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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(λ) 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(λ) 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(λ) 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 ($p = 0.53$).

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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 ($r(45) = 0.89$, $p = 1.5 \times 10^{-16}$). 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 $\alpha = 160.2$, 150.4, 159.2, and $\gamma = 435.2$, 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.

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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

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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).

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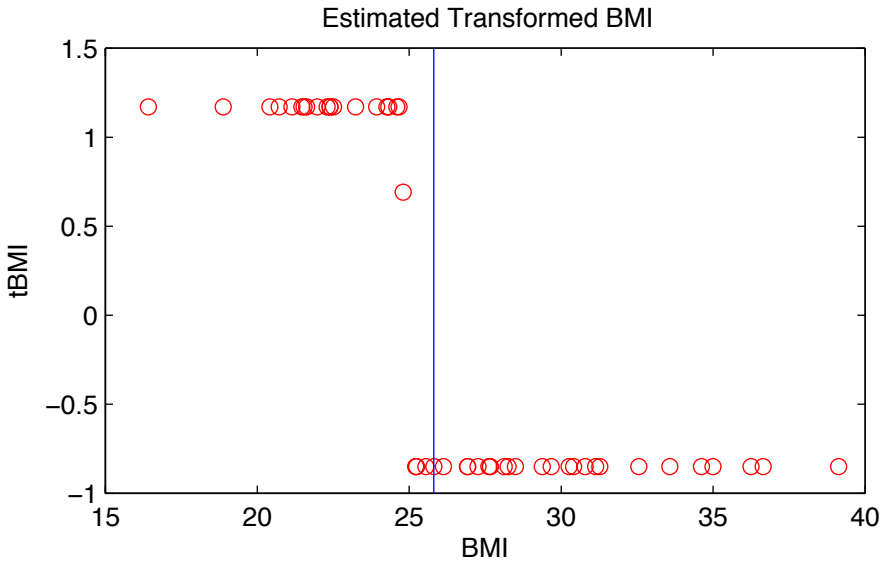

Figure S1: The best-fitting estimated transformation function. See Equation 4 in the main text. Red circles are individual participants, the blue line is the median BMI (used in the median-split). Untransformed BMIs are on the x-axis, and transformed values on the Y-axis. As can be seen, the transformation 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.

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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.

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