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Dissociable roles of glucocorticoid and noradrenergic activation on social discounting

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ABSTRACT

People often exhibit prosocial tendencies towards close kin and friends, but generosity decreases as a function of increasing social distance between donor and recipient, a phenomenon called social discounting. Evidence suggests that acute stress affects prosocial behaviour in general and social discounting in particular. We tested the causal role of the important stress neuromodulators cortisol (CORT) and noradrenaline (NA) in this effect by considering two competing hypotheses. On the one hand, it is possible that CORT and NA act in concert to increase generosity towards socially close others by reducing the aversiveness of the cost component in costly altruism and enhancing the emotional salience of vicarious reward. Alternatively, it is equally plausible that CORT and NA exert dissociable, opposing effects on prosocial behaviour based on prior findings implicating CORT in social affiliation, and NA in aggressive and antagonistic tendencies. We pharmacologically manipulated CORT and NA levels in a sample of men (N = 150) and found that isolated hydrocortisone administration promoted prosocial tendencies towards close others, reflected in an altered social discount function, but this effect was offset by concurrent noradrenergic activation brought about by simultaneous yohimbine administration. These results provide inceptive evidence for causal, opposing roles of these two important stress neuromodulators on prosocial behaviour, and give rise to the possibility that, depending on the neuroendocrine response profile, stress neuromodulator action can foster both tend-and-befriend and fight-or-flight tendencies at the same time.

1. Introduction

Although almost all people engage in prosocial behaviour at times, generosity tends to decrease with increasing social distance between donor and recipient. After all, while many of us do not hesitate to donate money to our close family members in need, very few of us would be willing to give the same amount to disadvantaged strangers. This decline in generosity as a function of increasing social distance is called social discounting, a phenomenon which has triggered significant research interest in recent years (Jones and Rachlin, 2006; Kalenscher, 2017; Margittai et al., 2015; Strang et al., 2017; Strombach et al., 2015, 2014; Vekaria et al., 2017).

Due to the high prevalence of acute stress in daily life, research focusing on how it impacts social decision making has increased manifold in recent years (Porcelli and Delgado, 2017; Starcke and Brand, 2012). Acute stress is associated with the activation of the hypothalamic-pituitary-adrenal axis (HPA axis) system as well as autonomic arousal (Selye, 1950), and increases in two main neuromodulators, cortisol (CORT) and noradrenaline (NA) respectively. These substances impact brain function in a symphonic, time-dependent fashion, with imminent elevations of NA, shortly followed by non-genomic CORT effects after stress onset, and subsequent genomic CORT response in the aftermath of stress (Hermans et al., 2014; Joëls and Baram, 2009).

In stark contrast to the canonical view that acute stress primarily leads to fight-or-flight, it has now been reliably shown that it can also foster prosocial behaviour in some situations, in both men and women (Buchanan and Preston, 2014; Margittai et al., 2015; Taylor et al., 2000; Tomova et al., 2017; Von Dawans et al., 2012).

In recent work (Margittai et al., 2015), we specifically focused on whether social closeness is a determining factor in acute stress effects on prosocial behaviour, and thus investigated how it altered social discounting. Results showed that exposure to psychosocial stress (Trier Social Stress Test for Groups, Von Dawans et al., 2011) increased generosity, but only towards individuals who were socially close to the decision maker. These findings were interpreted in the context of the

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tend-and-befriend hypothesis (Taylor, 2006), a coping mechanism that helps to counteract the negative effects of stress by investing into social networks providing help and comfort. As socially close others are more likely to offer protection in time of need, it is reasonable to focus affiliative efforts, and thus become more prosocial only towards them. Extending these findings Berger et al. (2016) demonstrated, that CORT responses to psychosocial stress were positively correlated with the tendency to affiliate amongst men, lending support to the idea that CORT plays a key role in social affiliative coping and thus in prosocial behaviour after stress. Furthermore, CORT has already been implicated as a positive predictor of empathy, a concept indisputably related to prosocial behaviour (Zilioli et al., 2015). The role of NA in prosocial behaviour, and its putative interaction with CORT, is less clear. CORT and NA acting in concert reduce loss aversion (Margittai et al., 2018), promote attention to salient stimuli (Hermans et al., 2011), and sharpen vigilance contrasts, and NA-related arousal caused by observing another person in distress has been found to be related to subsequent costly helping (Hein et al., 2011). This may suggest that generosity towards socially close others after stress might be boosted by the conjoint action of CORT and NA, by reducing the aversiveness of the costs in costly altruism, and at the same time enhancing the emotional salience of vicarious reward signals and feelings of warm glow. By contrast, NA has been widely associated with arousal and aggression both in animal and human studies (Nelson and Trainor, 2007), and it is known to reduce social play and affiliation in animals (Achterberg et al., 2016). Thus, it is equally plausible that CORT by itself promotes prosocial behaviour, particularly towards socially close others, while the concomitance of NA inhibits these prosocial tendencies.

Here, we set out to decide between these two competing hypotheses by investigating the causal effect of CORT and NA manipulation on social discounting. We pharmacologically manipulated CORT and NA levels by oral, exogenous administration of hydrocortisone or yohimbine (an alpha-2 adrenergic receptor antagonist) respectively. These substances were given separately or concomitantly in a placebo-controlled double-blind experimental design. We measured how elevations in CORT and NA level impact on social discounting using the same task that has been reported by (Margittai et al., 2015).

2. Materials and methods

2.1. Participants

One hundred and fifty male participants took part in the experiment. We opted to employ male participants only because there is evidence of gender differences in HPA-axis reactivity as well as effects of oral contraceptives and menstrual cycle phase on HPA-axis reactivity in female participants (Kirschbaum et al., 1999). Sample size was determined using G*Power (Faul et al., 2007). Assuming a medium effect size (also see Margittai et al., 2015), the sample size necessary to achieve a power of 0.8 was n = 128. We eventually opted to collect data from 150 participants, thus exceeding the minimum sample size requirement, to have a contingency for potential exclusions or other problems. Hence, we are confident that our study was sufficiently powered to detect the required effects.

Before participation individuals completed a screening interview and those who reported regular use of medication, chronic physical or mental illness, heavy smoking, drinking or drug use or being students of Psychology or Economics were not invited to participate. 7 participants disclosed after the experiment that they either had illnesses or were taking medication, and they were consequently excluded from further analyses. All participants had fluent knowledge of German, gave their written, informed consent and received financial compensation for participation. The study was approved by the ethics committee of the University Hospital Düsseldorf and conformed to the regulations of the Declaration of Helsinki. Participants were instructed not to engage in sexual activities, take medication or alcohol for 24 h prior to participation, not to smoke, or drink anything containing caffeine for 4 h prior to participation, and to refrain from physical exercise, eating and drinking anything other than water for 2 h before participation. These criteria were similar to what had been employed in other studies (e.g. Vinkers et al., 2013).

2.2. Trait measures

Prior to being invited to the laboratory, all participants completed a number of trait questionnaires online, designed to exclude potential confounds between the experimental groups:

We measured trait anxiety (State-Trait Anxiety Inventory – STAI, (Spielberger et al., 1983), impulsivity (Barratt Impulsiveness Scale – BIS-15, (Meule et al., 2011), reward and punishment sensitivity (BIS/BAS scale, Carver and White, 1994), social desirability (Social Desirability Scale – SDS-17, Ströber, 2001), empathy (Saarbrücker Persönlichkeitsfragebogen – SPF, Paulus, 2007), chronotype (reduced version of the Morningness-Eveningness Questionnaire − rMEQ, Randler, 2013) and general willingness to take risks. Additionally we recorded age, BMI, baseline salivary cortisol, baseline salivary alpha-amylase, baseline subjective feelings of stress (VAS) and mood (PANAS; Watson et al., 1988).

2.3. Pharmacological manipulation, physiological and subjective stress measures

Participants were randomly assigned to one of four experimental conditions: (A) placebo (PLAC, N = 36), (B) placebo + yohimbine (YOH, 20 mg, Cheplapharm, N = 38), (C) placebo + hydrocortisone (CORT, 20 mg, Jenapharm, N = 38), (D) yohimbine + hydrocortisone (YOHCORT, 20 mg each, N = 38). The number of tablets taken was identical in the four conditions, thus participants were unable to guess which condition they were in on the basis of the number of pills. The dosage was chosen to be in line with previous studies (Margittai et al., 2018, 2016; Schwabe et al., 2012, 2010). To assess increases in cortisol levels and noradrenergic activation, saliva samples (using Salivette devices from Sarstedt, Germany) were collected at baseline and +30, +60 and +75 min after pill ingestion and subsequently frozen at −20 °C until transport and analysis using the same method as reported by (Rohleder et al., 2004). 25 of the 1500 samples were compromised and thus could not be analysed. These values were excluded from analyses. All other samples were analysed for concentrations of salivary cortisol (CORT) and salivary alpha amylase (sAA), an indirect marker of noradrenergic activity. For each participant, two samples were taken approximately 10 min and 20 min before pill intake and their values averaged to determine individual baseline. In case one of the values was missing, we used the remaining value as the baseline. Subjective feelings of stress (using visual analogue scales − VAS) were taken at the same time as the saliva samples. Changes in positive and negative mood were assessed once at baseline and once 60 min after drug intake (shortly before the experimental tasks), using PANAS (Watson et al., 1988) scales. Change scores were calculated by subtracting baseline from the later measure.

2.4. Elicitation of social environment and experimental task

Our aim was to investigate how the decline in generosity across social distance is affected by CORT and NA. Thus, we asked participants prior to pill intake to describe their social environment using a similar method reported by Margittai et al. (2015) and Strombach et al. (2014, 2015). Individuals were asked to give the names of representatives for social distances (SD) 1, 2, 3, 5, 10 and 20, with SD 1 representing the person they feel closest to, with decreasing closeness as a function of increasing social distance. Although we also included distances 50 and 100 in the experiment, participants were not asked to provide a name for these, as they represent remote individuals or strangers whose

names are likely to be unknown to the participant.

The social discounting task used was identical to that reported in Margittai et al. (2015) consisting of 24 rounds of a dictator game presented in randomized order, where participants had to indicate how much of a given endowment (EUR13, EUR15 and EUR17) they would be willing to donate to the individuals at the 8 social distance levels mentioned before. Our dependent variable was the percentage of money shared at each SD. The task was fully incentive compatible, thus, participants were informed that, subsequent to task performance, one of their choices would be selected randomly and paid out, potentially resulting in payment for the participant and another person. The other person either received the money via cheque, or if the choice was about remote individuals or strangers (SD 50 and SD 100), the money was distributed randomly at the university campus.

2.5. Social discounting function

To assess social distance dependent changes in generosity, we fitted a standard hyperbolic function (Eq. (1)) to the percentage of money shared at each social distance level, using robust nonlinear regression with an iterative least square estimation procedure. Fits were done both individually for each participant and at a group level (separately for each experimental group), similarly to the method described in Margittai et al. (2015), Fig. 3A.

$$v = \frac{V}{(1 + kD)} \quad (1)$$

Eq. (1) is identical to that employed by Jones and Rachlin (2006); Margittai et al. (2015); Strombach et al. (2014, 2015) & Takahashi, (2007), with v representing the discounted other-regarding value of the percentage of money shared, V referring to the height of the function which can be interpreted as generosity at close social distance, D as a measure of social distance and k describing the degree of discounting. We used individual V and k parameters as a measure of a participants' generosity at close social distance (parameter V), and the decrease in generosity as a function of social distance (parameter k).

2.6. Procedure

Individuals arrived at the laboratory between 2:00PM and 6:00PM for their experimental sessions in order to control for diurnal variations of cortisol levels. After providing informed consent, participants completed a number of baseline measures as detailed in Table 1, and completed a questionnaire aimed at eliciting the social environment. Thereafter, participants ingested the drugs and a waiting period commenced, during which instructions for the experimental task were given, followed by a quiz to ensure comprehension. Subsequently, participants were free to read a number of magazines that were provided by the experimenters, but they were instructed not to leave the room or to communicate. The experimental task started approximately 65 min after pill intake and lasted less than 10 min to complete.

3. Results

3.1. Trait and baseline measures

To ensure that there was no difference between the four experimental groups in baseline and trait variables that could confound our findings, we carried out a number of univariate analyses of variance (ANOVA) with the between subject factor experimental group (placebo, yohimbine, hydrocortisone, yohimbine + hydrocortisone) and the trait and baseline measures listed in 2.2 above. We found no significant differences between the groups on any of these measures, see Table 1 for a detailed description.

3.2. Pharmacological manipulation check

Baseline corrected changes in CORT and NA concentration values over time were analysed using mixed ANOVAs with the within subject variable timepoint of testing (+30, +60 and +75 min post pill intake) and between subject factors yohimbine intake (yohimbine vs. placebo) and hydrocortisone intake (hydrocortisone vs. placebo). Sphericity violations were corrected using Greenhouse-Geisser correction. Salivary cortisol increased over time in participants who received hydrocortisone (timepoint x hydrocortisone interaction: $F_{1.47,193.90} = 20.79$, $p < .001$, $\eta_p^2 = 0.14$), but not in those who received yohimbine (timepoint x yohimbine interaction: $F_{1.47,193.90} = 0.50$, $p = .550$, $\eta_p^2 = 0.00$), nor was there an interaction between yohimbine and hydrocortisone on salivary CORT changes over time (timepoint x yohimbine x hydrocortisone: $F_{1.47,193.90} = 0.25$, $p = .711$, $\eta_p^2 = 0.00$, Fig. 1A). Salivary alpha-amylase levels increased over time in those who received yohimbine (timepoint x yohimbine interaction: $F_{1.63,216.48} = 3.36$, $p < .05$, $\eta_p^2 = 0.03$), but not in those who received hydrocortisone (timepoint x hydrocortisone interaction: $F_{1.63,216.48} = 0.43$, $p = .613$, $\eta_p^2 = 0.00$), nor was there an interaction between hydrocortisone and yohimbine on sAA levels over time (timepoint x hydrocortisone x yohimbine: $F_{1.63,216.48} = 0.24$, $p = .742$, $\eta_p^2 = 0.00$, Fig. 1B).

3.3. Subjective stress and mood ratings

Baseline corrected changes in positive and negative mood and

Table 1
Trait and baseline measures.

	Placebo M (SD)	Yohimbine M (SD)	Hydrocortisone M (SD)	YohCort M (SD)	F-value	p-value	Effect size (η_p^2)
Age	24.80 (5.42)	23.44 (3.82)	26.59 (10.09)	26.00 (5.64)	1.56	0.201	0.03
BMI	22.53 (2.13)	22.79 (1.80)	22.85 (2.03)	23.58 (2.02)	1.80	0.150	0.04
Baseline cortisol (nmol/l)	19.34 (11.38)	15.36 (5.14)	20.42 (19.54)	15.98 (12.44)	1.27	0.288	0.03
Baseline alpha-amylase (U/mL)	58.62 (40.64)	45.31 (34.62)	67.30 (64.39)	57.26 (41.18)	1.35	0.259	0.03
VAS	11.18 (12.56)	11.56 (10.42)	13.34 (14.07)	14.77 (12.37)	0.63	0.598	0.01
PANAS positive mood	30.62 (6.33)	28.83 (6.42)	29.35 (5.74)	27.59 (7.48)	1.27	0.288	0.03
PANAS negative mood	12.03 (3.15)	12.94 (2.99)	12.39 (3.19)	12.57 (2.85)	0.55	0.652	0.01
STAI	38.46 (10.61)	43.08 (9.38)	39.65 (9.31)	38.51 (7.52)	1.96	0.122	0.04
BIS-15	29.06 (4.67)	32.06 (8.11)	32.27 (5.24)	31.74 (6.31)	2.05	0.110	0.04
BIS total	18.71 (3.94)	18.78 (4.12)	18.92 (3.55)	18.14 (3.50)	0.29	0.834	0.01
BAS drive	12.94 (1.97)	12.69 (2.20)	12.40 (1.82)	12.03 (1.76)	1.44	0.235	0.03
BAS fun seeking	11.91 (1.92)	12.42 (2.98)	12.65 (1.60)	12.40 (1.85)	0.98	0.406	0.02
BAS reward responsiveness	16.77 (1.86)	16.19 (2.76)	16.78 (2.26)	16.34 (2.11)	0.62	0.602	0.01
SDS-17	9.71 (3.09)	9.92 (2.48)	10.08 (2.71)	10.37 (2.41)	0.38	0.771	0.01
SPF	38.66 (7.79)	39.47 (6.12)	41.27 (7.22)	41.94 (4.29)	1.96	0.124	0.04
Chronotype	12.03 (4.42)	11.56 (3.08)	12.94 (3.95)	11.54 (3.58)	1.10	0.350	0.02
Risk taking	4.17 (1.10)	4.17 (.81)	4.14 (.89)	4.03 (1.20)	0.15	0.927	0.003

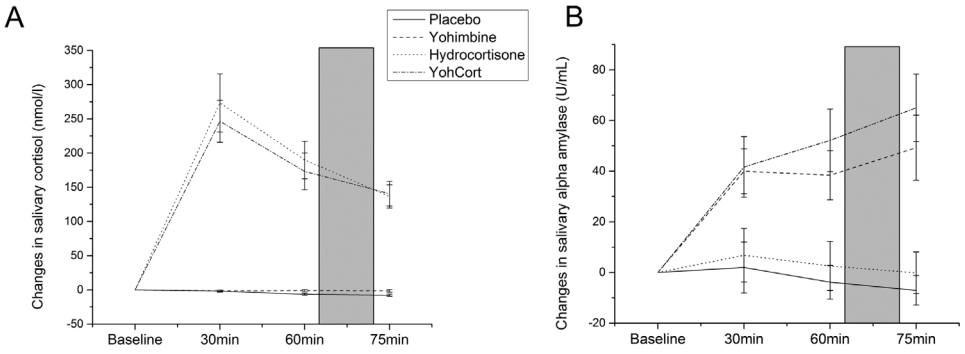

Fig. 1. (A) baseline corrected changes in salivary cortisol +30, +60 and +75 min after pill intake. Individuals who received hydrocortisone had increased salivary cortisol levels compared to those who did not. (B) baseline corrected changes in salivary alpha-amylase +30, +60 and +75 min after pill intake. Individuals who received yohimbine had higher concentrations of sAA than those who did not. The timing of experimental tasks is indicated by grey shaded bars. Error bars indicate ± 1 SEM.

baseline corrected changes in subjective feelings of stress +30 and +60 min after pill intake were analysed with ANOVAs with the between-subject factors yohimbine (yohimbine vs placebo) and hydrocortisone (hydrocortisone vs. placebo).

Baseline corrected change in positive affect from baseline to directly before the experimental task was not significantly affected by the treatment (main effect of hydrocortisone: $F_{1,132} = 2.83$, $p = .095$, $\eta_p^2 = 0.02$, main effect of yohimbine: $F_{1,132} = 0.004$, $p = .949$, $\eta_p^2 = 0.00$, yohimbine x hydrocortisone: $F_{1,132} = 1.19$, $p = .277$, $\eta_p^2 = 0.01$), but the decrease in negative mood was less pronounced in those who received yohimbine than in those who did not (main effect of yohimbine: $F_{1,137} = 4.61$, $p < .05$, $\eta_p^2 = 0.03$). Change in negative mood was not significantly affected by hydrocortisone intake ($F_{1,137} = 0.01$, $p = .930$, $\eta_p^2 = 0.00$), nor was there an interaction between the two substances on changes in negative mood ($F_{1,137} = 1.21$, $p = .273$, $\eta_p^2 = 0.01$, Fig. 2A).

We additionally carried out two one sample *t*-tests to compare baseline corrected changes in positive and negative mood against the value 0. These analyses confirmed that these changes were significantly different from 0 (Positive change: $M = -2.31$, $SD = 4.68$, $t(134) = -5.76$, $p < 0.001$: Negative change: $M = -0.57$, $SD = 2.16$, $t(139) = -3.16$, $p = .002$).

In a similar vein we also carried out two one-sample *t*-tests to compare baseline corrected changes in subjective feelings of stress at +60 min against the value 0. These analyses revealed that individuals who received yohimbine had a slight increase in feelings of stress, albeit only marginally significantly different from 0 ($M = 3.14$, $SD = 13.52$, $t(69) = 1.95$, $p = .056$), while those who received no yohimbine showed a marginally significant decrease ($M = -2.34$, $SD = 10.20$, $t(69) = -1.92$, $p = .059$). Though these changes were not significantly different from 0, due to their opposing trends we wanted to test whether there was a difference in feelings of stress between those who received yohimbine than those who did not. Baseline corrected increase in subjective feelings of stress directly before the experimental task (at the +60 min testing time point) were higher in those who received yohimbine than in those who did not (main effect of yohimbine: $F_{1,136} = 7.36$, $p < .05$, $\eta_p^2 = 0.05$), which is in line with prior research (e.g. Elman et al., 2012; Margittai et al., 2017). In contrast, hydrocortisone intake had no effect on subjective feelings of stress, nor was there an interaction between the two substances (main effect of hydrocortisone: $F_{1,136} = 0.53$, $p = .468$, $\eta_p^2 = 0.00$, hydrocortisone x yohimbine: $F_{1,136} = 0.13$, $p = .721$, $\eta_p^2 = 0.00$). Changes in subjective feelings of stress did not differ between the groups 30 min after pill intake (all $p > .184$, Fig. 2B). As changes in negative mood and subjective feelings of stress differed between the experimental groups, their potential confounding effects on our main findings were investigated (see Section 3.4).

3.4. Generosity to close others is boosted by hydrocortisone but this increase is offset by noradrenergic action

To investigate how CORT and NA impact social discounting in isolation as well as in combination, we analysed individual social discounting parameters *V* (representing generosity to close others) and *k* (representing the decline of generosity as a function of social distance) using 2 × 2 between subject ANOVAs with the factor yohimbine intake (yes/no) and hydrocortisone intake (yes/no). While we did not find any significant main effects on the *V* parameter (all $p > .284$), we found a significant interaction effect between yohimbine and hydrocortisone intake ($F_{1,139} = 5.94$, $p < .05$, $\eta_p^2 = 0.04$). Holm-Bonferroni corrected planned comparisons revealed that individuals who received hydrocortisone had higher *V* parameters, compared to those who received placebo ($t(64.72) = -2.30$, $p < .05$, $d = 0.54$), or cort + yohimbine ($t(59.77) = -2.00$, $p < .05$, $d = 0.55$, Fig. 3B). Thus, while CORT action alone increased generosity towards close others, additional YOH administration offset the CORT-induced boost in generosity. None of the other comparisons reached significance (all $p > .170$).

Subjective feelings of stress and changes in negative mood differed between the experimental groups at the +60 min timepoint (see Section 3.3), therefore we carried out a correlation analysis between the *V* parameter and subjective feelings of stress as well as changes in negative mood to exclude any potential confounding effects. The results of

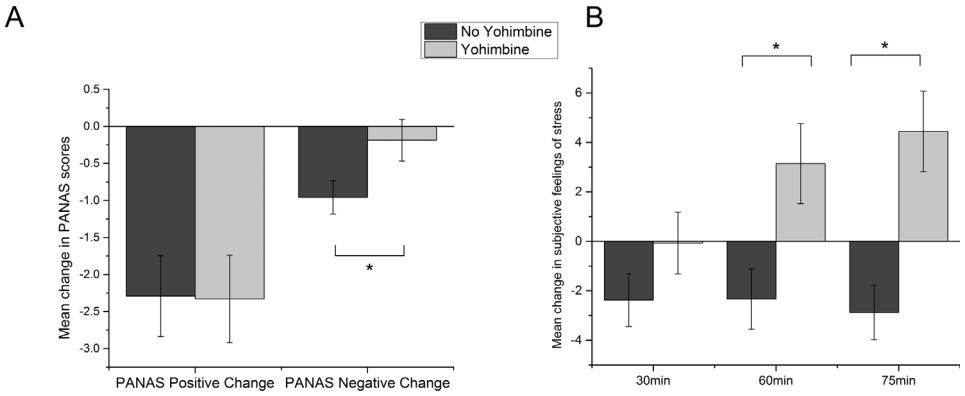

Fig. 2. (A) changes in positive and negative mood from baseline to directly before the experimental tasks. Individuals who received yohimbine had a smaller reduction in negative mood than those who received no yohimbine. Changes in positive mood were not affected by the treatment. (B) baseline corrected changes in subjective feelings of stress. Subjective levels of stress were perceived to be higher in those who received yohimbine than in those who did not +60 and +75 min post pill intake. Significant differences are indicated by an asterisk (* $p < .05$, ** $p < .01$, *** $p < .001$). Error bars indicate ± 1 SEM.

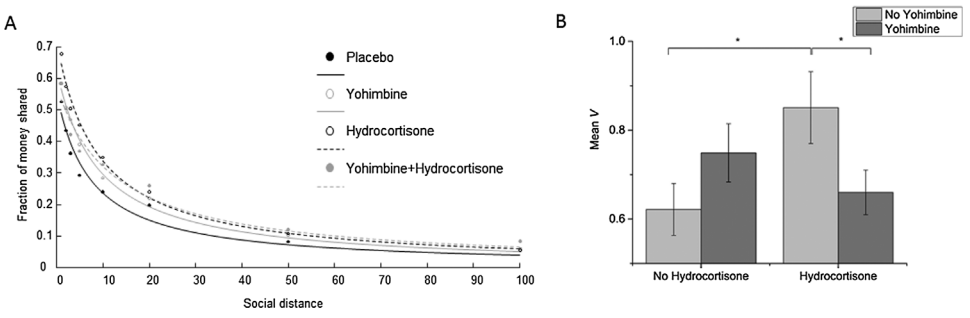

Fig. 3. (A) Decline in generosity across social distance in the four experimental groups as described by the hyperbolic model. (B) Individuals who received hydrocortisone had significantly higher V parameters, reflecting increased generosity at close social distance, which was offset by additional NA activation. Significant differences are indicated by an asterisk (* $p < .05$). Error bars indicate ± 1 SEM.

these analyses were not significant ($p = .164$ and $p = .670$ respectively). Furthermore, we repeated the main analyses with changes in negative mood and increases in subjective feelings of stress as covariates, which did not change the results. Thus subjective feelings of stress and changes in negative mood were unlikely to have interfered with the CORT- and NA-effects on *V*.

There were no main or interaction effects of CORT and YOH on the log-transformed *k* parameters (all $p > .285$), thus there was no evidence suggesting that CORT and NA affected the general decline in generosity across social distance.

In order to test whether belief about treatment may have influenced results, we asked participants to indicate at the end of the experiment whether they believe to have been in the treatment or placebo groups. A chi-square test revealed that participants who believed to have received placebo vs. active substances differed between the four experimental conditions (placebo: $belief_{placebo} = 27$, $belief_{treatment} = 8$, yohimbine: $belief_{placebo} = 26$, $belief_{treatment} = 10$, cortisol: $belief_{placebo} = 32$, $belief_{treatment} = 5$, yohcort: $belief_{placebo} = 16$, $belief_{treatment} = 19$; $\chi^2(3, N=143) = 15.72$, $p = .001$). However, a point-biserial correlation between treatment expectancy and individual *V* parameters did not reach significance ($r = -0.002$, $p = .979$), suggesting that treatment expectancy was unlikely to have interfered with our findings. We carried out a further chi-square test to investigate whether participants did better than chance in estimating what they received. This analysis showed that there was no difference from chance in their guessing performance ($\chi2(3, N = 143) = 3.08$, $p = .094$).

4. Discussion

Acute stress and associated elevations in CORT and NA have been known to impact social decision making (Buchanan and Preston, 2014; Starcke and Brand, 2012) with some studies showing that acute stress facilitates prosocial behaviour (Buchanan and Preston, 2014; Margittai et al., 2015; Taylor et al., 2000; Tomova et al., 2017; Von Dawans et al., 2012), in stark contrast to the traditionally held view that the primary reaction to acute stress is fight-or-flight. In support of the tend-and-befriend hypothesis, we recently showed that psycho-social stress boosts giving behaviour towards socially close others from whom support can be expected in stressful times, but not towards socially distant others who are less likely to help (Margittai et al., 2015). Here, we asked if the effects of psycho-social stress on social discounting are mediated by the stress neuromodulators CORT and/or NA. Crucially, we contrasted two competing hypotheses about how CORT and NA could be involved in the observed effect: both neuromodulators could either act in concert to boost generosity, or, alternatively CORT and NA may have opposing roles, with CORT fostering generosity, and NA inhibiting CORT-induced prosocial tendencies. Our results support the latter hypothesis: exogenous administration of hydrocortisone alone led to increased prosocial behaviour towards socially close recipients, reflected in higher *V* parameters in the social discount function, but additional noradrenergic activation brought these levels back to baseline. In line with prior findings (Margittai et al., 2015), neither drug affected the slope of the social discount function.

Taken together, the fact that CORT and NA had dissociable roles in promoting generosity, or inhibiting it, respectively, potentially resolves one of the most perplexing puzzles in the current stress literature: why does stress, or psychopharmacological challenges aimed to investigate the effects of the main stress neuromodulators, sometimes trigger tend-and-befriend (Margittai et al., 2015; Von Dawans et al., 2012), and at other times more socially antagonistic responses (FeldmanHall et al., 2015; Steinbeis et al., 2015)? Here, we propose that stress does not always provoke one *or* the other response, but *can boost either tendency,* depending on the intensity of the stressor, and the time-dependent dynamics of neuroendocrine action. Immediately after stress onset, noradrenergic activation is high, and NA and CORT (non-genomically) affect brain functioning in concert, but once the short-lived NA elevations subside, CORT dominates the endocrine stress response particularly via slow genomic actions (Hermans et al., 2014). Thus, our theory predicts that fight-or-flight tendencies should occur only in the acute phase of stress when NA- and arousal levels are high, but tend-and-befriend responses should predominantly emerge in the immediate or delayed aftermath of stress, where NA action fades while CORT action remains (Bendahan et al., 2017; Pabst et al., 2013). The implied timeframe of this hypothesis also fits with the general idea that fight-or-flight tendencies are aimed at ending, removing, or escaping from, the acute stressor, while tend-or-befriend responses are a putative coping strategy (Taylor, 2006) that becomes mostly relevant later.

As many prior studies neglected to measure noradrenergic activation and focused solely on cortisol increases after stress, it has so far been difficult to ascertain whether unmeasured noradrenergic activation may have explained some variance in the reported findings. This is particularly true for those studies that measured decision making at a time window where both NA and CORT should have been high, such as approximately 10–20 min after stress onset. As the interplay between the two stress hormones changes very rapidly over time (Pabst et al., 2013), a few minutes difference in the time of behavioural testing may lead to a shift in the balance of dominance between NA and CORT. This has made it difficult to disentangle the roles of the two stress neuromodulators on pro- and antisocial behaviour, and may explain the divergence in existing literature. The results presented here hope to make a valuable contribution to the resolution and reconciliation of these issues.

Our findings that CORT boosted generous behaviour corroborate and extend prior reports of a correlation between CORT elevations and social affiliation after stress (Berger et al., 2016). Furthermore, the fact that the increase in generosity was restricted to individuals socially close to the decision maker lend further support to the idea of a tend-and-befriend reaction (Margittai et al., 2015; Taylor et al., 2000; Von Dawans et al., 2012) by demonstrating that social affiliative efforts are primarily focused on individuals from whom help and protection can reasonably be expected, (Margittai et al., 2015) as opposed to indiscriminately befriending everyone. More broadly, our findings are in line with research focusing on the role of CORT in emotional contagion (Buchanan and Preston, 2014) in particular with those of Engert et al. (2014) who found that observing individuals undergo a stressful

situation resulted in cortisol responses in observers, which was particularly pronounced when the observer and the observed were socially close.

Importantly, our finding that the CORT-related boost in prosocial behaviour was offset by NA action provides novel insights into the role of NA in social cognition. However, although our findings are in line with prior studies demonstrating the role of NA in arousal and aggressive behaviour (Nelson and Trainor, 2007), we did not observe actual other-harming behaviour in our participants. Hence, one might plausibly ask why NA did not produce genuinely antagonistic tendencies, as would be expected from a true fight-or-flight reaction. It is possible that, instead of promoting antagonistic fight-or-flight responses, NA might simply inhibit CORT-induced prosocial motives, while leaving aggressive predispositions aimed at harming others unaffected. Alternatively, it is also conceivable that NA induces true aggression, but the nature of our task masked those putative NA-driven antagonistic tendencies. As our primary focus was to examine the psychopharmacology of *prosocial* behaviour, we used the dictator game (Kahneman et al., 1986) which is ideally suited to study prosociality, but it does not provide a real opportunity for probing other-harming behaviours. Thus, to extend these findings, future research should investigate whether, when given an opportunity for aggression, individuals with increased levels of NA indeed show a propensity to be more antisocial.

Although the pharmacological manipulation used in the present study presents an excellent opportunity to study the causal effects of CORT and NA on decision making, it is also important to consider that it does not directly parallel a naturally occurring stress response. For instance, the levels of hormone concentrations are significantly higher and longer-lasting after the pharmacological manipulation than after naturally occurring stress (Lupien et al., 1999; Margittai et al., 2016), and the subjective emotional experience also differs between the two situations (Margittai et al., 2017). Furthermore, CORT increases in natural stress always happen subsequent to and in combination with NA, which is different from administering the two substances in isolation.

A further question that arises is what neural mechanisms may underlie the observed effects. Speculatively we propose that the right temporoparietal junction (rTPJ) may play a crucial role the effect of stress neuromodulators on social discounting. Two research papers from our group and collaborators have highlighted the prominent role of this brain region in social discounting. Strombach et al. (2015) demonstrated that rTPJ activation facilitated generous decision making by overcoming the bias to be egoistic and Soutschek et al. (2016) applied transcranial magnetic stimulation to the rTPJ and found altered social discounting which was accompanied by perspective taking deficits. As stress is known to affect TPJ function (e.g. Hermans et al., 2014), the stress-neuromodulator effects on social discounting reported here might be mediated by changes in TPJ operation. To elucidate the exact neural underpinnings of our findings, future neuroimaging studies are necessary.

As we only tested male participants, it is important to consider whether the results presented here also apply to women. Gender differences in stress effects on social cognition (Smeets et al., 2009; Tomova et al., 2014) have already been documented. For instance, Tomova et al. (2014) found that exposure to acute stress leads to decreased self-other distinction in men, with the opposite pattern being observed in women. Smeets et al. (2009) showed that cortisol elevations after stress were negatively correlated with social cognition in men and positively in women. Thus, the present results cannot readily be generalized across genders.

A further point to clarify is related to potential expectancy effects of the drugs received. Although we asked participants about the drugs they thought they had received, it is plausible that this question alone was not sufficient to quantify expectancy effects. Popular belief of a drug's effect might influence how participants behave during psychopharmacological challenges. However, even if participants had been aware of what they had ingested, it is unclear if, and how, popular belief about hydrocortisone and yohimbine action affect behavior, as these drugs are not as clearly associated with an expected psychological effect in general public perception in the same way that, for example, testosterone is believed linked to aggression.

Overall, our results demonstrate dissociable roles of CORT and NA on prosocial behaviour. We show that CORT in isolation promotes prosocial tendencies, particularly towards close others, evidential of increased social affiliative tendencies. Furthermore, concurrent noradrenergic activation prevents this CORT-related increase in generosity from occurring. Our findings contribute to the understanding of the neurobiological basis of acute stress effects on social behaviour, and they suggest the intriguing possibility that the neuroendocrine stress response triggers both tend-and-befriend as well as fight-or-flight responses in chorus.

Conflict of interest declaration

The authors declare no conflict of interest.

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