Supporting Information

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SI Text

Data Collection

There were two instances of technical malfunction that lead to error in data collection. In the first session, nine players, in three different groups, saw a phantom additional "other player" when contributions for round 1 of the No Punishment game were summarized. For these nine players, the lagged mean group contributions for round 1 of the No Punishment game were adjusted for analyses according to what they saw. Three players, one in each of the same groups, saw a phantom additional "self." For two of these players, no contribution was entered and the phantom contribution was 0. For one player, he or she reentered his/her initial contribution (10 tokens). These three players were informed by the researcher that a technical error had occurred and so their "phantom self" contributions were disregarded in all analyses.

In the Punishment game of a later session, negative tokens for four players, in four different groups, were not applied, because of a technical error (i.e., if/when other players assigned negative tokens to one of these four, the recipient did not receive the information, nor was his or her income reduced). The negative tokens these four players assigned to others remained uncorrupted and were included in analyses. The contributions of these four players were also included in calculations of the group mean contribution, but contributions these four individuals made during the Punishment game were excluded from analyses.

Data Analysis

Haplotype Classification. Our schema for grouping haplotypes is similar to that of ref. 1, which classified haplotypes at the serotonin 2A receptor gene [*5-hydroxytryptamine* (*serotonin*) *receptor 2A*, *G protein-coupled*, or *HTR2A*] and the serotonin transporter gene [*solute carrier family 6* (*neurotransmitter transporter*, *serotonin*), *member 4*, or *SLC6A4*] as predicted high or low expression based on the results of previously published molecular studies. We note that a more appropriate description may be differential expression haplotypes instead of high and low expression haplotypes. This is because of increasing evidence that the effect of these variants on expression is under epigenetic regulation. For *SLC6A4*, we characterize haplotypes that include the short allele at 5-HTTLPR and the 12-repeat allele at serotonin transporter intron 2 variable number of tandem repeats (STin2 VNTR) as *SLC6A4* 1 (*SH1*) and haplotypes with the long allele at 5-HTTLPR or the short allele at 5-HTTLPR and the 10-repeat allele at the STin2 VNTR as *SH2* (Table S1). Gene by environment studies show an association between the short allele and behavioral plasticity (2). Both the 5-HTTLPR and STin2 VNTR can regulate in vitro expression (3). Using a reporter gene assay (4) demonstrated that regulation of expression is dependent upon both the 5-HTTLPR and the STin2 VNTR alleles. The reporter gene construct with both the short allele at 5-HTTLPR and the 12-repeat allele at the STin2 VNTR supported the highest levels of activity in the absence of CCCTC-binding factor and the lowest levels of activity in its presence (4).

For *HTR2A,* we characterize haplotypes with the ancestral alleles at reference single nucleotide polymorphism 6311 (rs6311) and rs6313 (G and C) as *HTR2A* 1 (*HH1*) and those with the derived alleles at rs6311 and rs6313 (A and T) as *HH2* (Table S1). A potentially recombinant haplotype, represented by two chromosomes in our sample, with the ancestral allele at rs6311 (which is in the promoter) and the derived allele at rs6313, are included in this grouping. Gene by environment studies suggest that behavioral outcomes for individuals with the derived T allele at rs6313 are more susceptible to a positive environment (5). The derived alleles at rs6311 and rs6313 result in the loss of methylation sites (6). Methylation levels at both SNPs can affect *HTR2A* expression (6, 7). The derived allele at rs6311 also creates a transcription factor binding site, and a recent study suggests that regulation of *HTR2A* transcription is affected by a complex interaction among rs6311 genotype, promoter methylation, transcription factor binding, and cortisol levels (8).

The outcome of the reporter gene construct study cited above (4) and increased variability in expression for individuals with the C allele at rs6313 (6, 7) suggest that *SH1* and *HH1* may enable increased expression flexibility relative to *SH2* and *HH2*. However, this remains speculative until further work has been done. Below, we investigate the robustness of our results to the haplotype groupings used for *SLC6A4* and *HTR2A*.

Robustness of Contribution Inferences. ***Binomial model.*** The contribution data are discrete and censored, with contributions of multiples of five common, violating assumptions of normality. Thus, we refit the best candidate model (model 3 in Table 1) to the data, assuming a binomial distribution for the outcome variable, and checked for consistency with the Gaussian model. Coefficients for the binomial model are presented in Table S2 and are consistent with those for the Gaussian model. Inspection of a plot of predicted contributions from this model revealed little change from the predictions from the Gaussian model.

Ordered logit model. We refit the best candidate model to the data, this time modeling the number of tokens contributed as an ordinal variable, and checked for consistency with the Gaussian and binomial models. Coefficients for the ordered logit model are presented in Table S2 and are consistent with those for the Gaussian and binomial models. Inspection of a plot of predicted contributions from this model revealed little change from the predictions from the Gaussian and binomial models. Because all evidence indicates that the best candidate Gaussian model performs remarkably well despite the discrete and censored nature of the outcome variable, downstream analyses were conducted using this model as a starting point.

Sex. We assessed whether the inclusion of sex in the best candidate model altered the effect of *SH1* or *HH1* on contributions. We followed the same approach as for the genes; that is, we included *Sex* as a main effect and then iterated over the base model, interacting *Sex* with each of the six variables from the base model. Akaike Information Criterion (AIC) weights for the seven resulting models were assessed, and models with weights greater than 0.05 were combined until more complex models were not supported. The model that receives the most support includes interactions between *Sex* and *P game* and *Sex* and *Round*. The coefficients for *HH1* and *SH1* change little from those in Table 1: *SH1* = 1.323 (0.57, 2.08); *SH1* × *Lag MCO* = −0.087 (−0.14, −0.03); *SH1* × *Lag punished* = −0.231 (−0.38, −0.08); *HH1* = 0.009 (−0.86, 0.88); *HH1* × *P game* = 1.011 (0.30, 1.72).

Population structure. A number of participants in later sessions were foreign students, primarily from Asian countries. One concern is that the genetic effects on contributions that we observe in our study are actually cultural. That is, the observed variation in contribution behavior could be largely driven by differences in cultural norms within our participant pool. If these cultural norms are associated with differences in haplotype frequency, then we

could erroneously infer an effect of haplotype on contribution behavior.

Self-reported biological ancestry was collected during the experiment. One hundred twenty-one individuals self-identified as Northern European. No other category has more than 13 individuals (13 participants self-identified as East Asian), so participants were combined into the following categories: European (136), Asian (33), and African (7). Regional ancestry is unidentifiable for eight participants.

Haplotype frequencies for participants grouped by regional ancestry were estimated in PHASE. Consistent with the observations of ref. 1 haplotype frequencies at both loci vary among participants by regional ancestry. Claw et al. show that the 5-HTTLPR short allele and *SH1* further characterized by a transversion at rs1042173 are higher in frequency among individuals sampled from Asian populations compared with those sampled from European and African populations (1). There are 169 individuals for which we have *SLC6A4* data and self-reported biological ancestry. In our study, *SH1* is higher in frequency among individuals who claim Asian ancestry (0.53; $\sigma = 0.02$) than among those who claim European (0.34; $\sigma = 0.01$) or African (0.06; $\sigma = 0.04$) ancestry. There are 166 individuals for whom we have *HTR2A* data and self-reported biological ancestry. Similar to the observation of ref. 1, the frequency of *HH1* (referred to as the −1438G/102C haplotype by ref. 1) is higher among individuals in our study who claim European ancestry (0.57; $\sigma = 0.00004$) or African ancestry (0.60; $\sigma = 0.00063$) than those who claim Asian ancestry (0.47; $\sigma = 0.00011$).

To assess whether a correlation between haplotype frequency and cultural norms could underlie our results, we checked whether the observed relationship between haplotype and contribution behavior can be recovered in a subset of the data defined by regional ancestry. We fit the best candidate (Gaussian) model to two subsets of the data, European and Asian. We have *SLC6A4* and *HTR2A* data for all 33 individuals claiming Asian biological ancestry and *SLC6A4* and *HTR2A* data for 130 and 128 individuals, respectively, claiming European ancestry. Predicted contributions from this model fit to the European and Asian subsets of the data are shown in Fig. S4.

The major results from the full dataset are clearly replicated with the European subset of the data. That is, individuals with one or two copies of *SH1* contribute more in the No Punishment game (Fig. S4*A*), and individuals with one or two copies of *HH1* contribute more in the Punishment game (Fig. S4*B*). Table S5 shows that the results are replicated even with the small number of individuals in the Asian subset of the data; individuals with *SH1* contribute more in the No Punishment game, and those with *HH1* contribute more in the Punishment game. Predicted contributions are plotted in Fig. S4 *C* and *D*.

Thus, the effects of *SH1* and *HH1* on contributions persist when only participants with European ancestry are considered. Although not all of the participants with European ancestry grew up in the United Kingdom (we can confirm that 12 did not; countries of origin include France, Romania, and the United States), there is no evidence that the European subset of the data contains a substantial number of participants sharing a common biological and cultural origin outside of the United Kingdom (or a distinct biological and cultural origin within the United Kingdom), as would be required for a spurious association between haplotype and contribution behavior.

We note that although similar results are achieved when the subset of participants with Asian ancestry are considered separately, this should not be considered as a replication of the study in a culturally and biologically distinct population. Aside from the very small sample size (33 individuals), this subset of the data represents both individuals of South Asian ancestry who have grown up in the United Kingdom and individuals who recently arrived in the United Kingdom.

Characterization of haplotypes. SLC6A4. Our grouping of *SLC6A4* haplotypes (i.e., haplotypes with the short allele at 5-HTTLPR and the 10-repeat allele at STin2 VNTR are classed as *SH1* with all haplotypes with the 5-HTTLPR long allele, as shown in Table S1) is based on results from a reporter gene assay (4). However, a large number of studies have considered the 5-HTTLPR alone. In our sample, over 93% of chromosomes with the short allele at 5-HTTLPR also have the 12-repeat allele at STin2 VNTR. The effect of *SLC6A4* on contributions is similar when only 5-HTTLPR genotype is considered; participants with one or two copies of the short allele contribute more in the No Punishment game, and this difference is attenuated in the Punishment game. Fig. S3*A* shows predicted contributions for the best candidate model fit to data for 5-HTTLPR genotypes instead of haplotypes.

Claw et al. (1) observed the strongest linkage disequilibrium at *SLC6A4* for a haplotype characterized by the short allele at 5-HTTLPR, the 12-repeat allele at STin2 VNTR, and the derived allele, G, at rs1042173 [position 23966 relative to the start of transcription, exon 14 (3′ untranslated region)]. They referred to this haplotype as "S/12/G." The frequency of this haplotype varies dramatically across world regions; without even considering sub-Saharan Africa, it ranges from 10 to 75% (1). Despite its overall high frequency, this haplotype has very little background variation (1). This pattern does not appear to be explained solely by demography and may be partly attributable to directional selection (1). Moreover, the estimated most recent common ancestor of this haplotype is 19,000 ± 4,000 y ago (1).

The S/12/G haplotype corresponds to the subset of *SH1* with a G at rs1042173. We genotyped our participants for this SNP as well but have no expectation for its function and, so, for our main analyses did not differentiate participants with *SH1* on the basis of this SNP. To determine whether the result we observe with *SH1* is still apparent with the S/12/G haplotype, we fit the best candidate model to the subset of data that includes only participants of European ancestry and substituted the S/12/G haplotype for *SH1*. Twenty-four of the 136 participants in this dataset have the S/12/G haplotype. Predicted contributions are shown in Fig. S3*B*. As with the full dataset and the *SH1*, participants with the S/12/G haplotype contribute more in the No Punishment game, and this difference is attenuated with the introduction of punishment. A similar result is observed when the entire dataset is considered (i.e., all participants are included irrespective of ancestry).

HTR2A. Over 98% of chromosomes that we sampled have one of two *HTR2A* haplotypes. In most studies of *HTR2A* variation, only one of the SNPs in these haplotypes is genotyped, and complete linkage disequilibrium is assumed. We observe four haplotypes that are potential recombinants. We note that because of our grouping of these four potential recombinants (Table S1), our *HTR2A* data and results are exactly what we would have achieved had we only genotyped the commonly studied promoter polymorphism rs6311 (position −1438 relative to the start of transcription). We tried excluding data for the four individuals with potentially recombinant haplotypes. The resulting fixed effect regression coefficients [*HH1* = −0.03 (−0.93, 1.23); *HH1* × *P game* = 0.89 (0.16, 1.61)] can be compared with those for model 3 in Table 1. The effect of *HH1* on contributions in the Punishment game does not change substantially with exclusion of the four individuals with potentially recombinant haplotypes.

1. Claw KG, Tito RY, Stone AC, Verrelli BC (2010) Haplotype structure and divergence at human and chimpanzee serotonin transporter and receptor genes: Implications for behavioral disorder association analyses. *Mol Biol Evol* 27(7):1518–1529.

2. Belsky J, et al. (2009) Vulnerability genes or plasticity genes? *Mol Psychiatry* 14(8): 746–754.
3. Haddley K, et al. (2008) Molecular genetics of monoamine transporters: Relevance to brain disorders. *Neurochem Res* 33(4):652–667.
4. Ali FR, et al. (2010) Combinatorial interaction between two human serotonin transporter gene variable number tandem repeats and their regulation by CTCF. *J Neurochem* 112(1): 296–306.
5. Keltikangas-Järvinen L, Salo J (2009) Dopamine and serotonin systems modify environmental effects on human behavior: A review. *Scand J Psychol* 50(6):574–582.
6. Polesskaya OO, Aston C, Sokolov BP (2006) Allele C-specific methylation of the 5-HT_{2A} receptor gene: Evidence for correlation with its expression and expression of DNA methylase *DNMT1*. *J Neurosci Res* 83(3):362–373.
7. Abdolmaleky HM, et al. (2011) Epigenetic dysregulation of *HTR2A* in the brain of patients with schizophrenia and bipolar disorder. *Schizophr Res* 129(2-3):183–190.
8. Falkenberg VR, Gurbaxani BM, Unger ER, Rajeevan MS (2011) Functional genomics of serotonin receptor 2A (*HTR2A*): Interaction of polymorphism, methylation, expression and disease association. *Neuromolecular Med* 13(1):66–76.

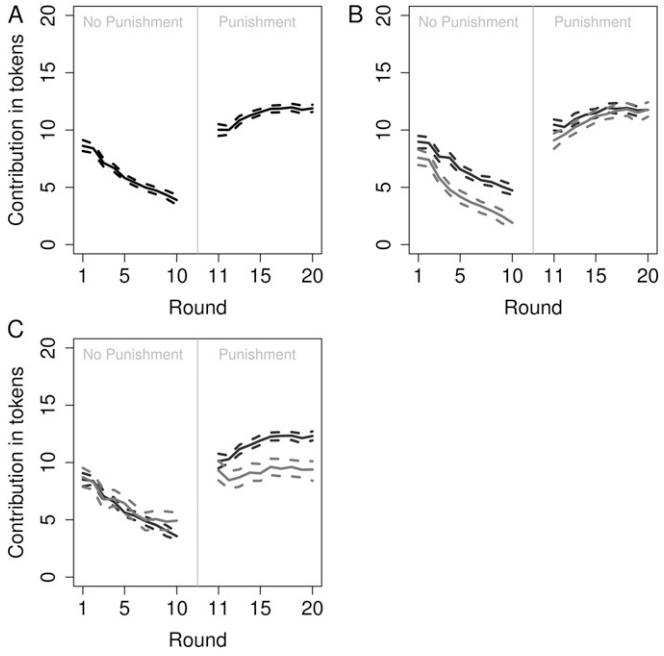

Fig. S1. Predicted contributions for Gaussian base model and best candidate model with genetic data. Dotted lines illustrate 95% confidence intervals. (*A*) Base model. (*B*) *SLC6A4*. (*C*) *HTR2A*. For *B*, *SH1* homozygotes and heterozygotes are in dark gray and *SH2* homozygotes are in light gray. For *C*, *HH1* homozygotes and heterozygotes are in dark gray and *HH2* homozygotes are in light gray.

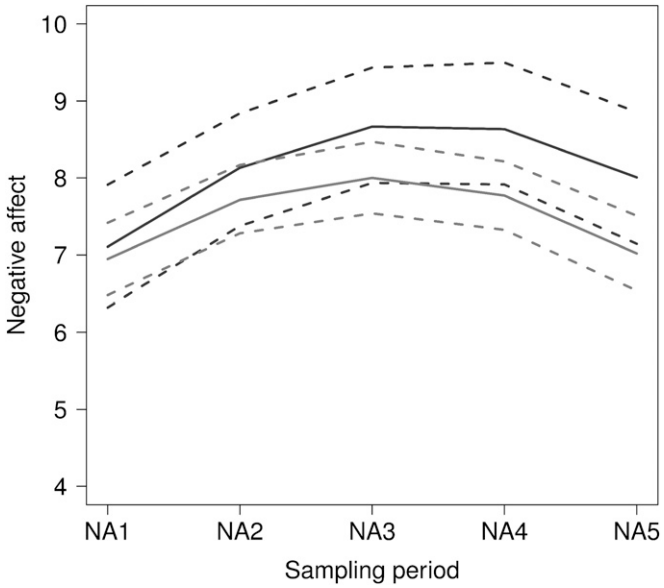

Fig. S2. Effect of *HTR2A* on NA. Model specifies a recessive relationship between *HH1* and phenotype, with an interaction between phenotype and sampling period. Dotted lines illustrate 95% confidence intervals. *HH1* homozygotes are in dark gray and heterozygotes and *HH2* homozygotes are in light gray. Sampling periods: NA1, beginning of the experiment; NA2, after reading the PGG instructions (No Punishment version) and before commencing the No Punishment game; NA3, immediately after the No Punishment game; NA4, after reading instructions and before commencing the Punishment game; and NA5, immediately after the Punishment game.

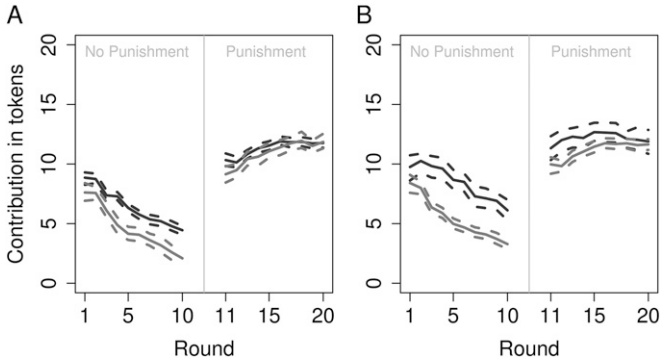

Fig. S3. For both *A* and *B*, dotted lines illustrate 95% confidence intervals. (*A*) Predicted contributions for best candidate model fit to data for 5-HTTLPR genotypes instead of *SLC6A4* haplotypes. Participants with one or two copies of the 5-HTTLPR short allele in dark gray and two copies of the long allele in light gray. (*B*) Predicted contributions for best candidate model fit to the S/12/G haplotype. Only participants of European ancestry were included. Participants with one or two copies of the S/12/G haplotype are in dark gray and those without the haplotype are in light gray.

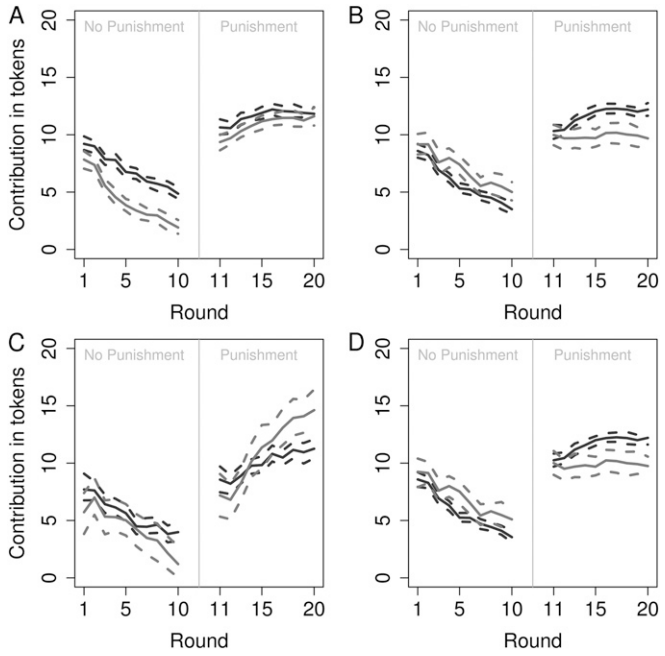

Fig. S4. Predicted contributions for best candidate model fit to subsets of the data. Dotted lines illustrate 95% confidence intervals. (*A*) *SLC6A4*, participants with European ancestry only. (*B*) *HTR2A*, participants with European ancestry only. (*C*) *SLC6A4*, participants with Asian ancestry only. (*D*) *HTR2A*, participants with Asian ancestry only. For *A* and *C*, *SH1* homozygotes and heterozygotes are in dark gray, and *SH2* homozygotes are in light gray. For *B* and *D*, *HH1* homozygotes and heterozygotes are in dark gray and *HH2* homozygotes are in light gray.

Table S1. *SLC6A4* and *HTR2A* haplotype classification and sample sizes

N	Gene	Haplotype	Differential expression haplotype	Frequency
144	*SLC6A4*	5HTTLPR-S / STin2 VNTR.12	*SH1*	0.407
24	*SLC6A4*	5HTTLPR-S / STin2 VNTR.10	*SH2*	0.068
4	*SLC6A4*	5HTTLPR-L / STin2 VNTR.9	*SH2*	0.011
95	*SLC6A4*	5HTTLPR-L / STin2 VNTR.10	*SH2*	0.268
87	*SLC6A4*	5HTTLPR-L / STin2 VNTR.12	*SH2*	0.246
189	*HTR2A*	rs6311G / rs6313C	*HH1*	0.543
2	*HTR2A*	rs6311G / rs6313T	*HH1*	0.006
155	*HTR2A*	rs6311A / rs6313T	*HH2*	0.445
2	*HTR2A*	rs6311A / rs6313C	*HH2*	0.006

Table S2. Fixed-effects regression coefficients and variance components for Gaussian, binomial, and ordered logit models of the number of tokens contributed to the group fund

	Gaussian model			Binomial model			Ordered logit model		
Parameter	Estimate	2.5%	97.5%	Estimate	2.5%	97.5%	Estimate	2.5%	97.5%
Fixed effects									
Intercept	0.01 (0.54)	−1.046	1.075	−2.85 (0.183)	−3.21	−2.49			
SH1	1.38 (0.39)	0.619	2.132	0.48 (0.132)	0.22	0.74	0.57 (0.19)	0.18	0.938
SH1 × *Lag MCO*	−0.09 (0.03)	−0.143	−0.034	−0.03 (0.005)	−0.04	−0.02	−0.04 (0.01)	−0.06	−0.009
SH1 × *Lag punished*	−0.23 (0.08)	−0.382	−0.081	−0.06 (0.011)	−0.08	−0.04	−0.11 (0.04)	−0.18	−0.035
HH1	0.02 (0.45)	−0.855	0.897	0.07 (0.162)	−0.25	0.39	0.09 (0.22)	−0.34	0.531
*HH1 * P game*	1.01 (0.36)	0.298	1.719	0.21 (0.055)	0.10	0.32	0.27 (0.17)	−0.05	0.607
P game	0.66 (0.34)	−0.004	1.316	0.37 (0.050)	0.27	0.47	0.53 (0.16)	0.22	0.831
Round	−0.06 (0.03)	−0.113	−0.003	−0.02 (0.004)	−0.03	−0.01	−0.03 (0.01)	−0.06	−0.004
First round	7.61 (0.32)	6.995	8.232	2.06 (0.045)	1.98	2.15	3.46 (0.16)	3.15	3.777
Lag contribution	0.32 (0.02)	0.286	0.355	0.07 (0.002)	0.06	0.07	0.16 (0.01)	0.14	0.174
Lag MCO	0.56 (0.03)	0.502	0.613	0.18 (0.004)	0.17	0.19	0.26 (0.02)	0.23	0.290
Lag punished	0.25 (0.07)	0.122	0.379	0.06 (0.009)	0.04	0.08	0.11 (0.03)	0.04	0.171
Variance components									
Participant	3.27 (1.81)			0.60 (0.775)			0.92 (0.07)		
Residual	16.04 (4.01)								

Based on results of the model selection process, dominant relationships between both *SH1* and *HH1* and phenotype are assumed. Parentheses contain SEs or, for the variance components and for the fixed effects estimates for the ordered logit model, SDs of the estimates. Lag refers to the previous round. *First round*, the initial round of either game (i.e., round 1 or round 11); *Lag contribution*, the lagged contribution of ego; *Lag MCO*, the lagged mean contribution of the group, excluding ego; *Lag punished*, the lagged number of negative tokens ego received; *P game*, the punishment game.

Table S3. Fixed-effects regression coefficients and variance component for the effect of *HH1* on NA

Parameter	Estimate	2.5%	97.5%
Fixed effects			
Intercept	1.754 (0.084)	1.59	1.92
Sampling period	0.240 (0.047)	0.15	0.33
HH1 Hr	0.007 (0.077)	−0.14	0.16
Sampling period^2	−0.035 (0.007)	−0.05	−0.02
Sampling period × *HH1 Hr*	−0.028 (0.019)	−0.07	0.01
Variance component			
Participant	0.057 (0.240)		

SEs (SD for the variance component) are in parentheses. *Hr*, a recessive relationship between *HH1* and phenotype.

Table S4. Regression coefficients for the effect of *HH1* on total cortisol secretion during interval 2

Parameter	Estimate	2.5%	97.5%
Intercept	5.67 (0.70)	4.30	7.04
HH1 Hd	−0.90 (0.78)	−2.43	0.63
Female	−3.48 (1.00)	−5.43	−1.53
Male	−0.82 (0.83)	−2.45	0.81
MDI	−0.14 (0.18)	−0.50	0.22
HH1 Hd × *Female*	3.68 (1.09)	1.54	5.82
HH1 Hd × *Male*	0.76 (0.92)	−1.05	2.57
HH1 Hd × *MDI*	0.16 (0.20)	−0.23	0.56
Female × *MDI*	0.79 (0.26)	0.29	1.30
Male × *MDI*	0.20 (0.23)	−0.25	0.64
HH1 Hd × *Female* × *MDI*	−0.83 (0.28)	−1.38	−0.28
HH1 Hd × *Male* × *MDI*	−0.14 (0.25)	−0.62	0.35

SEs are in parentheses. *Female*, females who were not taking hormonal contraceptives; *Hd*, a dominant relationship between *HH1* and phenotype; *MDI*, the square root of the Major Depression Inventory.

Table S5. Fixed effects coefficients and variance components for the best candidate Gaussian model of the number of tokens contributed to the group fund, fit to subsets of the data

	Model fit to subset of data*			Model fit to subset of data†		
Parameter	Estimate	2.5%	97.5%	Estimate	2.5%	97.5%
Fixed effects						
Intercept	0.53 (0.62)	−0.68	1.75	−2.41 (1.24)	−4.85	0.02
SH1	1.33 (0.44)	0.47	2.19	2.03 (0.98)	0.10	3.96
*SH1 * Lag MCO*	−0.07 (0.03)	−0.14	−0.02	−0.18 (0.08)	−0.33	−0.03
*SH1 * Lag punished*	−0.28 (0.09)	−0.45	−0.11	0.02 (0.22)	−0.41	0.44
HH1	−0.44 (0.53)	−1.48	0.60	0.69 (0.81)	−0.89	2.28
*HH1 * P game*	0.85 (0.42)	0.03	1.68	1.39 (0.69)	0.05	2.74
P game	0.81 (0.39)	0.05	1.57	0.01 (0.65)	−1.26	1.28
Round	−0.07 (0.03)	−0.14	−0.01	0.05 (0.06)	−0.07	0.17
First round	7.77 (0.36)	7.06	8.47	7.43 (0.66)	6.14	8.71
Lag contribution	0.32 (0.02)	0.28	0.36	0.39 (0.04)	0.32	0.47
Lag MCO	0.55 (0.03)	0.49	0.61	0.62 (0.08)	0.46	0.78
Lag punished	0.26 (0.07)	0.11	0.40	0.10 (0.21)	−0.30	0.51
Variance components						
Participant	3.38 (1.84)			2.32 (1.52)		
Residual	15.31 (3.91)			13.41 (3.66)		

Dominant relationships between both *SH1* and *HH1* and phenotype are assumed. Lag refers to the previous round. *First round*, the initial round of either game (i.e., round 1 or round 11); *Lag contribution*, the lagged contribution of ego; *Lag MCO*, the lagged mean contribution of the group, excluding ego; *Lag punished*, the lagged number of negative tokens ego received; *P game*, the punishment game. Parentheses contain SEs or, for the variance components, SDs of the estimates.

*Data from 128 participants who claim European ancestry.

†Data from 33 participants who claim Asian ancestry.