Supporting Information

Saphire-Bernstein et al. 10.1073/pnas.1113137108

SI Text

Additional Details on Construction of Factor Scores. Exploratory factor analysis of the combined items from the Beck Depression Inventory-IA (BDI-IA) and from the three measures of psychological resources revealed a reasonably clear two-factor solution (Table S1). Four items from the BDI-IA loaded more strongly (negatively) on the resources factor than on the symptoms factor. These items (BDI-IA #s 2, 3, 7, and 8) each assess the absence of self-esteem or positive self-feeling, and so the cross-loadings on resources are not surprising. In addition, one item from the mastery scale (MAS #7) had a stronger loading on the depressive symptomatology factor (-0.31) than it did on the resources measure (0.30). In addition, three items (MAS #2 and BDI-IA #s 14 and 19) failed to achieved loadings greater than 0.20 on either factor (see Table S1 for the full pattern matrix of factor loadings).

After the elimination of these eight items, a satisfactory simple structure solution was produced by extracting two factors, which combined to account for 29.2% of the total item variance. All items attained a loading greater than 0.30 on the intended factor and none displayed loadings greater than 0.30 on the other factor. The correlation between the two factors in this second exploratory factor analysis was -0.433. Factor scores were estimated by averaging the items loading on each factor in the second analysis, after first standardizing each item to assure the equivalence of item scaling across measures. Thus, 21 items were used to compute the psychological resources factor, and 14 items were used to compute the depressive symptomatology factor (see Table S1 for more details). Unit-weighting was used to compute factor scores, as this method is believed to avoid overfitting to the sample at hand and therefore to yield factor scores that are more replicable across samples (1, 2). The factor scores for psychological resources and depressive symptomatology were standardized to enable the direct comparison of the bootstrapped estimates of the indirect effects.

Ethnicity Analyses. Molecular genetic findings regarding human behavior may not generalize across different ethnic groups (3–5). For example, significant moderation by race (African-American relative to Caucasian) has been reported for an association between the serotonin transporter promoter length polymorphism (5HTTLPR) and levels of 5-hydroxyindoleacetic acid (5-HIAA) in cerebrospinal fluid (3). Previous studies of OXTR rs53576 in mixed-ethnicity samples (Asians and Caucasians) have reported significantly greater prevalence of A alleles relative to G alleles in individuals of Asian ancestry relative to Caucasians (6-8). As our sample was characterized by a relatively high degree of ethnic heterogeneity (as noted in the main text), we explored the extent to which the effects uncovered in the present study were generally consistent across the largest ethnic subgroups. In the analyses that follow, we first investigated whether the effects of OXTR were similar for individuals in the largest ethnic subgroup, Asians and Asian-Americans (n = 117), and for individuals in the remainder of the sample (n = 209). Follow-up analyses were then conducted on a subset of the sample consisting exclusively of individuals from the three largest ethnic subgroups: Asian, Caucasian (n = 87), and Hispanic (n = 49). Together, these three ethnicities accounted for 77.6% of the study participants (combined n = 253).

A series of multiple regression analyses were conducted to examine whether the effects of *OXTR* A-allele carrier status on psychological resources and depressive symptomatology were moderated by or confounded with ethnicity. Initial models included a term for the interaction of *OXTR* and ethnicity, but no significant interaction effects were detected in any of the analyses of ethnicity and *OXTR*, including additional analyses described below. The absence of significant interaction effects indicates that ethnicity did not moderate the effect of *OXTR* on any of the dependent variables included in the study, and this possibility is not considered or discussed further.

We next investigated whether the effects of OXTR are confounded with ethnicity by regressing the psychological resources and depressive symptomatology factor scores on OXTR and ethnicity simultaneously, absent the interaction term. These analyses demonstrated that the variance in psychological resources accounted for by OXTR A-allele carrier status partially overlaps with the variance explained by Asian ethnicity, as the effect of OXTR on psychological resources was reduced and no longer significant $(\beta = -0.094, P = 0.097; \text{ from } \beta = -0.168, P = 0.002 \text{ without}$ ethnicity in the model), whereas the effect of Asian ethnicity remained significant ($\beta = -0.229, P < 0.001$). These results indicate that lower resources were reported by Asians relative to non-Asians and by A-allele carriers relative to G-allele homozygotes, although the latter effect was not significant. Follow-up analyses restricted to participants of Asian, Caucasian, and Hispanic ancestry (n = 253) found that the effect of OXTR on resources in this subsample remained significant ($\beta = -0.142, P = 0.029$) when controlling for both Asian ($\beta = -0.232$, P = 0.001) and Hispanic ethnicity ($\beta = -0.029, P = 0.665$). Caucasian ethnicity served as the comparison group for this analysis. As with the preceding analysis, the results indicated lower resources among A-allele carriers relative to G-allele homozygotes and among Asians (but not Hispanics) relative to Caucasians. Note that the zero-order effect of OXTR A-allele carrier status was somewhat larger in the subsample of Asians, Hispanics, and Caucasians ($\beta = -0.222, P < 0.222$ 0.001) than it was in the full sample ($\beta = -0.168$), a difference that may have contributed to the greater robustness of the OXTR effect in this subsample.

With respect to depressive symptomatology, the effect of Asian ethnicity was not significant ($\beta = 0.050$, P = 0.391) when entered simultaneously with *OXTR* A-allele carrier status, the effect of which fell just shy of significance ($\beta = 0.111$, P = 0.057). This situation was somewhat reversed in the subsample of the three largest ethnicities, as the effect of carrying the *OXTR* A allele was not significant ($\beta = 0.108$, P = 0.107), but the effect of Asian ethnicity ($\beta = 0.111$, P = 0.050) was right at the threshold of nominal significance, and the effect of Hispanic ethnicity was significant ($\beta = 0.172$, P = 0.014). These results indicate higher levels of depressive symptomatology among both Asians and Hispanics, relative to Caucasians, and a nonsignificant trend for more depressive symptomatology in *OXTR* A-allele carriers.

One factor that may account in part for the shared variance between the A allele of rs53576 and Asian ethnicity is the greater prevalence of the A allele in Asian individuals, relative to individuals in all other ethnic groups (Table S2). Of the 117 Asians and Asian-Americans in our sample, only 15 (12.8%) had the G/G genotype, whereas 102 (87.2%) were A-allele carriers (of the carriers, 58 were heterozygotes and 44 were A-allele homozygotes) (Table S2). In contrast, A-allele homozygotes were a relative rarity among the non-Asian participants in our study, numbering only 21 in total, and they were even rarer (n = 3 of 87) among Caucasian participants (see Table S2 for complete information on the distributions of genotype by ethnicity). It may be the case that *OXTR* rs53576 variation in Caucasians is best studied using a dominant model, whereas the consequences of variation at this locus for Asian individuals may be better captured by an additive model, in which each additional A allele contributes added risk for negative outcomes. In support of this notion, we found that when the number of A alleles (i.e., 0, 1, or 2, coded as -1, 0, and 1, respectively) was used to predict psychological resources instead of the A-allele carrier contrast in the full sample, the effect of OXTR genotype survived the addition of Asian ethnicity to the model (for *OXTR*, $\beta = -0.115$, P = 0.050; for Asian ethnicity, $\beta = -0.214$, P < 0.001; model adjusted $R^2 = 0.073$). Likewise, the effect of OXTR on psychological resources in the reduced sample of Asian, Caucasian, and Hispanic participants was more robust using the additive model: OXTR genotype was significantly related to psychological resources ($\beta = -0.189$, P = 0.005) even when controlling for both Asian ($\beta = -0.197$, P = 0.009) and Hispanic ethnicity $(\beta = -0.011, P = 0.871; \text{ model adjusted } R^2 = 0.092).$

Separate analyses of the effects of *OXTR* on each of the dependent variables are provided for the three largest ethnic groups (Asians, Caucasians, and Hispanics) and for non-Asians as a whole in Table S4. Although none of the effects are significant when the sample is stratified by ethnicity because of the reduction in sample size, comparison of the effect sizes obtained in each ethnic group reveals that the effects of *OXTR* on the individual resource measures and the psychological resources factor are consistently positive and moderately comparable across Asians, Caucasians, and Hispanics, although some variation in the size of the effect is present. The effect of *OXTR* on depressive symptomatology was also present in Asians, non-Asians overall, and in Hispanics, but was less evident for Caucasians (Table S4).

Finally, the mediation model held for both Asians and non-Asians when examined separately by ethnicity, but the effects of *OXTR* were once again not significant because of the reduction in sample size. Correlations between the psychological resources and depressive symptomatology factor scores were significant at P < 0.001 in each subsample: for Asians (r = -0.36), for Caucasians (r = -0.47), Hispanics (r = -0.55), and non-Asians overall (r = -0.53). Bootstrapped estimates of the indirect effect were: for Asians [0.0648, 95% confidence interval (CI): -0.0137, 0.1456], for Hispanics (0.0741, 95% CI: -0.0395, 0.2027), and for Caucasians (0.0304, 95% CI: -0.0532, 0.1147).

- 1. Floyd FJ, Widaman KF (1995) Factor analysis in the development and refinement of clinical assessment instruments. *Psychol Assess* 7:286–299.
- Russell DW (2002) In search of underlying dimensions: The use (and abuse) of factor analysis in Personality and Social Psychology Bulletin. Pers Soc Psychol Bull 28: 1629–1646.
- Williams RB, et al. (2003) Serotonin-related gene polymorphisms and central nervous system serotonin function. *Neuropsychopharmacology* 28:533–541.
- Propper C, Willoughby M, Halpern CT, Carbone MA, Cox M (2007) Parenting quality, DRD4, and the prediction of externalizing and internalizing behaviors in early childhood. *Dev Psychobiol* 49:619–632.

Our supplemental analyses provide support for the hypothesis that the effect of *OXTR* on psychological resources documented in the present study (see main text) is roughly similar for Asians, Caucasians, and Hispanics. Nevertheless, future research should confirm that the rs53576 SNP is a marker for functionally similar genetic effects in individuals from different ethnicities.

Sex Analyses. The distribution of OXTR alleles did not differ significantly between males and females $[\chi^2(2) = 3.50, P = 0.173],$ and there were no significant sex differences in self-esteem, optimism, depressive symptomatology, and the psychological resources and depressive symptomatology factors (see Table S5 for more details). We also tested for interactions between OXTR and sex in their effects on each of these measures, and none were significant. A significant difference did emerge on the mastery scale, with men scoring higher on average (M = 3.17, SD = 0.43) than women: (M = 3.05, SD = 0.48), t(324) = 2.37, P = 0.018, $d = 0.27, R^2 = 0.018$. Simultaneous regression analysis revealed this sex effect to be largely independent from the effect of OXTR, as significant effects were observed for both OXTR A-allele carriers ($\beta = -0.116$, P = 0.035) and sex ($\beta = -0.134$, P = 0.015), indicating lower levels of mastery in women and OXTR A-allele carriers. The two variables combined to explain 2.4% of the variance in self-reported mastery. As with the other dependent variables, the interaction between OXTR and sex was not significant in predicting mastery (P = 0.745). Similar results were obtained when the effect of OXTR genotype was assessed using the additive model (for *OXTR* genotype, $\beta = -0.137$, P = 0.013; for sex, $\beta = -0.127$, P = 0.021; model adjusted $R^2 = 0.030$). Furthermore, although the effect of sex on psychological resources did not reach the threshold for nominal significance when entered on its own ($\beta = -0.102$, P = 0.066), the P value for the sex effect $(\beta = -0.107, P = 0.051)$ was only slightly greater than 0.05 when entered simultaneously with the OXTR A-allele carrier contrast (the effect of *OXTR* was not appreciably different, $\beta = -0.171$, P = 0.002), indicating lower levels of psychological resources among females and among A-allele carriers, relative to men and to GG homozygotes, respectively. Finally, correlations between the psychological resources and depressive symptomatology factor scores were significant at P < 0.001: for men, r = -0.44; and women, r = -0.49.

- Widom CS, Brzustowicz LM (2006) MAOA and the "cycle of violence:" Childhood abuse and neglect, MAOA genotype, and risk for violent and antisocial behavior. *Biol Psychiatry* 60:684–689.
- Kim HS, et al. (2010) Culture, distress, and oxytocin receptor polymorphism (OXTR) interact to influence emotional support seeking. Proc Natl Acad Sci USA 107:15717–15721.
- Kim HS, et al. (2011) Gene-culture interaction: Oxytocin receptor polymorphism (OXTR) and emotion regulation. Soc Psychol Pers Sci, 10.1177/1948550611405854.
- Sasaki JY, Kim HS, Xu J (2011) Religion and well-being: The moderating role of culture and the oxytocin receptor (OXTR) gene. J Cross-Cultural Psychol, 10.1177/ 0022022111412526, in press.

	Factor I	oading		Factor loading		
Item	I	П	Item	I	II	
SE6	0.80	0.07	MAS3	0.39	-0.10	
SE5	0.75	0.15	OPT1	0.39	-0.01	
SE7	0.68	-0.08	OPT3	0.37	-0.23	
SE10	0.67	-0.07	MAS2	0.24	0.00	
SE2	0.66	0.12	BDI-IA18	0.01	0.54	
SE1	0.65	0.06	BDI-IA15	-0.05	0.53	
SE3	0.63	-0.05	BDI-IA17	0.01	0.53	
SE9	0.62	-0.02	BDI-IA13	-0.06	0.51	
SE4	0.59	0.09	BDI-IA10	0.02	0.44	
OPT4	0.58	0.01	BDI-IA4	-0.23	0.43	
SE8	0.55	-0.04	BDI-IA1	-0.23	0.42	
OPT10	0.54	-0.11	BDI-IA16	0.02	0.42	
OPT9	0.50	-0.13	BDI-IA5	-0.19	0.38	
BDI-IA7	- 0.49	0.32	BDI-IA11	0.02	0.37	
OPT7	0.49	-0.15	BDI-IA21	0.10	0.37	
MAS6	0.48	-0.20	BDI-IA12	-0.11	0.36	
MAS5	0.43	0.12	BDI-IA6	-0.13	0.32	
BDI-IA8	-0.43	0.29	MAS7	0.30	-0.31	
MAS1	0.42	-0.01	BDI-IA20	-0.07	0.31	
MAS4	0.41	0.06	BDI-IA14	-0.21	0.27	
BDI-IA2	-0.40	0.29	BDI-IA19	0.07	0.23	
BDI-IA3	-0.40	0.31				

Table S1. Factor loadings from exploratory factor analysis

Loadings with an absolute value greater than or equal to 0.20 are displayed in boldface text. Items excluded from the computation of the factor scores are italicized.

Table S2. Distributions of OXTR genotypes by ethnicity

Ethnic grouping	G/G	A/G	A/A
White (<i>n</i> = 87)	42 (47.7%)	42 (48.8%)	3 (3.5%)
Asian (<i>n</i> = 117)	15 (12.8%)	58 (49.6%)	44 (37.6%)
Hispanic (<i>n</i> = 49)	21 (42.9%)	17 (34.7%)	11 (22.4%)
Other (<i>n</i> = 73)	30 (41.9%)	36 (48.6%)	7 (9.5%)

Table S3. Scale means by ethnic group

PNAS PNAS

	Non-Asian	Asian		Hispanic	t test – Asian vs. Other	F-test – three ethnicities
Scale	(<i>n</i> = 209)	(<i>n</i> = 117)	White <i>n</i> = 87)	(<i>n</i> = 49)	(<i>df</i> = 324)	(df = 2, 250)
Self-esteem	3.36 (0.49)	3.09 (0.52)	3.38 (0.44)	3.28 (0.57)	4.70 <i>P</i> < 0.001	8.62 <i>P</i> < 0.001
Mastery	3.16 (0.46)	2.98 (0.43)	3.15 (0.43)	3.15 (0.57)	3.55 <i>P</i> < 0.001	4.35 <i>P</i> = 0.014
Optimism	3.70 (0.83)	3.41 (0.82)	3.73 (0.80)	3.77 (0.83)	3.08 P = 0.002	5.29 <i>P</i> = 0.006
BDI sum	5.55 (5.37)	6.98 (5.91)	4.62 (4.50)	6.76 (5.67)	-2.18 <i>P</i> = 0.031	5.15 <i>P</i> = 0.006
Resources factor	0.19 (0.96)	-0.35 (0.99)	0.22 (0.87)	0.13 (1.05)	4.83 <i>P</i> < 0.001	9.99 <i>P</i> < 0.001
BDI factor	-0.06 (0.98)	0.11 (1.03)	-0.25 (0.80)	0.19 (1.06)	–1.55 <i>P</i> = 0.122	4.68 <i>P</i> = 0.010

Cell values indicate group means. SDs are in parentheses.

Scale	G/G	G/A/A/A	Effect sizes
Self-esteem			
Asian (<i>n</i> = 117)	3.17 (0.51)	3.07 (0.52)	$d = 0.20, R^2 = 0.009$
Non-Asian (<i>n</i> = 209)	3.41 (0.44)	3.32 (0.52)	$d = 0.19, R^2 = 0.009$
Caucasian ($n = 87$)	3.40 (0.39)	3.35 (0.48)	$d = 0.13, R^2 = 0.004$
Hispanic ($n = 49$)	3.40 (0.52)	3.19 (0.60)	$d = 0.38, R^2 = 0.033$
Male (<i>n</i> = 127)	3.41 (0.47)	3.26 (0.50)	$d = 0.29, R^2 = 0.020$
Female ($n = 199$)	3.36 (0.45)	3.16 (0.55)	$d = 0.38, R^2 = 0.035$
Mastery			
Asian (<i>n</i> = 117)	3.04 (0.46)	2.97 (0.43)	$d = 0.17, R^2 = 0.007$
Non-Asian (<i>n</i> = 209)	3.19 (0.44)	3.14 (0.48)	$d = 0.11, R^2 = 0.003$
Caucasian (<i>n</i> = 87)	3.18 (0.43)	3.11 (0.43)	$d = 0.16, R^2 = 0.007$
Hispanic (<i>n</i> = 49)	3.19 (0.51)	3.11 (0.62)	$d = 0.14, R^2 = 0.005$
Male (<i>n</i> = 127)	3.23 (0.44)	3.14 (0.42)	$d = 0.22, R^2 = 0.011$
Female (<i>n</i> = 199)	3.13 (0.44)	3.00 (0.49)	$d = 0.27, R^2 = 0.018$
Optimism			
Asian (<i>n</i> = 117)	3.74 (0.80)	3.36 (0.81)	$d = 0.48, R^2 = 0.053$
Non-Asian (<i>n</i> = 209)	3.74 (0.79)	3.68 (0.87)	$d = 0.08, R^2 = 0.002$
Caucasian (<i>n</i> = 87)	3.86 (0.75)	3.60 (0.83)	$d = 0.33, R^2 = 0.027$
Hispanic (<i>n</i> = 49)	3.95 (0.66)	3.64 (0.94)	$d = 0.39, R^2 = 0.035$
Male (n = 127)	3.78 (0.84)	3.60 (0.86)	$d = 0.22, R^2 = 0.012$
Female (<i>n</i> = 199)	3.72 (0.76)	3.48 (0.85)	$d = 0.28, R^2 = 0.020$
BDI–IA sum			
Asian (<i>n</i> = 117)	5.13 (4.19)	7.25 (6.09)	$d = 0.36, R^2 = 0.031$
Non-Asian (<i>n</i> = 209)	5.02 (4.52)	5.96 (5.95)	$d = 0.17, R^2 = 0.007$
Caucasian (n = 87)	4.69 (5.00)	4.53 (4.06)	$d = -0.04, R^2 = 0.000$
Hispanic (<i>n</i> = 49)	5.19 (4.57)	7.93 (6.19)	$d = 0.50, R^2 = 0.058$
Male (<i>n</i> = 127)	4.10 (3.74)	6.66 (5.74)	$d = 0.49, R^2 = 0.056$
Female (<i>n</i> = 199)	5.59 (4.77)	6.50 (6.25)	$d = 0.16, R^2 = 0.006$
Resources, factor			_
Asian (<i>n</i> = 117)	-0.03 (1.00)	-0.38 (1.00)	$d = 0.38, R^2 = 0.034$
Non-Asian (<i>n</i> = 209)	0.27 (0.83)	0.12 (0.94)	$d = 0.17, R^2 = 0.007$
Caucasian (<i>n</i> = 87)	0.30 (0.77)	0.16 (0.85)	$d = 0.23, R^2 = 0.013$
Hispanic (<i>n</i> = 49)	0.30 (0.97)	-0.07 (0.96)	$d = 0.42, R^2 = 0.042$
Male (<i>n</i> = 127)	0.30 (0.89)	0.01 (0.95)	$d = 0.31, R^2 = 0.023$
Female (<i>n</i> = 199)	0.19 (0.84)	-0.20 (1.02)	$d = 0.41, R^2 = 0.039$
BDI-IA factor			_
Asian (<i>n</i> = 117)	-0.11 (0.71)	0.15 (1.01)	$d = 0.33, R^2 = 0.027$
Non-Asian (<i>n</i> = 209)	-0.16 (0.72)	0.01 (0.96)	$d = 0.22, R^2 = 0.011$
Caucasian (n = 87)	-0.20 (0.85)	-0.20 (0.70)	$d = 0.03, R^2 = 0.000$
Hispanic (<i>n</i> = 49)	-0.09 (0.85)	0.39 (1.17)	$d = 0.46, R^2 = 0.049$
Male (<i>n</i> = 127)	-0.32 (0.60)	0.13 (0.96)	$d = 0.57, R^2 = 0.074$
Female (<i>n</i> = 199)	-0.05 (0.77)	0.04 (1.01)	$d = 0.12, R^2 = 0.004$

	Table S4.	Means of ma	or variables for	G/Gs and A	carriers b	y ethnicity	/ and sex
--	-----------	-------------	------------------	------------	------------	-------------	-----------

Cell values indicate group means. SDs are in parentheses.

Tal	ble !	55.	Means	for	stud	y var	iab	les	by	sex
-----	-------	-----	-------	-----	------	-------	-----	-----	----	-----

Male (<i>n</i> = 127)	Female (<i>n</i> = 199)	t test (df = 324)	Effect sizes
3.31 (0.49)	3.23 (0.53)	1.34 <i>P</i> = 0.180	$d = 0.15 R^2 = 0.006$
3.17 (0.43)	3.05 (0.48)	2.37 <i>P</i> = 0.018	$d = 0.27 R^2 = 0.018$
3.65 (0.85)	3.56 (0.83)	0.97 <i>P</i> = 0.334	$d = 0.11 R^2 = 0.003$
5.86 (5.31)	6.19 (5.79)	-0.52 P = 0.602	$d = 0.06 R^2 = 0.001$
0.13 (0.94)	-0.08 (1.03)	1.84 <i>P</i> = 0.066	$d = 0.21 R^2 = 0.011$
-0.02 (0.93)	0.02 (1.05)	-0.34 P = 0.734	$d = 0.04 R^2 = 0.000$
	Male (n = 127) 3.31 (0.49) 3.17 (0.43) 3.65 (0.85) 5.86 (5.31) 0.13 (0.94) -0.02 (0.93)	Male (n = 127) Female (n = 199) 3.31 (0.49) 3.23 (0.53) 3.17 (0.43) 3.05 (0.48) 3.65 (0.85) 3.56 (0.83) 5.86 (5.31) 6.19 (5.79) 0.13 (0.94) -0.08 (1.03) -0.02 (0.93) 0.02 (1.05)	Male $(n = 127)$ Female $(n = 199)$ t test $(df = 324)$ 3.31 (0.49) 3.23 (0.53) 1.34 $P = 0.180$ 3.17 (0.43) 3.05 (0.48) 2.37 $P = 0.018$ 3.65 (0.85) 3.56 (0.83) 0.97 $P = 0.334$ 5.86 (5.31) 6.19 (5.79) $-0.52 P = 0.602$ 0.13 (0.94) $-0.08 (1.03)$ 1.84 $P = 0.066$ $-0.02 (0.93)$ 0.02 (1.05) $-0.34 P = 0.734$

Cell values indicate group means. SDs are in parentheses.

PNAS PNAS