Helping hands, healthy body? Oxytocin receptor gene and prosocial behavior interact to buffer the association between stress and physical health

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Abstract

Providing help or support to others buffers the associations between stress and physical health. We examined the function of the neurohormone oxytocin as a biological mechanism for this stress-buffering phenomenon. Participants in a longitudinal study completed a measure of charitable behavior, and over the next two years provided assessments of stressful life events and physician-diagnosed physical ailments. Results indicated that charitable behavior buffered the associations between stressful events and new-onset ailments among individuals with the AA/AG genotypes of oxytocin receptor gene (OXTR) variant rs53576, but not among those with the GG genotype. These results suggest that oxytocin function may significantly affect health and may help explain the associations between prosocial behavior and health. More broadly, these findings are consistent with a role for the caregiving behavioral system in health and well-being.

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Introduction

Providing help or support to others, while often depicted as burdensome, is robustly associated with better health and well-being. Indeed, volunteering or providing care for close others predicts reduced morbidity and mortality (e.g., Brown et al., 2003; Konrath et al., 2012; O'Reilly et al., 2008), and increased psychological well being (e.g., Brown et al., 2008; Poulin et al., 2010; see Post, 2007, for an overview).

The benefits of engaging in prosocial behavior may be due to stress-buffering features of helping. Helping or supporting others predicts reduced associations between stress and mortality (Krause, 2006; Okun et al., 2010; Poulin et al., in press) as well as depression (Brown et al., 2008). Laboratory research indicates that people respond to acute stress by increasing their prosocial behavior (von Dawans et al., in press), and that helping behavior reduces physiological response to stress (e.g., Floyd et al., 2007), raising the possibility that prosociality may serve as a coping strategy.

We test the prediction that the stress-buffering effects of prosocial behavior are a function of the caregiving behavioral system, and specifically of the neurohormone oxytocin. To do so, we examine the joint role of charitable behavior, stressful life events, and oxytocin receptor (OXTR) genotype in predicting new-onset physical ailments.

Prosocial behavior, caregiving, and oxytocin

Engaging in prosocial behavior may reduce stress in several ways, such as increasing positive affect or perceived control (Krause, 2006). Theoretical models of the caregiving behavioral system further suggest that prosocial behavior may also buffer stress more directly (Brown and Brown, 2006; Goetz et al., 2010). The caregiving system, which evolved to facilitate parental behavior, motivates efforts to reduce the suffering and/or increase the well-being of any individual thought to be in need (Bell and Richard, 2000; Collins et al., 2010; Shaver et al., 2010). Recent models of this system suggest it may do so by facilitating social approach behaviors, at least in part via anxiety reduction (Brown and Brown, 2006; Goetz et al., 2010).

Prior research indirectly links the caregiving system with health by showing that prosocial behavior only promotes health and well-being when accompanied by other-focused motivations (Gillath et al., 2005; Konrath et al., 2012) or when extended towards valued others (Poulin et al., 2010). However, a more direct way to study the role of caregiving in health is to examine a key biological mechanism that supports caregiving: the function of the neurohormone oxytocin. In both humans and
The present study

The present study tests whether oxytocin function, as indicated by OXTR rs53576 genotype, moderates the stress-buffering effects of prosocial behavior in predicting subsequent longitudinal assessments of health status. We predicted that, adjusting for baseline health status and other relevant covariates, greater charitable involvement would predict a lessened association between stress and new-onset ailments (i.e., a stress-buffering pattern). In addition, we predicted that this stress-buffering effect would be qualified by an interaction (either compensatory or synergistic) between OXTR genotype and charitable involvement.

Method

Participants and procedure

Data were collected through Internet-based surveys of a large, nationally representative sample (N=2729; Silver et al., 2006) recruited using stratified random-digit-dial telephone sampling by Knowledge Networks Inc. (KN). KN panel members are compensated with Internet access (if needed), points used to obtain merchandise, and cash incentives for completing surveys. Data used for this investigation were collected at several time points, described below.

Life event and health surveys

The participants completed a survey on mental/physical health and lifetime and ongoing stress by September, 2002 (Wave 1; N=1916). They were subsequently invited to participate in two similar follow-up surveys 12 months (Wave 2; N=1571, 82% of the Wave 1 sample) and 24 months after Wave 1 (Wave 3; N=1771, 92% of the Wave 1 sample).

Social and political survey

A subset of those who completed the Wave 1 survey had completed a KN-administered survey on social attitudes and involvement, including charitable behavior, between April, 2000 and March, 2003. This sample (n=924) was the base sample for all analyses involving charitable behavior.

DNA collection

In 2008, KN re-contacted available participants (N=1296) from the larger longitudinal study to request their participation in the genetic study. Most participants (54.7%; N=711) agreed, and provided saliva for genotyping using OraGene test kits (http://www.dnagenotek.com/) mailed to their homes. Kits were sent to The Centre for Applied Genomics (TCAG; http://www.tcag.ca/) for genotyping. There were 704 participants for whom OXTR rs53576 was successfully genotyped (99% call rate), and of these, 631 had completed the Wave 1 survey. This sample (n=631) was the base sample for all analyses involving OXTR genotype.

Final sample

Because not all participants provided data on either charitable behavior or genetics, analyses in the present study are not based on a single sample size, but on the largest, most representative sample providing data for all variables in each analysis. For analyses involving just charitable behavior and health, n=924; for analyses involving just OXTR genotype and health, n=631; and for analyses involving both charitable behavior and OXTR genotype, n=365. Across these separate analyses, data from a total of N=1195 people are examined.

Measures

OXTR

The OXTR variant of interest, rs53576, consists of a locus at which either the nucleobase adenine or guanine (denoted as “A” or “G”) can occur. The rs53576 SNP genotyping identified 361 “GG”, 284 “AG”, and 59 “AA” individuals. It was in Hardy–Weinberg equilibrium \( (X^2 = 1.1; p = .30) \) with no genotype-by-sex differences \( (X^2 = 1.32; p = .52) \) or genotype-by-ethnicity differences \( (X^2 = 7.22; p = .30) \). We followed the same grouping strategy used in prior studies addressing genotype-related psychological and social phenotypes—GG respondents were compared to individuals carrying a high risk A allele \( (GG=1, AA/AG=0) \) (e.g., Poulin et al., 2012; Rodrigues et al., 2009; Tost et al., 2010). This approach maintains consistency with prior studies and ensures sufficient statistical power to detect differences related to the high risk A allele.
Stressful life events

Assessment of lifetime exposure to stressful events was completed by Wave 1 using a count of 37 negative events (e.g., serious illness or injury, natural disaster) a respondent reported experiencing (see Silver et al., 2002). This measure was modified from the Diagnostic Interview Schedule section on trauma (Robins et al., 1981), expanded using open-ended coding of lifetime traumas reported by a primary care sample (Holman et al., 2000), and has provided rates of specific events in this sample comparable to surveys conducted on other community samples (e.g., Breslau et al., 1998). The total number of lifetime stressful events reported was used as a measure of lifetime adversity. At Waves 2 and 3, respondents were asked which of those same events had occurred in the past 12 months. The total count of events reported at each wave—excluding events directly related to health, our dependent variable—represented recent stressful events experienced between Waves 1 and 2 and between Waves 2 and 3, respectively.

Charitable behavior

The social and political survey also asked whether participants had engaged in the following activities in the past 12 months specifically as a way of being socially involved in their communities: donating blood, giving money to or working for a charity, attending PTA meetings, or attending a community group meeting. The total number of these activities was used as a measure of involvement in charitable behaviors. Asking participants about participation in specific, concrete activities provides the best possible estimate of long-term charitable involvement (as well as group membership; see below), and has been validated for psychological (e.g., Omoto et al., 2010), sociological (Wilson, 2000), and governmental (U.S. Bureau of Labor Statistics, 2010) research.

Group membership

The social and political survey also asked the participants whether they participated in any of the following groups, without tying such participation to community service: a club or fraternal organization, a veterans group, a religious group, a senior citizen’s center or group, a women’s group, an issue-oriented political organization, a non-partisan civic organization, a school club or association, a hobby club, a sports team, a youth club, a neighborhood association or community group, or a group representing racial/ethnic issues. The total number of these group memberships was computed as an index of group membership.

Physical ailments

At Waves 1–3, health data were collected using a questionnaire modified from the Centers for Disease Control’s National Center for Health Statistics annual National Health Interview Survey (NHIS; U.S. Department of Health and Human Services, 2000). Respondents were asked, “Has a medical doctor ever diagnosed you as suffering from any of the following ailments?” with prompts for 33 physical ailments. Evidence for the validity of this measure comes from a study of 25,000 KN panelists (Baker et al., 2003): when compared to the 2000 NHIS, prevalence rates for common health outcomes (e.g., heart problems, cancer, diabetes, hypertension, ulcer, migraine, and stroke) differed in the KN panel by an average of less than 1.5%. From this list of ailments, we created a count variable of the total number of physical ailments as the dependent variable in our analyses.

Mental ailments

The KN health questionnaire also included questions about doctor-diagnosed psychological ailments (anxiety disorder and depression). We created a count variable of the total number of psychological ailments as a covariate in our analyses.

Analytic strategy

Analyses were conducted using Stata 11.0 (Stata Corp. College Station, TX). Multilevel Poisson regression models were built using Stata’s xtpois module1 to examine whether OXTR genotype, recent stressors, and charitable behaviors would predict incidence of physical ailments. These analyses were conducted to predict increased ailment incidence at Waves 2 and 3 by controlling for ailments at Wave 1. Because the dependent variable was assessed at more than one point in time, analyses took the form of multilevel regression models (mixed effects or hierarchical linear models; Singer and Willett, 2003), which examine outcomes across multiple waves without increasing Type I error. Since physical ailments was a count variable, these analyses were conducted as Poisson regressions. Poisson regression models yield regression coefficients that can be exponentiated as $e^b$ and interpreted as incidence rate ratios (IRRs). IRRs reflect the ratio by which the predicted count of the outcome (e.g., number of physical ailments) would change given a one-unit increase in the predictor. IRRs of <1 indicate a relative decrease in the outcome’s incidence while IRRs of >1 indicate a relative increase in the outcome’s incidence, and IRRs = 1 indicate no association between the predictor and the outcome.

The construction of all models presented involved screening two sets of control variables before entering the variables for recent stress, OXTR genotype, and charitable behavior: (a) demographics (age, sex, ethnicity, education, and income level) and (b) mental health history (number of lifetime stressful events, number of physician-diagnosed mental health ailments at each wave).

Results

Descriptive statistics

Across the different analyses reported, a total of 1195 people contributed data. Ages ranged from 18 to 89 (M = 52.97), females comprised 46%, 79% were European-American, 8% were African American, 8% were Latino/a, and 6% were of another ethnicity. At Wave 1, participants reported an average of 3.60 physician-diagnosed ailments (SD = 3.24) and those who provided data on charitable activities reported engaging in an average of 1.31 out of 5 possible charitable behaviors (SD = 1.08).

Attrition analysis

Results of a multiple logistic regression predicting participation revealed that individuals who were genotyped for the present study (n = 631) did not differ from those not genotyped in the Wave 1 sample in terms of age, sex, ethnicity, income, education, number of psychological or physical ailments, or past-year stressful events. Those genotyped, however, reported slightly more lifetime adverse events (M = 9.27) than those not genotyped (M = 8.34; OR = 1.02, p = .04). A separate multiple logistic regression examined differences between those who provided data on charitable behavior (N = 924) versus other Wave 1 participants. Respondents with data on charity were older (M = 54.95) than other Wave 1 participants (M = 44.31, OR = 1.05, p < .001), less likely to be female (40% of the sample with charity data versus 62% of the sample without charity data, OR = 0.32, p < .001) and more likely to be of European-American ethnicity (81% of the sample with charity data versus 69% of the sample without charity data, OR = 0.63, p < .001).

Following Wave 1, some individuals did not participate in all subsequent waves, but this type of missing data is acceptable in multilevel modeling, because individuals contribute to estimation of the model at particular time points even if they cannot do so at all time points.

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1 To address possible overdispersion, negative binomial models were also examined; results were substantively identical.
analyses (see Table 1) and oxytocin is associated with many factors (Rodrigues et al., 2009), female sex was a significant covariate in our analyses (Poulin et al., 2012; Kim et al., 2010). A follow-up analysis tested a three-way interaction among genotype, stress, and ethnicity (European-American versus other). This interaction was not significant (p < .001; Table 1, Model 2). Results of this model indicated that group membership did not significantly buffer the association between stress and health (IRR = 1.00, p = .64), but the charity × recent stress interaction remained significant (IRR = 0.96, p = .01). We again examined whether our results differed by sex; a second follow-up analysis examined whether the stress-buffering role of charitable behavior differed between males and females. A three-way interaction among charitable behavior, stress, and sex (female versus male) revealed no significant differences in stress buffering between females (n = 321) and males (n = 310; p = .15). A final follow-up analysis tested whether the OXTR GG × stress interaction was present in the sample of individuals who had complete data on all variables in our study (n = 365). Results indicated that this interaction was not significant in the smaller sample (IRR = 0.98, p = .58).

Charitable behavior, OXTR, stress, and health

Our prediction that charitable behavior would interact with OXTR genotype to buffer the association between recent stressful events and ailment incidence suggested a three-way interaction among charitable behavior, OXTR genotype, and recent stressors. However, before testing this hypothesis, we examined the independent stress-buffering roles of OXTR genotype and charitable behavior identified in prior research.

OXTR and stress buffering

A multilevel Poisson regression tested the interaction between OXTR genotype and recent stressors, along with relevant controls, among all participants with data for those variables (n = 631; Table 1, Model 1). Results indicated a significant OXTR GG × recent stress interaction (IRR = 0.90, p = .001). Examining the simple effects of recent stress for GG versus other genotype by recoding the genotype variable revealed that recent stress predicted increased ailment incidence among AA/AG individuals (IRR = 1.09, p < .001), but not among GG individuals (IRR = 0.99, p = .51; Fig. 1, Panel A).

As prior research has identified inter-ethnic differences in OXTR rs53576, with greater proportions of GG individuals among Caucasians (Kim et al., 2010), a follow-up analysis tested a three-way interaction among genotype, stress, and ethnicity (European-American versus other). This interaction was not significant (p = .20), indicating no ethnic differences in the stress-buffering role of OXTR rs53576; moreover, the magnitude of the OXTR GG × stress interaction was very similar between Caucasians (IRR = 0.91) and those of other ethnic groups (IRR = 0.87). While prior research on OXTR rs53576 has found no sex differences (e.g., Poulin et al., 2012; Rodrigues et al., 2009), female sex was a significant covariate in our analyses (see Table 1) and oxytocin is associated with many female-specific functions such as childbirth and lactation (Carter, 1998). Therefore, a second follow-up analysis examined whether the stress-buffering role of OXTR rs53576 differed between males and females. Testing a three-way interaction among genotype, stress, and sex (female versus male) revealed no significant differences in stress buffering between females (n = 321) and males (n = 310; p = .15). A final follow-up analysis tested whether the OXTR GG × stress interaction was present in the sample of individuals who had complete data on all variables in our study (n = 365). Results indicated that this interaction was not significant in the smaller sample (IRR = 0.98, p = .58).

Charity and stress buffering

A second multilevel Poisson regression tested the interaction between charitable behavior and recent stressors, along with relevant controls, among all participants with data for those variables (n = 924; Table 1, Model 2). Results indicated a significant charity × recent stress interaction (IRR = 0.96, p < .001). To examine the simple effects of recent stressors predicting ailment incidence, charitable behavior was centered at low and high values (1 SD below and above the mean, respectively). Recent stress predicted increased ailment incidence more strongly at low levels of charitable behavior (IRR = 1.15, p < .001), than at high levels of charitable behavior (IRR = 1.04, p = .02; Fig. 1, Panel B).

To assess whether the stress-buffering role of charitable behavior was specific to prosocial activities as opposed to general social connection, a follow-up analysis included group membership and a group membership × recent stress interaction term alongside the charitable behavior variables reported in Table 1, Model 2. Results of this model indicated that group membership did not significantly buffer the association between stress and health (IRR = 1.00, p = .64), but the charity × recent stress interaction remained significant (IRR = 0.96, p = .01). We again examined whether our results differed by sex; a second follow-up analysis examined whether the stress-buffering role of charitable behavior differed between males and females. Testing a three-way interaction among charitable behavior, stress, and sex (female versus male) revealed no significant differences in stress buffering between females (n = 364) and males (n = 560; p = .41). A final follow-up analysis tested whether the charity × stress interaction was present in the sample of individuals who had complete data on all variables in our study examined (n = 365). Results indicated that this interaction was not significant in the smaller sample (IRR = 0.98, p = .15).

Charity, OXTR, and stress buffering

Poisson regression tested the three-way interaction among charitable behavior, OXTR genotype, and recent stressors, along with relevant controls (Table 1, Model 3). There was a significant charity × OXTR GG × stress interaction (IRR = 1.11, p = .002). Examining the simple two-way (charity × stress) interactions for different genotypes by recoding the genotype variable (as GG = 0 or AA/AG = 0) revealed that charitable behavior significantly interacted with recent stress to predict ailment incidence among AA/AG individuals (IRR = 0.94, p < .001), but not among GG individuals (IRR = 1.05, p = .12).

Simple effects of recent stressors predicting ailment incidence were examined for both genotypes, with charitable behavior centered at low and high values (1 SD below and above the mean, respectively). Results indicated that recent stress did not predict ailment incidence for GG individuals, regardless of whether they had engaged in low (IRR = 0.96, p = .42) or high amounts of charitable behavior (IRR = 1.06, p = .14). However, for AA/AG individuals, recent stress specifically predicted increased ailment incidence among individuals who engaged in few charitable behaviors (IRR = 1.16, p = .001), but not among those who engaged in many charitable behaviors (IRR = 1.01, p = .80). In sum, charitable behavior buffered the association between recent stressors and health for AA/AG individuals, but not for GG individuals, among whom there was no stress/health association (Fig. 2).

To estimate the magnitude of the contribution of OXTR rs53576, we computed the effect size of the charity × stress interaction as predicted for AA/AG individuals and for GG individuals. To do so, we computed the change in Wald $\chi^2$ (the omnibus test of the fit of a
Poisson model) when the charity×stress interaction was deleted from the model, and converted this statistic to the corresponding effect size estimate, phi ($\phi$) by dividing the $\chi^2$ by n and taking the square root of the result. This procedure revealed that the effect size of the charity×stress interaction was $\phi = .34$, a “medium” effect size, for AA/AG individuals, but for GG individuals, the same interaction had an effect size of $\phi = .09$, a “small” effect size—and one that Fig. 2 indicates is in the opposite direction.

A follow-up analysis examined whether the OXTR GG×charity×stress interaction varied by ethnicity (European-American versus other). We did not expect to be able to test a four-way interaction (ethnicity×OXTR GG×charity×stress), however, we explored the possibility of ethnic differences by testing the three-way interaction separately in Caucasians and those of other ethnicities. As in our analysis of ethnicity and the OXTR GG×stress interaction, the magnitude of the OXTR GG×charity×stress interaction was very similar between Caucasians (IRR=1.14) and those of other ethnic groups (IRR=1.12) with no significant differences between the two groups.

A second follow-up analysis examined whether the OXTR GG×charity×stress interaction differed between males and females. As with ethnicity, we did not expect to be able to test a four-way interaction (sex×OXTR GG×charity×stress), however, we explored the possibility of sex differences by testing the three-way interaction separately for females and males. The magnitude of the OXTR GG×charity×stress interaction was very similar between females (IRR = 1.15; n = 224) and males (IRR = 1.12; n = 141).

**Tests of replicability**

While our analyses were conducted in a single sample, we conducted further analyses to provide evidence of the replicability of these findings by testing our models separately in randomly selected halves of our sample. Using random digits from the website random.org (http://www.random.org) we randomly designated each participant a member of subsample 1 or subsample 2. All results reported above were replicated and achieved significance independently in both subsamples. The OXTR GG stress-buffering effect (OXTR GG×stress interaction) was present in subsample 1 (n = 320, IRR = 0.91, p = .01) and subsample 2 (n = 311, IRR = 0.89, p = .02). Similarly, the charity stress-buffering effect (charity×stress interaction) was present in subsample 1 (n = 445, IRR = 0.96, p = .04) and subsample 2 (n = 479, IRR = 0.95, p = .002). Finally, the three-way interaction among genotype, charity, and stress was significant in both subsample 1 (n = 185, IRR = 1.13, p = .01) and subsample 2 (n = 180, IRR = 1.11, p = .04).

![Fig. 1. Number of new ailments per wave, graphed by number of recent stressors (0–2). Note. Panel A represents stress–ailment associations graphed by OXTR rs53576 genotype (GG versus AA/AG). Panel B represents stress-ailment associations graphed by high and low levels of charitable behavior (1 SD above and below the mean, respectively).](image1)

![Fig. 2. Number of new ailments per wave, graphed by number of recent stressors (0–2), amount of charitable behavior, and OXTR rs53576 genotype (GG versus AA/AG). Note. High and low values of charitable behavior represent amounts 1 SD above and below the mean, respectively. Separate panels represent the charity×recent stress interaction for the AA/AG genotype (Panel A) and for the GG genotype (Panel B).](image2)
Discussion

While prior research has demonstrated positive associations between prosocial behavior and health, including the stress-buffering role of prosocial behavior, the mechanisms for these associations have not been clear. Drawing on research and theory on the caregiving behavioral system, we predicted that the stress-buffering effects of prosocial behavior would be explained by the function of the neurohormone oxytocin—specifically that oxytocin receptor (OXTR) genotype would interact with prosocial behavior to buffer the association between stress and health. Our findings support this hypothesis: engaging in charitable behaviors and OXTR rs53576 GG genotype both buffered the association between stress and health. However, examining them in combination revealed that charity only buffered the association between stress and health for respondents with the OXTR rs53576 AA/AG genotypes, which are thought to render individuals less sensitive to oxytocin than the GG genotype—a compensatory effect. These findings provide the first evidence of a link between oxytocin receptor genotype (rs53576) and human health outcomes, and are consistent with the possibility that oxytocin accounts for the stress-buffering role of prosocial behavior in predicting health.

Helping, oxytocin, and health

Our findings add to a growing literature that indicates that prosocial behavior bolsters physical health, and that it specifically does so by buffering the association between stress and health (Brown et al., 2008; Krause, 2006; Okun et al., 2010; Poulin et al., 2012). However, our findings also extend prior research by suggesting a plausible mechanism for the effects of prosocial behavior: the function of the neurohormone oxytocin. Notably, our findings suggest that individual differences in the OXTR gene can predict stress-related physical health problems. For individuals with AA/AG genotypes, stressful life events significantly predicted new-onset ailments. For individuals with the GG genotype, there was no such association. This finding alone, while a result of one study only, is worth future investigation.

An even more relevant finding for the oxytocin-as-mechanism hypothesis is that charitable behavior buffered the association between stress and health among those with AA/AG genotypes. This effect is consistent with the possibility that engaging in charitable behavior provides a sufficient boost in oxytocin to compensate for the relative lack of oxytocin sensitivity thought to characterize these genotypes. This compensatory effect is made plausible by the fact that prosociality has been linked to our need for support, or for the mere presence of others, and that the human need for social contact has implications for physical health. While this need is often interpreted as a need for support, or for the mere presence of others, our findings, along with those from previous studies (e.g., Bell and Hansford, 2000; Brown and Brown, 2006; Sober and Wilson, 1998).

One implication of a need to invest in others is that seeking opportunities to help or provide support to others might be as natural and important during times of adversity as seeking support from others. Recent research supports this view: under acute stress, individuals can become more, not less, prosocial (von Dawans et al., in press). Paradoxically, however, seeking to support others for the express purpose of benefiting the self may be self-defeating, given that prior research has found that such motivations actually undermine the benefits of prosocial behavior (Gillath et al., 2005; Konrath et al., 2012). These prior findings indicate that it may be impractical to advise individuals to cope with stress by engaging in prosocial behavior. Such advice might deserve further qualification as our findings suggest that the benefits of engaging in prosocial behavior may be limited to OXTR rs53576 AA/AG individuals.

Contributions, limitations, and future directions

The present study is the first study using prospective data from a diverse real-world sample to (a) demonstrate an association between the oxytocin system and human health, and (b) provide evidence suggesting that oxytocin is the mechanism linking prosocial behavior with health. We also extend prior research (e.g., Poulin et al., 2012) indicating that the effects of OXTR genotype depend on social context. Despite these strengths, we acknowledge the limitations of our study. First, this study featured a relatively small sample of individuals with all of the necessary data to test interactions among charitable behavior, OXTR genotype, and stress. Even though we found a significant three-way (OXTR GG × charity × stress) interaction among these variables in this small sample, we did not detect significant OXTR GG × stress and charity × stress two-way interactions in individuals with all data, but only in larger groups of individuals who had just the relevant data for those analyses. However, the presence of the three-way (OXTR GG × charity × stress) interaction result may help explain this phenomenon. Because both of these two-way interactions are qualified by a third variable—i.e., there is a three-way OXTR GG × charity × stress interaction—any simple two-way effect combines individuals for whom the two-way effect is present with individuals for whom the effect is absent. This lowers the effect size of the two-way interaction, making it probabilistically more difficult to detect in a smaller versus a larger sample.

Another implication of our relatively small sample is that our findings about the OXTR rs53576 genotype should be considered preliminary, and in need of exact replication (Sullivan, 2007). However, the fact that our results replicated exactly in randomly-selected subsamples of our data boosts our confidence in the replicability of these findings.

Next, given that this was a non-experimental study, it is important to emphasize that the causal effects of OXTR and charity on health remain unproven. The longitudinal design of our study, including controls for baseline health that allow for prediction of new-onset ailments, provide some evidence that the associations we found were not solely due to health status predicting levels of charitable involvement. However, we acknowledge the need for converging evidence from experimental and field studies.

In addition, while we assessed several common types of prosocial involvement, our charitable behaviors assessment was not comprehensive. Other approaches may identify different patterns of associations among charitable behaviors, OXTR genotype, and stress. For example, it is possible that charitable behaviors were not stress-buffering for GG individuals because they engaged in more day-to-day supportive activities that buffered their stress (cf. Kogan et al., 2011). Moreover, while we examined OXTR genotypes as a way of making inferences about the effects of oxytocin, it is possible that, over the course of a life span, individual differences in OXTR genotype may also shape
aspects of people's personalities and social environments, potentially confounding the association between OXTR and health. Ideally, future work could examine proximal as well as distal indicators of oxytocin function and health, not all of which share this limitation, such as peripheral oxytocin assessment (e.g., Gouin et al., 2010). Finally, it was beyond the scope of the present research to examine the physiological mechanisms (e.g., modulated HPA axis and cardiovascular stress reactivity) by which charitable behavior and oxytocin might buffer the impact of stressful events (Chen et al., 2011; Norman et al., 2012; Rodrigues et al., 2009). Future research should examine whether the OXTR rs53576 SNP and prosocial behavior interact in a compensatory manner to buffer physiologic markers of stress, and if so, whether these effects can predict health outcomes.

Conclusion

The results of this study provide novel insights into the links between social behavior and health, identifying significant roles of charitable behavior, oxytocin, and stress. Importantly, these findings shed light on how the evolutionarily-preserved caregiving system, by way of the neurohormone oxytocin, may contribute to the biological underpinnings of stress-related illness. We hope that these findings encourage future research not only on the mechanisms linking stress and health, but on novel therapeutic approaches to help individuals adjust to adversity.

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