11-12-2012

Salivary cortisol and interpersonal functioning: An event-contingent recording study in the offspring of parents with bipolar disorder

Mark A. Ellenbogen
Concordia University

Anne-Marie Linnen
Concordia University

Jonathan Bruce Santo
University of Nebraska at Omaha, jsanto@unomaha.edu

Marije aan het Rot
University of Groningen

Sheilagh Hodgins
Université de Montréal

Follow this and additional works at: https://digitalcommons.unomaha.edu/psychfacpub

Part of the Psychology Commons

Please take our feedback survey at: https://unomaha.az1.qualtrics.com/jfe/form/
SV_8cchtFmpDyGfBLE

Recommended Citation

Ellenbogen M.A., Linnen A.M., Santo J.B., aan het Rot, M., Hodgins S. & Young, S. (2013). Salivary cortisol and interpersonal functioning: An event-contingent recording study in the offspring of parents with bipolar disorder. Psychoneuroendocrinology, 38(7), 997-1006. https://doi.org/10.1016/j.psyneuen.2012.10.005

Authors

Mark A. Ellenbogen, Anne-Marie Linnen, Jonathan Bruce Santo, Marije aan het Rot, Sheilagh Hodgins, and Simon N. Young

Salivary cortisol and interpersonal functioning: An event-contingent recording study in the offspring of parents with bipolar disorder

Mark A. Ellenbogen[a, 1], Anne-Marie Linnen[a, 1], Jonathan B. Santo[b], Marije aan het Rot[c], Sheilagh Hodgins[d], Simon N. Young[e]

_____

[a] Centre for Research in Human Development, Department of Psychology, Concordia University, Montréal, Québec, Canada

[b] Department of Psychology, University of Nebraska at Omaha, Omaha, NE, USA

[c] Heymans Institute for Psychological Research, University of Groningen, Groningen, The Netherlands

[d] Department of Psychiatry, Université de Montréal, Québec, Canada

[e] Department of Psychiatry, McGill University, Montréal, Québec, Canada

Corresponding author at: Centre for Research in Human Development, Concordia University, 7141 Sherbrooke Street West, Montréal, Québec H4B 1R6, Canada. Tel.: +1 514 848 2424x7543; fax: +1 514 848 2815.

1 These authors contributed equally to the manuscript.

Summary

Despite a large body of research in non-human primates, the relationship between naturalistic patterns of social behaviour and basal cortisol levels has been understudied in humans. The present study examined the relationship between patterns of interpersonal functioning and cortisol levels in 23 offspring of parents with bipolar disorder (BD), at high risk for the development of an affective disorder, and 22 offspring of parents with no affective disorder (controls) in late adolescence and young adulthood. Using event-contingent recording, participants rated their dominance, submissiveness, quarrelsomeness, and agreeableness in naturally occurring social interactions over 14 consecutive days and provided salivary cortisol twice daily in the afternoon over the same period. In the full sample, multilevel modeling analyses revealed that dominance was a significant positive predictor of afternoon basal cortisol levels, $t_{(35)} = 2.58$, $p < 0.05$. Moreover, risk group (having a parent with BD or parents with no affective disorder) significantly interacted with mean levels of quarrelsomeness to predict afternoon cortisol levels, $t_{(29)} = 2.06$, $p < 0.05$. Offspring of parents with BD who reported more frequent quarrelsome behaviours exhibited lower levels of afternoon cortisol relative to high-risk offspring reporting few quarrelsome behaviours and control offspring. The results are consistent with evidence that dominance is associated with high cortisol levels in an unstable environment, and suggest that quarrelsomeness among high risk youth contributes to altered hypothalamic—pituitary—adrenal activity.

Keywords: Interpersonal functioning, cortisol, bipolar disorder, social behaviours

1. Introduction

Poor interpersonal functioning has been identified as an important factor in the pathogenesis of various disease states and mental illness (Holt-Lunstad et al., 2010; Patterson and Veenstra, 2010), particularly for the affective disorders (Hirschfeld et al., 2000; Hammen and Cohen, 2004; Eberhart and Hammen, 2006). Researchers have attempted to identify mechanisms that underlie the association between social factors and health outcomes (Norman et al., 2012). Accordingly, particular attention has been paid to the relationship between interpersonal behaviour and the functioning of the hypothalamic—pituitary—adrenal (HPA) axis. Among nonhuman primates, social submissiveness has been associated with higher basal cortisol levels (Abbott et al., 2003) and increased cortisol reactivity to a pharmacological challenge (Czoty et al., 2009).

The relationship between submissive behaviour and elevated cortisol levels has been partially corroborated among humans. A significant positive relationship between social submissiveness and basal cortisol levels has been identified among Dominican men living in a pre-industrial society (Decker, 2000) and among individuals who are bullied in the work place (Kudielka, 2004). Similar findings have been reported in children (Gunnar et al., 2003). At the beginning of the school year, children with dominant traits secrete higher basal cortisol levels as they clash with one another to establish social standing. However, later in the school year, shy children with submissive traits are victimized by peers and exhibit higher basal cortisol levels (Gunnar, 1994). Accordingly, elevated cortisol levels have been reported in

both behaviourally inhibited and shy children (Kagan et al., 1988; Schmidt et al., 1997), both of whom are at risk for the development of social phobia (Hirshfeld-Becker et al., 2007).

Links between cortisol levels and interpersonal behaviours have also been found in studies of externalizing problems in children and adolescents (Virkkunen, 1985; Holi et al., 2006; Alink et al., 2008). A negative association between basal cortisol levels and disruptive behaviours has been observed among some clinical samples (i.e. disruptive behaviour disorder or conduct disorder; Pajer et al., 2001, 2006; Popma t al., 2007), but not others (Azar et al., 2004). Studies of aggression and delinquency conducted among non-clinical samples have also varied considerably (Alink et al., 2008), with reports of an inverse association between basal cortisol levels and aggressive behaviours in some studies (Shoal et al., 2003; Loney et al., 2006; Haltigan et al., 2011), but not in others (Gerra et al., 1997; Klimes-Dougan et al., 2001). Overall, the conflicting results render it challenging to draw any strong conclusions regarding the relationship between HPA activity and disruptive behaviours in adolescence and young adulthood.

Some of the inconsistencies in the literature may be related to methodological issues. Studies of cortisol and interpersonal behaviour have varied greatly in research design (i.e. number of samples and time of day). Because the HPA axis is highly sensitive to environmental (i.e. physical activity; van der Pompe et al., 1999) and psychological factors (i.e. anticipatory appraisal; Gaab et al., 2005), the collection of small numbers of samples is susceptible to the influence of confounds and therefore may not reflect true basal cortisol levels. Cortisol levels have been seldom measured repeatedly over the course of multiple days to control for day to day variations in HPA activity. Differences in how interpersonal behaviours are assessed may also alter the relationship between basal cortisol levels and disruptive behaviours. Research in this area has focused exclusively on questionnaires and laboratory observations, which can lead to differences in reported levels of disruptive behaviours (McEvoy et al., 2003). Thus, methodological variations in this literature may be central to the reported discrepancies described previously.

The present study, as its primary aim, intended to improve on the methodology of past studies of cortisol and social behaviours by examining interpersonal behaviours using an event-contingent recording method developed by Moskowitz (1994). Event-contingent recording is a reliable and validated method in which participants record their behaviours and affect as they occur in the natural environment (Reis and Gable, 2000). Interpersonal behaviours are measured along two independent axes of behaviour. The ''status'' axis encompasses submissive and dominant behaviours whereas the ''affiliation'' axis includes quarrelsome and agreeable behaviours. The two axes are not significantly correlated with one another, and each end point of the axis represents an independent measure of social behaviour (Moskowitz, 1994). A major advantage of this technique is that it is not subject to the retrospective biases associated with selfreport questionnaires (Reis and Gable, 2000).

The relationship between event-contingent-recordings of social behaviour and afternoon cortisol levels in the natural environment, assessed during two weeks of daily sampling, was examined among adolescents and young adults having either a parent with bipolar disorder (BD) or parents with no affective disorder selected from a larger longitudinal study (Ellenbogen and Hodgins, 2004). The offspring of parents with BD are at high risk for the development of major affective disorders and other mental disorders (Lapalme et al., 1997; Birmaher et al., 2009), and therefore represent a unique opportunity to study the antecedents of affective disorders. In the present sample, we found no robust differences in interpersonal functioning

in the natural environment between the offspring of parents with BD and the offspring of parents with no affective disorder, despite higher self-report ratings of externalizing behaviours among high risk offspring relative to controls (Linnen et al., 2009). The offspring of parents with BD, however, had higher cortisol levels in the afternoon over a 14-day period than the control offspring (Ellenbogen et al., 2010b), similar to a previous finding (Ellenbogen et al., 2006a). In the present study, we explore the possibility that high cortisol levels in the offspring of parents with BD may be related to interpersonal difficulties in the natural environment. We have recently shown, in a different data collection, that the offspring of parents with BD were more biologically sensitive to interpersonal stressors in the natural environment than the offspring of parents with no affective disorder (Ostiguy et al., 2011). The offspring of parents with BD secreted higher levels of cortisol in the afternoon when exposed to severe interpersonal stressful life events, relative to high risk offspring exposed to less severe stress and the control offspring. Thus, as a secondary goal, the present study tested whether high risk offspring are more biologically reactive to interpersonal difficulties in the natural environment than control offspring.

Three hypotheses were put forth. First, in light of evidence that social submissiveness has been associated with heightened HPA activity, we expected to find a significant positive relationship between mean levels of submissive behaviour and basal cortisol levels in the afternoon. Second, we predicted a significant negative relationship between mean levels of quarrelsome behaviour and afternoon cortisol levels. Although the research in this area is inconsistent (Alink et al., 2008), we expected to detect this negative relationship by using an extended sampling protocol and sensitive behavioural measures. Third, as suggested by our previous work on sensitivity to naturalistic stress (Ostiguy et al., 2011), we hypothesized that high risk offspring who display frequent submissive behaviour in the natural environment would secrete higher cortisol levels than high risk offspring with low submissive behaviour and control offspring. Given the small sample size, the examination of statistical interactions was considered exploratory. Other interactions examined in this study included those between sex and social interactions, and risk group and quarrelsome behaviour.

2. Methodology

2.1. Participants

Twenty-six offspring of parents with BD ("high-risk") and 24 offspring of parents with no affective disorder ("control") were recruited into the study. Sixty-four potential participants were initially contacted to participate in the study. They were selected at random from a subject pool of 189 15—25 year olds participating in a longitudinal study of offspring with a parent having BD or no affective disorder (Ellenbogen and Hodgins, 2004). Out of 64 candidates contacted, 3 high-risk offspring and 11 control offspring refused to participate. Of those who agreed to participate, 2 participants failed to perform event-contingent recording and 3 were non-compliant with the cortisol sampling instructions. Therefore, the final sample consisted of 23 high-risk offspring (22 having a parent with BD-1 and one having a parent with BD-2) and 22 control offspring. All participants were administered the Structured Clinical Interview for DSM-IV (SCID-I), Patient edition (First et al., 1997). Demographic and clinical information is presented by group in Table 1.

Parents with BD and their spouses were originally recruited from general hospitals and consumer groups in the Canadian province of Quebec. Parents with no affective disorder were selected from the same geographical regions as parents with BD. All parents were administered the Structured Clinical Interview

for the DSM-III-R by experienced doctoral-level clinical psychologists, and the psychiatric records of the parents with BD were examined to confirm the presence of the disorder.

2.2. Event contingent recording of social interactions

Event-contingent recording requires participants to provide information about designated specific events immediately after they occur. Using standardized forms, participants recorded their behaviours during social interactions occurring throughout the day (see procedure). They also recorded the time and location of the interaction, the gender and role of the (primary) person they interacted with, and the presence or absence of additional others. Moreover, if alcohol had been consumed within 3 h of the interaction, participants were asked to write down the number of alcoholic beverages ingested.

Social behaviours were measured by asking participants to identify, from a list of items on each form, specific behaviours that they performed during each reported interaction. Participants were told to endorse as many or as few items that applied. Four different forms, containing different items, were administered on alternating days to minimize response biases. The original item pool described by Moskowitz (1994) contained 46 items classified as dominant behaviours (e.g. "I told the other(s) what to do" and "I voiced an opinion"), submissive behaviours (e.g. ''I let others make decisions'' and "I did not express my feelings"), quarrelsome items (e.g. "I ignored other(s) comments" and "I confronted the other(s)"), and agreeable items (e.g. "I listened attentively" or "I expressed affection"). Mean rates of social behaviours in this sample are reported elsewhere (see Linnen et al., 2009).

2.3. Cortisol sampling

Cortisol was measured via saliva samples obtained at 1300 h and 1500 h across the 14 days. Saliva was absorbed into a small cotton roll and expressed through a plastic tube into a sterile vial (''salivette'' device). Saliva samples were frozen at -20°C until assayed for cortisol by a sensitive radioimmunoassay (Lupien et al., 1996) using a commercial kit from Diagnostic Systems Laboratory (DSL-2000; Sanofi Diagnostics, Montreal, CAN). The sensitivity of the assay was set at 0.01 μg/dl (or 0.276 nmol/l). The inter- and intra-assay coefficient of variation for the assays were 3.6% and 4.6% (on a range of 0.01—10 μg/dl dose) respectively. Assays were conducted in the laboratory of Dr. C.-D. Walker at the Douglas Hospital Research Centre (Montreal, Canada). Mean salivary cortisol levels in this sample are reported elsewhere (Ellenbogen et al., 2010b).

2.4. Procedure

Participants were contacted by telephone and those interested in participating in the study were scheduled for a laboratory visit. At the laboratory, participants provided informed consent. If the participant was under the age of 18, informed consent was obtained both from the participant and from a parent. Participants then underwent a diagnostic interview by an experienced clinician.

Participants were provided with three individually coloured booklets containing the event-contingent recording forms (each booklet included forms for four days), times for saliva sampling on each day, as well as detailed written instructions of the procedures they were to follow. Participants were asked to complete up to a maximum of 10 event-contingent recording forms per day over a consecutive period of 14 days, and to report on social interactions occurring over the entire course of the day. Participants were instructed to provide saliva samples at designated times and were asked to record the time at which they

provided each saliva sample, as well as their activities prior to sampling. Participants were instructed to remove lipstick, to refrain from drinking water 5 min before sampling, and to refrain from eating, drinking (except water), smoking and brushing teeth at least 60 min before sampling.

Participants were provided with a pre-paid envelope and asked to mail back their first booklet after completion, as well as saliva samples collected over the first four days. Booklets were reviewed to ascertain that participants were carrying out the instructions properly. At the end of the two weeks, a laboratory member picked up the remaining two booklets and saliva samples, and participants were remunerated one hundred dollars (CAD) for their participation. The study was approved by the Human Research Ethics Committee of Concordia University (Montre´al, Canada).

2.5. Data analysis

Interpersonal behaviours were sampled along four scales, quarrelsomeness, agreeableness, dominance, and submissiveness. For every specified interaction, ipsitized scores on each scale were computed by dividing the number of items endorsed for each scale by the total number of items that could have been endorsed for that scale. This quotient is subtracted from the total number of items endorsed divided by the total number of items that could have been endorsed (n = 12). The ipsitizing procedure was deemed necessary because individuals vary in their rate of responding with some participants generally checking off more items than others (Moskowitz, 1994). An ipsitized score reflects the frequency with which items corresponding to each behavioural scale are endorsed, while adjusting for participants' general rate of endorsing. Social interactions revealing that alcohol had been consumed within 1 h of the interaction were excluded from all analyses.

The analyses were conducted with the multilevel modeling program HLM 6 (Raudenbush et al., 2004). In these analyses individual data points for each participant were "nested" within each individual. While the time-dependent data served for within-subject comparisons (the level 1 units of the analysis), the participants' characteristics (i.e. interpersonal behaviours) were used for between-subject comparisons (the level 2 units of the analysis; Raudenbush and Bryk, 2002). In the within-subject analyses, the participants' cortisol levels (in mg/dl) were used as the dependent variable and the timing of the data collection were used as the predictors. In the between-subject analyses, the characteristics of participants were used to account for variability observed in the within-subject effects. Correlations between the variables are provided in Table 2.

The analyses were conducted as follows. First, variables used as statistical controls including risk group, sex, age, medication use, subjective compliance to the sampling protocol (in minutes before or after the designated sampling time), were entered into the model. Next, mean ipsitized scores for submissiveness, dominance and quarrelsomeness were entered. Interactions between social behaviours and risk group, and social behaviours and sex, were then added to the model. Although agreeableness was measured during the study, it was highly correlated to quarrelsomeness ($r = -.71$, $p < 0.05$). This strong negative relationship led to multi-collinearity problems during preliminary analyses of the data. Since there was no hypothesis based on agreeableness in the analyses, the variable was excluded.

Post hoc latent class analyses were also conducted using the M-Plus program (Muthe´n and Muthe´n, 2006). A latent class analysis is a statistical method for identifying subtypes of related cases (latent classes) from multivariate data.

3. Results

3.1. Interpersonal behaviour and afternoon cortisol A within-subject ''unconditional model'' including only the dependent variable (i.e., cortisol levels) revealed that 69.94% of the variance in cortisol levels during 14 consecutive days of sampling was due to within-subject variability and the rest was due to between-subject variability. The level-1 analysis examining the linear effect of the timing of the data revealed, as expected, a significant decrease in cortisol over the course of the afternoon (b = -0.012, SE = 0.004, $t_{(43)}$ = 3.47, $p < 0.05$). This effect explained 1.11% of the within-subject variability.

Next, between-subject effects (level 2) were examined. Since between-subject variability in the linear effect of time was not statistically significant ($\chi^2_{(42)}$ = 58.13, $p > 0.05$), the slope was set as fixed at level 2. A significant amount of variability in the cortisol afternoon intercept was found ($\chi^2_{(42)}$= 71.21, $p <$ 0.05), meaning that participants did differ in cortisol values at the beginning of the afternoon. The between-subject control variables (risk group, sex, age, medication use, and compliance to the sampling protocol) had no statistically significant effect (at $p < 0.05$) on cortisol intercept, nor did submissive or quarrelsome behaviour. However, dominance had a significant positive main effect on the cortisol intercept (b = 0.003, SE = 0.001, $t_{(35)}$ = 2.58, $p < 0.05$) which explained 4.35% of the between-subject variability. Dominance was positively associated with cortisol levels.

Exploratory interactions between risk group and sex with dominance, submissiveness and quarrelsomeness were added to the model. Only one of the interactions had a statistically significant effect. There was a significant risk by quarrelsome interaction (b = -.019, SE = 0.009, $t_{(29)}$ = 2.06, $p <$ 0.05). The risk group by quarrelsome interaction explained an additional 13.63% of the remaining between-subject variability on the cortisol intercept. Interestingly, the effect of dominance on cortisol levels reported above did not differ across the risk groups.

Simple slope analyses were conducted to examine the effect of risk group on cortisol levels among participants reporting low levels of quarrelsome behaviours (1 standard deviation below the mean) and high levels of quarrelsome behaviours (1 standard deviation above the mean). In control offspring, the slope was not significantly different from zero (b = 0.001, $t_{(29)}$ = 0.90, $p > 0.05$). In high risk offspring, the slope depicted a negative relationship between quarrelsome behaviours and cortisol levels, which was significantly different from zero (b = -.003, $t_{(29)}$ = 1.78, $p < 0.05$). That is, elevated levels of quarrelsome behaviour were associated with decreases in cortisol levels among the high-risk offspring but not control offspring (Fig. 1).

Finally, we examined whether the presence of mental disorders in high risk participants accounted for the reported findings regarding quarrelsome behaviour. We repeated the analyses described above replacing the medication control variable with lifetime history of any mental disorder. The quarrelsomeness × risk group interaction still predicted the cortisol intercept (b = -.020, SE = 0.009, $t_{(29)}$ = 2.32, $p < 0.05$).

3.2. Latent class analyses

Given the different patterns of findings for the interpersonal variables, event-contingent ratings of dominance, submissiveness and quarrelsomeness were subjected to latent class analysis to identify whether there were groupings of individuals with different profiles on these three variables. A three class solution was identified as the best fit to the data with a significant bootstrapped likelihood ratio test for

two versus three classes ($p < 0.05$), acceptable class proportions (>5%), and acceptable average latent class probabilities for most likely latent class membership (>95%). The groups were labelled as follows: (1) an average group (80% of the sample), consisting of offspring with means on dominance, submissiveness and quarrelsomeness that were not statistically different from the overall mean, (2) a low dominance group (11% of the sample), consisting of offspring with a dominance mean significantly below the overall mean ($p < 0.05$) and (3) a high dominance/low submissiveness group (9% of the sample), consisting of offspring with a dominance mean significantly above the overall mean ($p < 0.05$) and a submissiveness mean significantly below the overall mean ($p < 0.05$).

The group classifications were then included in multilevel modelling analyses, to determine whether the groups differed in cortisol levels. The high dominance/low submissiveness group had significantly higher cortisol levels than the average and low dominant groups ($b = 0.135$, SE $= 0.033$, $t_{(33)} = 4.42$, $p < 0.05$), even after controlling for risk group, sex, age, medication use, and sampling compliance.

4. Discussion

As the primary aim of the study, we examined the relationship between interpersonal functioning and afternoon cortisol levels across 14 consecutive days. Unique to this area of research, interpersonal behaviours associated with status and affiliation were assessed during naturally occurring social interactions. On the status axis, we failed to confirm our hypothesis that social submissiveness would be positively associated with afternoon cortisol levels. Rather, we found a significant positive relationship between reported mean levels of dominant behaviours and cortisol levels. On the affiliation axis, we had expected to find a significant negative association between quarrelsome behaviours during social interactions and cortisol levels. The hypothesis was partially supported in that the negative relationship was observed among the offspring of parents with BD but not among offspring of parents having no affective disorder.

Individuals who reported frequent dominant behaviours during their social interactions exhibited elevated afternoon cortisol levels over the 14 days of data collection. Latent class analyses of the afternoon data revealed that this effect was largely driven by a subgroup of participants high in dominance and low in submissiveness. These participants displayed significantly higher afternoon basal cortisol levels than individuals who reported either average or low levels of dominant behaviours, as well as those reporting average levels of quarrelsome and submissive behaviours. The positive relationship between social dominance and basal cortisol is inconsistent with several studies in human and non-human primates indicating that social subordination, relative to social dominance, incurs greater psychological stress and heightened HPA activity (Sapolsky, 1990; Scerbo and Kolko, 1994; Shively et al., 1997; Decker, 2000; Gunnar et al., 2003). However, research on basal HPA activity and social status has been equivocal, and the nature of this relationship may vary across social context (Abbott et al., 2003). For example, some studies of non-human primates have reported a positive relationship between basal cortisol and dominance (Mendoza et al., 1978; Kimura et al., 2000; Czoty et al., 2009). Research among olive baboons has shown that during periods of social stability, subordinate males are exposed to more stressors than dominant males, and secrete higher basal cortisol levels than dominant males (Sapolsky, 1990). Conversely, during periods of social instability, when dominant males can descend in social standing, they display higher basal cortisol levels than subordinate males, who have an opportunity to rise in social standing (Sapolsky, 1992). Similar observations have been reported among children. Compared with shy

and submissive children, dominant children exhibit higher basal cortisol levels at the beginning of the school year as they struggle to establish social standing, followed by lower mid-year cortisol levels when their peer relationships have stabilized (Gunnar, 1994).

Therefore, one possible explanation of the present finding linking high dominance to high cortisol levels is that dominant offspring were interacting within an unstable social environment. The age range of the current sample indicates that most participants were studied during the transition from adolescence to adulthood. During adolescence, there is evidence that peer and romantic relationships are generally unstable (Zimmer-Gembeck, 1999; Bowker, 2004). Adolescents high in social dominance may therefore find themselves in a precarious, and possibly stressful, situation. Social dominance might also induce psychological stress among young adults who are transitioning to college and/or the work force, and are attempting to establish social standing in new environments. Instability in the developmental transition from adolescence and adulthood is further magnified, in one half of the sample, by having a parent with BD. The offspring of parents with BD, for example, report more chronic interpersonal and non-interpersonal stress than the offspring of parents with no affective disorder (Ostiguy et al., 2009). Unfortunately, data on developmental transitions or social instability were not collected in the present study; future research should test this hypothesis directly.

Other factors might also influence the relationship between social dominance and the HPA axis. Wirth et al. (2006) demonstrated that the degree to which individuals seek dominance over others (termed implicit power motivation) influences their cortisol responses to victory or defeat during a competitive computer task. A strong desire for dominance was associated with a cortisol increase in response to defeat, but not in response to victory. In the present study, dominant behaviours were expressed in efforts to impact other people. However, it is not known to what extent dominant offspring's ability to impact others was successful. A general inability to dominate others and/or a heightened sensitivity to social failure may have increased stress and stimulated the HPA axis. In order to empirically test this hypothesis, future studies would need to examine the corollaries associated with dominant behaviours during social interactions.

As a secondary goal of the study, we examined whether risk group, as defined by having a parent with BD or having two parents with no affective disorder, was associated with increased reactivity to social interactions in the natural environment. It was predicted that the offspring of parents with BD who reported high levels of social submissiveness would secrete higher levels of cortisol than participants low in submissiveness or control offspring. No support of the hypothesis was found, which was inconsistent with a previous study showing that elevated interpersonal stress was associated with higher cortisol levels in the offspring of parents with BD relative to the offspring of parents with no affective disorder (Ostiguy et al., 2011). The divergent results of these studies suggest that submissiveness in response to social interactions is not a central component of the interpersonal stress reported by Ostiguy et al. (2011), which was assessed by clinical interview and focused on broad areas of chronic stress over a six month period. Moreover, because the measurement of social behaviour was so different between studies, it is difficult to make meaningful direct comparisons. Increased cortisol reactivity to interpersonal stress among the offspring of parents with BD, detected by Ostiguy et al. (2011) but not in the present study, may indicate that the heightened reactivity is more closely related to chronic stress and exposure to multiple negative life events than normative daily social interactions.

In contrast to the data on submissiveness during social interactions, risk group moderated the relationship between quarrelsome social interactions and cortisol levels. The offspring of parents with BD who reported high social quarrelsomeness had lower levels of cortisol than high risk offspring with low quarrelsomeness and control offspring. Because of the small sample size, this finding should be interpreted with due caution. Both a flattened diurnal slope and low levels of cortisol have been associated with antisocial behaviours in adolescence (Shoal et al., 2003; Haltigan et al., 2011; Ruttle et al., 2011), particularly among clinical samples (Pajer et al., 2001, 2006; Popma et al., 2007). Some studies of non-clinical samples have failed to replicate this pattern of association (Klimes-Dougan et al., 2001). It is likely that abnormal HPA activity is more strongly related to overt expressions of aggression and delinquency that are characteristic of more severe externalizing problems (Alink et al., 2008). Within the present sample, high risk offspring self-report significantly more aggressive and delinquent behaviours on the Child Behaviour Checklist (Achenbach and Rescorla, 2001) than control offspring (Linnen et al., 2009). Although high risk offspring do not report significantly more quarrelsome behaviours in their social interactions than control offspring, it is possible that high risk offspring exhibit more severe forms of quarrelsome behaviours when interacting with others. Accordingly, among high risk offspring who develop BD, there is evidence of a sub-group characterized by antisocial behaviour during childhood and adolescence who exhibit a more severe course of BD, including more hospitalizations and episodes, and a higher prevalence of psychotic symptoms during manic episodes (Carlson and Weintraub, 1993; Carlson et al., 2000). It is possible that within this sub-group, cortisol levels are inversely associated with conduct problems and represent a biological marker for the onset BD.

The finding of low cortisol levels among quarrelsome offspring of parents with BD is contrary to other studies in this high risk population, where elevated cortisol levels have been reported (Ellenbogen et al., 2006a, 2010b). High cortisol levels, rather than low levels, predict the prospective development of an affective disorder (Ellenbogen et al., 2011). However, the findings associated with elevated cortisol levels may pertain to the development of major depression rather than BD. Clearly, there is heterogeneity in the developmental trajectories and outcomes of the offspring of parents with BD (Reichart et al., 2004; Klimes-Dougan et al., 2010), and the present findings may represent one such example of this. Future research in larger samples will be needed to better delineate distinct developmental trajectories among the offspring of parents with BD.

The present study has several limitations. First, even though event-contingent recording reduces the retrospective bias associated with self-report questionnaires, it remains a subjective measure intended to assess one's perceptions of their behaviours during naturally occurring social interactions. Therefore, it is not known whether participants reported behaviours that accurately depicted how they actually behaved during their social interactions, or whether participants are biased in the selection of interactions they choose to record. Second, the system of event-contingent recordings used in this study did not code for the behaviour of the person the participant was interacting with. Rather, recordings were limited to the behaviours of the participants. As described previously, the absence of information on the response to a participants' behaviour meant that it was impossible to assess the effectiveness or success of participants' social behaviours on their social environment. Third, because our study employed a correlational design, we cannot infer the direction of causation between interpersonal behaviours and cortisol levels. For example, we cannot rule out the possibility that individuals with higher basal cortisol levels were predisposed to report more dominant behaviours, or to appraise their behaviour as being more dominant, or to act in a more dominant fashion during social interactions. Cortisol reactivity to stress is associated

with faster shifts of attention towards, and slower disengagement from, pictures depicting threat and anger (Ellenbogen et al., 2006b, 2010a), which could signal a dominance-related response. To elucidate the nature of this relationship, it would be interesting to assess changes in cortisol reactivity in response to dominant behaviours during social interactions, or to examine how exogenous glucocorticoids influence laboratory assessments of dominance. It would also be useful to measure basal testosterone levels in addition to cortisol levels. Testosterone has been established as a neuroendocrinological marker of dominance (Bernhardt, 1997) and appears to interact with cortisol levels to predict dominant behaviour (Mehta et al., 2008; Mehta and Josephs, 2010). Lastly, the present study lacks power to adequately identify subtypes of behavioural patterns that may contribute to HPA abnormalities and the development of mental disorder. Future studies in larger samples are needed to replicate these effects.

In conclusion, these data support the view that HPA functioning is sensitive to status-related (dominance-submissiveness) social behaviour in late adolescence and young adulthood. A two-week protocol of repeated saliva sampling and event-contingent recordings of social interactions in the natural environment revealed a novel positive relationship between cortisol levels and dominant behaviour. Similar to indices of chronic stress (Ostiguy et al., 2011), dominant behaviours during social interactions in late adolescence and young adulthood may exert a physiological cost on HPA functioning. Among the offspring of parents with BD, a different pattern emerged. Relations between cortisol levels and status-related behaviours were absent. Instead, elevated levels of quarrelsomeness during social interactions among the offspring of parents with BD were associated with hypoactivation of the HPA axis, possibly identifying an important sub-group of high risk offspring at risk for externalizing problems and more severe course of BD. Unfortunately, the mechanisms by which these relationships occur is not known, so future studies need to address direct and indirect pathways from interpersonal relations to neuroendocrine function.

Conflict of interest

The authors declare that they have no conflicts of interest.

References

Abbott, D.H., Keverne, E.B., Bercovitch, F.B., Shively, C.A., Mendoza, S.P., Saltzman, W., Snowdon, C.T., Ziegler, T.E., Banjevic, M., 2003. Are subordinates always stressed? A comparative analysis of rank differences in cortisol levels among primates. Horm. Behav. 43, 67—82.

Achenbach, T.M., Rescorla, L.A., 2001. Manual for the ASEBA School- Age Forms & Profiles. University of Vermont, Research Center for Children, Youth, & Families, Burlington, VT.

Alink, L.R., van Ijzendoorn, M.H., Bakermans-Kranenburg, M.J., Mesman, J., Juffer, F., Koot, H.M., 2008. Cortisol and externalizing behavior in children and adolescents: mixed meta-analytic evidence for the inverse relation of basal cortisol and cortisol reactivity with externalizing behavior. Dev. Psychobiol. 50, 427—450.

Azar, R., Zoccolillo, M., Paquette, D., Quiros, E., Baltzer, F., Tremblay R.E., 2004. Cortisol levels and conduct disorder in adolescent mothers. J. Am. Acad. Child Adolesc. Psychiatry 43, 461—468.

Bernhardt, P.C., 1997. Influences of serotonin and testosterone in aggression and dominance: convergence with social psychology. Curr. Dir. Psychol. Sci. 6, 44—48.

Birmaher, B., Axelson, D., Monk, K., Kalas, C., Goldstein, B., Hickey, M.B., Obreja, M., Ehmann, M., Iyengar, S., Shamseddeen, W., Kupfer, D., Brent, D., 2009. Lifetime psychiatric disorders in school-aged offspring of parents with bipolar disorder: the Pittsburgh Bipolar Offspring Study. Arch. Gen. Psychiatry 66, 287—296.

Bowker, A., 2004. Predicting friendship stability during early adolescence. J. Early Adolesc. 24, 85—112.

Carlson, G.A., Weintraub, S., 1993. Childhood behavior problems and bipolar disorder — relationship or coincidence? J. Affect. Disord. 28, 143—153.

Carlson, G.A., Bromet, E.J., Sievers, S., 2000. Phenomenology and outcome of subjects with early- and adult-onset psychotic mania. Am. J. Psychiatry 157, 213—219.

Czoty, P.W., Gould, R.W., Nader, M.A., 2009. Relationship between social rank and cortisol and testosterone concentrations in male cynomolgus monkeys (Macaca fascicularis). J. Neuroendocrinol. 21, 68—76.

Decker, S.A., 2000. Salivary cortisol and social status among Dominican men. Horm. Behav. 38, 29—38.

Eberhart, N.K., Hammen, C.L., 2006. Interpersonal predictors of onset of depression during the transition to adulthood. Pers. Relationship 13, 195—206.

Ellenbogen, M.A., Hodgins, S., 2004. The impact of high neuroticism in parents on children's psychosocial functioning in a population at high risk for major affective disorder: a family-environmental pathway of intergenerational risk. Dev. Psychopathol. 16, 113—136.

Ellenbogen, M.A., Hodgins, S., Walker, C.D., Adam, S., Couture, S., 2006a. Daytime cortisol and stress reactivity in the offspring of parents with bipolar disorder. Psychoneuroendocrinology 31, 1164—1180.

Ellenbogen, M.A., Schwartzman, A.E., Stewart, J., Walker, C.D., 2006b. Automatic and effortful emotional information processing regulates different aspects of the stress response. Psychoneuroendocrinology 31, 373—387.

Ellenbogen, M.A., Carson, R.J., Pishva, R., 2010a. Automatic emotional information processing and the cortisol response to acute psychosocial stress. Cogn. Affect. Behav. Neurosci. 10, 71—82.

Ellenbogen, M.A., Santo, J.B., Linnen, A.M., Walker, C.D., Hodgins, S., 2010b. High cortisol levels in the offspring of parents with bipolar disorder during two weeks of daily sampling. Bipolar Disord. 12, 77—86.

Ellenbogen, M.A., Hodgins, S., Linnen, A.M., Ostiguy, C.S., 2011. Elevated daytime cortisol levels: a biomarker of subsequent major affective disorder? J. Affect. Disord. 132, 265—269.

First, M., Spitzer, R.L., Gibbon, M., Williams, J.B.W., 1997. Structured Clinical Interview for DSM-IV Disorders. Biometrics Research Department, New York.

Gaab, J., Rohleder, N., Nater, U.M., Ehlert, U., 2005. Psychological determinants of the cortisol stress response: the role of anticipatory cognitive appraisal. Psychoneuroendocrinology 30, 599—610.

Gerra, G., Zaimovic, A., Avanzini, P., Chittolini, B., Giucastro, G., Caccavari, R., Palladino, M., Maestri, D., Monica, C., Delsignore, R., Brambilla, F., 1997. Neurotransmitter-neuroendocrine responses to experimentally induced aggression in humans: influence of personality variable. Psychiatry Res. 66 33—43.

Gunnar, M., 1994. Psychoneuroendocrine studies of temperament and stress in early childhood: expanding current models. In: Bates, J.E., Wachs, T.D. (Eds.), Temperament: Individual Differences at the Interface of Biology and Behavior. American Psychological Association, Washington, DC, pp. 175—198.

Gunnar, M.R., Sebanc, A.M., Tout, K., Donzella, B., van Dulmen, M.M.H., 2003. Peer rejection, temperament, and cortisol activity in preschoolers. Dev. Psychobiol. 43, 346—358.

Haltigan, J.D., Roisman, G.I., Susman, E.J., Barnett-Walker, K., Monahan, K.C., Natl Inst Child Health Human Dev, 2011. Elevated trajectories of externalizing problems are associated with lower awakening cortisol levels in mid-adolescence. Dev. Psychol. 47, 472—478.

Hammen, C., Cohen, A.N., 2004. Psychosocial functioning. In: Johnson, S.L., Leahy, R.L. (Eds.), Psychological Treatment of Bipolar Disorder. Guilford Press, New York, pp. 17—34.

Hirschfeld, R.M.A., Montgomery, S.A., Keller, M.B., Kasper, S., Schatzberg, A.F., Moller, H.J., Healy, D., Baldwin, D., Humble, M., Versiani, M., Montenegro, R., Bourgeois, M., 2000. Social functioning in depression: a review. J. Clin. Psychiatry 61, 268—275.

Hirshfeld-Becker, D.R., Biederman, J., Henin, A., Faraone, S.V., Davis, S., Harrington, K., Rosenbaum, J.F., 2007. Behavioral inhibition in preschool children at risk is a specific predictor of middle childhood social anxiety: a five-year follow-up. J. Dev. Behav. Pediatr. 28, 225—233.

Holi, M., Auvinen-Lintunen, L., Lindberg, N., Tani, P., Virkkunen, M., 2006. Inverse correlation between severity of psychopathic traits and serum cortisol levels in young adult violent male offenders. Psychopathology 39, 102—104.

Holt-Lunstad, J., Smith, T.B., Layton, J.B., 2010. Social relationships and mortality risk: a meta-analytic review. PLoS Med. 7,e1000316.

Kagan, J., Reznick, J.S., Snidman, N., 1988. Biological bases of childhood shyness. Science 240, 167—171.

Kimura, K., Shimizu, K., Hayashi, M., Ishikawa, T., Ago, Y., 2000. Pituitary-adrenocortical responses to the first dyadic encounters in male rhesus monkeys: effect of dominance relationship. Am. J. Primatol. 50, 247—256.

Klimes-Dougan, B., Hastings, P.D., Granger, D.A., Usher, B.A., Zahn-Waxler, C., 2001. Adrenocortical activity in at-risk and normally developing adolescents: individual differences in salivary cortisolbasal levels, diurnal variation, and responses to social challenges. Dev. Psychopathol. 13, 695—719.

Klimes-Dougan, B., Long, J.D., Lee, C.-Y.S., Ronsaville, D.S., Gold, P.W., Martinez, P.E., 2010. Continuity and cascade in offspring of bipolar parents: a longitudinal study of externalizing, internalizing, and thought problems. Dev. Psychopathol. 22, 849—866.

Kudielka, B.M., 2004. Cortisol day profiles in victims of mobbing (bullying at the work place): preliminary results of a first psychobiological field study. J. Psychosom. Res. 56, 149—150.

Lapalme, M., Hodgins, S., LaRoche, C., 1997. Children of parents with bipolar disorder: a meta-analysis of risk for mental disorders. Can. J. Psychiatry 42, 623—631.

Linnen, A.M., aan het Rot, M., Ellenbogen, M.A., Young, S.N., 2009. Interpersonal functioning in adolescent offspring of parents with bipolar disorder. J. Affect. Disord. 114, 122—130.

Loney, B.R., Butler, M.A., Lima, E.N., Counts, C.A., Eckel, L.A., 2006. The relation between salivary cortisol, callous-unemotional traits, and conduct problems in an adolescent non-referred sample. J. Child Psychol. Psychiatry 47, 30—36.

Lupien, S.J., Lecours, A.R., Schwartz, G., Sharma, S., Hauger, R.L., Meaney, M.J., Nair, N.P., 1996. Longitudinal study of basal cortisol levels in healthy elderly subjects: evidence for subgroups. Neurobiol. Aging 17, 95—105.

McEvoy, M.A., Estrem, T.L., Rodriguez, M., Olson, M.L., 2003. Assessing relational and physical aggression among preschool children: intermethod agreement. Top. Early Child. Spec. 23, 53—63.

Mehta, P.H., Jones, A.C., Josephs, R.A., 2008. The social endocrinology of dominance: basal testosterone predicts cortisol changes and behavior following victory and defeat. J. Pers. Soc. Psychol. 94, 1078—1093.

Mehta, P.H., Josephs, R.A., 2010. Testosterone and cortisol jointly regulate dominance: evidence for a dual-hormone hypothesis. Horm. Behav. 58, 898—906.

Mendoza, S.P., Coe, C.L., Lowe, E.L., Levine, S., 1978. The physiological response to group formation in adult male squirrel monkeys.

Psychoneuroendocrinology 3, 221—229. Moskowitz, D.S., 1994. Cross-situational generality and the interpersonal circumplex. J. Pers. Soc. Psychol. 66, 921—933.

Muthe´n, L.K., Muthe´n, B.O., 2006. Mplus: Statistical Analysis with Latent Variables, Fourth edition. Muthe´n & Muthe´n, Los Angeles, CA.

Norman, G.J., Hawkley, L.C., Cole, S.W., Berntson, G.G., Cacioppo, J.T., 2012. Social neuroscience: the social brain, oxytocin, and health. Soc. Neurosci. 7, 18—29.

Ostiguy, C.S., Ellenbogen, M.A., Linnen, A.M., Walker, E.F., Hammen, C., Hodgins, S., 2009. Chronic stress and stressful life events in the offspring of parents with bipolar disorder. J. Affect. Disord. 114, 74—84.

Ostiguy, C.S., Ellenbogen, M.A., Walker, C.D., Walker, E.F., Hodgins, S., 2011. Sensitivity to stress among the offspring of parents with bipolar disorder: a study of daytime cortisol levels. Psychol. Med. 41, 2447—2457.

Pajer, K., Gardner, W., Rubin, R.T., Perel, J., Neal, S., 2001. Decreased cortisol levels in adolescent girls with conduct disorder. Arch. Gen. Psychiatry 58, 297—302.

Pajer, K., Tabbah, R., Gardner, W., Rubin, R.T., Czambel, R.K., Wang, Y., 2006. Adrenal androgen and gonadal hormone levels in adolescent girls with conduct disorder. Psychoneuroendocrinology 31, 1245—1256.

Patterson, A.C., Veenstra, G., 2010. Loneliness and risk of mortality: a longitudinal investigation in Alameda County, California. Soc. Sci. Med. 71, 181—186.

Popma, A., Vermeiren, R., Geluk, C.A., Rinne, T., van den Brink, W., Knol, D.L., Jansen, L.M., van Engeland, H., Doreleijers, T.A., 2007. Cortisol moderates the relationship between testosterone and aggression in delinquent male adolescents. Biol. Psychiatry 61, 405—411.

Raudenbush, S.W., Bryk, A.S., 2002. Hierarchical Linear Models: Applications and Data Analysis Methods, 2nd edition. Sage, Thousand Oaks, CA.

Raudenbush, S.W., Bryk, A.S., Cheong, Y.F., Congdon, R., du Toit, M., 2004. HLM: 6 Hierarchical Linear and Non-linear Modeling. Scientific Software International, Lincolmwood, IL.

Reichart, C.G., Wals, M., Hillegers, M.H.J., Ormel, J., Nolen, W.A., Verhulst, F.C., 2004. Psychopathology in the adolescent offspring of bipolar parents. J. Affect. Disord. 78, 67—71.

Reis, H.T., Gable, S.L., 2000. Event-sampling and other methods for studying everyday experience. In: Reis, H.T., Judd, C.M. (Eds.), Handbook of Research Methods in Social and Personality Psychology. Cambridge University Press, New York, pp. 558—580.

Ruttle, P.L., Shirtcliff, E.A., Serbin, L.A., Fisher, D.B., Stack, D.M., Schwartzman, A.E., 2011. Disentangling psychobiological mechanisms underlying internalizing and externalizing behaviors in youth: longitudinal and concurrent associations with cortisol. Horm. Behav. 59, 123—132.

Sapolsky, R.M., 1990. Adrenocortical function, social rank, and personality among wild baboons. Biol. Psychiatry 28, 862—878.

Sapolsky, R.M., 1992. Cortisol concentrations and the social significance of rank instability among wild baboons. Psychoneuroendocrinology 17, 701—709.

Scerbo, A.S., Kolko, D.J., 1994. Salivary testosterone and cortisol in disruptive children: relationship to aggressive, hyperactive, and internalizing behaviors. J. Am. Acad. Child Adolesc. Psychiatr 33, 1174—1184.

Schmidt, L.A., Fox, N.A., Rubin, K.H., Sternberg, E.M., 1997. Behavioral and neuroendocrine responses in shy children. Dev. Psychobiol. 30, 127—140.

Shively, C.A., Laber-Laird, K., Anton, R.F., 1997. Behavior and physiology of social stress and depression in female cynomolgus monkeys. Biol. Psychiatry 41, 87—882.

Shoal, G.D., Giancola, P.R., Kirillova, G.P., 2003. Salivary cortisol, personality, and aggressive behavior in adolescent boys: a 5-year longitudinal study. J. Am. Acad. Child Adolesc. Psychiatry 42, 1101—1107.

van der Pompe, G., Bernards, N., Meijman, T.F., Heijnen, C., 1999. The effect of depressive symptomatology on plasma cortisol responses to acute bicycle exercise among post-menopausal women. Psychiatry Res. 85, 113—117.

Virkkunen, M., 1985. Urinary free cortisol secretion in habitually violent offenders. Acta Psychiatr. Scand. 72, 40—44.

Wirth, M.M., Welsh, K.M., Schultheiss, O.C., 2006. Salivary cortisol changes in humans after winning or losing a dominance contest depend on implicit power motivation. Horm. Behav. 49, 346—352.

Zimmer-Gembeck, M.J., 1999. Stability, change and individual differences in involvement with friends and romantic partners among adolescent females. J. Youth Adolesc. 28, 419—438.

Table 1 Demographic and clinical characteristics of the sample.

	Offspring of parents with BD	Offspring of parents with no affective disorder
n	23	22
Mean age, years (SD)	18.3 (2.7)	18 (2.3)
Gender	12 males/ 11 females	11 males/ 11 females
Lifetime diagnosis		
Bipolar disorder	3	0
Major depressive disorder	3	2
Substance abuse/ dependence[a]	5/1[b]	1/0
Anxiety disorders	1[c]	0
Current symptoms (past month)		
Bipolar disorder	1	0
Major depressive disorder	0	1
Substance abuse/ dependence	0	0
Anxiety disorders	1	0
Current psychotropic medication	2	0

Note. BD: bipolar disorder.
[a] Diagnoses included alcohol, cannabis, and cocaine.
[b] Cannabis dependence.
[c] Specific phobia.

Table 2 Inter-correlations between study variables (*n* = 45).

	Mean (SD)	1	2	3	4	5	6
1. Age	18.6 (2.5)	—					
2. Cortisol at 13:00 pm	.17 (.07)	.16	—				
3. Cortisol at 15:00 pm	.14 (.07)	.26	.80*	—			
4. Submissiveness	−5.7 (5.9)	.09	−.14	−.07	—		
5. Dominance	5.2 (5.9)	−.12	.11	.21	−.51*	—	
6. Quarrelsomeness	−11.79 (6.6)	−.02	.00	−.09	.18	−.32*	—

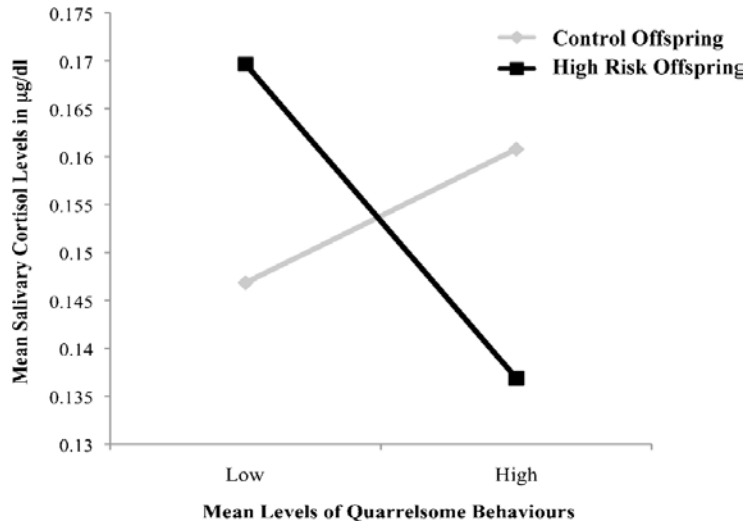* Correlation is significant at the 0.05 level (2-tailed).

Figure 1   Simple slopes depicting the relationship between quarrelsome behaviours and cortisol levels in the offspring of parents with bipolar disorder (high risk; n = 23) and offspring of parents with no affective disorder (control offspring; n = 22). Quarrelsome behaviours were sampled using event-contingent recording and were reported during naturally occurring social interactions over a 14- day period. Salivary cortisol levels were collected twice daily (1300 h and 1500 h) over the same 14-day period. Low (high) levels of quarrelsome behaviours are defined as one standard deviation below (above) the mean of the distribution of quarrelsome behaviours reported by the full sample. Simple slope analyses indicate that the slope in control offspring did not differ significantly from zero (b = 0.001, $t_{(29)}$ = 0.90, p > 0.05). The slope in high risk offspring, in contrast, was significantly different from zero (b = −.003, $t_{(29)}$ = 1.78, p < 0.05), revealing a significant negative relationship between quarrelsome behaviours and cortisol levels.