherwise healthy individual will be permissible. Other EKG abnormalities are permissible with cardiology approval or approval from the participant's primary outpatient medical doctor.
5) History of intubation from asthma
6) History of diagnosed asthma requiring use of a rescue inhaler, maintenance medication, or other treatment within the past 7 years
7) Diabetes mellitus requiring insulin replacement therapy
8) Uncontrolled thyroid disease
9) History of glaucoma or elevated ocular pressures
10) Active cocaine use (cocaine use within the past 2 months)
11) Clinical suspicion for pregnancy
12) Currently breast feeding
13) If they are taking the following medications for any reason:
    a. Alpha-adrenergic blocker
    b. Amioderone
    c. Beta-blocker
    d. Chlorpromazine
    e. Cimetidine
    f. Clonidine
    g. Digoxin
    h. Diazoxide
14) If they have a resting:
    a. heart rate of 55 beats per minute or below
    b. systolic blood pressure outside of the range of 90-160
    c. diastolic blood pressure outside of the range of 60-100
15) Younger than 18 year old

DS8

16) Older than 40 years old
17) Any additional condition or finding deemed to elevate medical risk in participation

Scientific Inclusion/Exclusion Criteria (Exclusions pertinent to data quality but not medical safety):
Inclusion:
1) Completed at least 1 year of college
2) Fluent English speaker

Exclusion:
1) Vision impairment not corrected to normal w/ glasses or contacts
2) Personal medical history of:
    a. Seizure disorder/epilepsy
    b. Significant head injury (loss of consciousness > 30 min)
3) History or current psychiatric diagnosis of:
    a. Schizophrenia
    b. Schizoaffective disorder
    c. Alcohol dependence
    d. Sedative-hypnotic dependence
    e. Cannabis dependence
    f. Opioid abuse or dependence
    g. Cocaine dependence
    h. Hallucinogen dependence
4) Anything else that may result in a deficit in the participant's ability to perform the task.