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Perceived early-life maternal care and the cortisol response to repeated psychosocial stress

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Background: In the past decade, a body of animal and human research has revealed a profound influence of early-life experiences, ranging from variations in parenting behaviour to severe adversity, on hypothalamic–pituitary–adrenal axis regulation in adulthood. In our own previous studies, we have shown how variations in early-life parental care influence the development of the hippocampus and modify the cortisol awakening response. **Methods:** In the present study, we investigated the influence of early-life maternal care on cortisol, heart rate and subjective psychological responses to the repeated administration of a psychosocial laboratory stressor in a population of 63 healthy young adults. Low, medium and high early-life maternal care groups were identified using the Parental Bonding Instrument. **Results:** Controlling for the effect of sex, we found an inverted u-shaped relation between increasing levels of maternal care and cortisol stress responsivity. Specifically, overall and stress-induced cortisol levels went from below normal in the low maternal care, to normal in the medium care, back to below normal in the high maternal care groups. We found no group differences with respect to heart rate and subjective psychological stress measures. Whereas low and high maternal care groups exhibited similarly low endocrine stress responses, their psychological profiles were opposed with increased levels of depression and anxiety and decreased self-esteem in the low care group. **Limitations:** Sex was unequally distributed among maternal care groups, whereby the number of men with low maternal care was too small to allow introducing sex as a second between-group variable. **Conclusion:** We discuss the potential significance of this dissociation between endocrine and psychological parameters with respect to stress vulnerability and resistance for each maternal care group.

Introduction

The hypothalamic–pituitary–adrenal (HPA) axis is one of the most important neuroendocrine stress systems.¹ Dysregulations of the HPA axis are implicated in the pathophysiology of stress-related disorders, such as depression and anxiety.^{2,3} In the past decade, a body of animal and human research has revealed a profound influence of early-life experiences, ranging from variations in parenting behaviour to severe adversity, on HPA axis regulation in adulthood.^{4,5} Systematically investigating this influence of early-life experiences might enhance our understanding of the development and pathophysiology of stress-related disorders.

In the laboratory setting, the Trier Social Stress Test (TSST)⁶ is the most frequently administered psychological tool used to induce a cortisol stress response. In its original version, the TSST comprises a free speech and a mental arithmetic challenge performed in front of at least 2 evaluating panelists. So far, only few studies have examined the effect of repeated TSST exposure, by either repeating the TSST daily⁷ or weekly⁸ for up to 5 repetitions. Results from these studies suggest that repeatedly high cortisol stress responses over 5 days are linked to specific personality profiles.^{7,9}

With respect to early-life experiences, previous TSST studies focused mainly on the influence of severe adversity and yielded conflicting results. Whereas Heim and colleagues¹⁰ and

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Rao and colleagues¹¹ showed that a history of early-life adversity determined increased neuroendocrine stress responses in adolescents and adult women, Carpenter and colleagues¹² and MacMillan and colleagues¹³ found attenuated neuroendocrine stress responses in maltreated adolescents and adults. There are only 2 human studies available, from our group, exploring the association between early-life parental care and stress responsivity. Using positron emission tomography (PET), we showed that young adults with self-reported low early-life maternal care exhibited increased cortisol and nucleus accumbens dopamine responses to stressful mental arithmetic when compared with a high care group.¹⁴ In an elderly population, we showed an association between low early-life parental care (including mother and father care ratings), decreased hippocampal volume and self-esteem and an increased cortisol response to the Montreal Imaging Stress Task (MIST).¹⁵ Further studies from our group have extended these findings by revealing an influence of early-life maternal care on hippocampal volume in young adult women¹⁶ and an influence of early-life parental care on the cortisol awakening response¹⁷ and the behavioural response to methylphenidate¹⁸ in young adults.

In the current study, we investigated the influence of early-life maternal care on single and repeated TSST exposure. We identified a low, medium and high early-life maternal care group using the Parental Bonding Instrument (PBI).¹⁹ Next to cortisol, heart rate and subjective psychological stress responses, we assessed key psychological variables. We expected to find the highest cortisol stress response in the low maternal care group, indicating stress vulnerability, and the lowest cortisol stress response in the high care group, indicating stress resistance. Further, we expected the low maternal care group to show a continuously high cortisol response upon repeated stress exposure.

Methods

Participants

We recruited participants between 18 and 30 years of age by posting ads on the electronic billboard of the McGill University website. We initially screened 495 individuals with the PBI. This questionnaire assesses care and overprotection received independently from mother and father during the first 16 years of life. To avoid a confounding effect of variation of parental care across the 2 parents, we included individuals in the study only if the care levels for both their parents fell within the same care category according to the normative scores established by Parker.²⁰ The normative range of care scores lies between 0 and 26 for low maternal care, 0 and 23 for low paternal care, 27 and 36 for high maternal care and 24 and 36 for high paternal care.²⁰ Individuals with mixed scores (low maternal care, high paternal care and vice versa) or who were unable to provide information on both parents were excluded from the study. Individuals with separated parents were not excluded from the study as long as they could provide information on both parents, or a parent and a stepparent (in this case, the closeness of the relationship determined whether parent or stepparent was re-

ferred to in answering the PBI). We contacted potential participants for a follow-up. If interested in the project, they underwent a telephone interview, which assessed information about recreational drug use, medical and psychological history. We excluded regular recreational drug users (cannabis within the past 2 months, any other recreational drug within the past year) and smokers (> 5 cigarettes/wk) from the study. Individuals reporting chronic illness (including current psychological disorders) or taking medication that might influence HPA axis activity were also excluded. Given an influence of gonadal steroids on HPA axis stress responsiveness,²¹ all women participating in the study were either on hormonal contraceptives or in the first half (corresponding to the follicular phase) of their cycle when stress testing took place. The local research ethics committee approved the study. All procedures were carried out with the full understanding and written informed consent of the participants.

Study outline

After completing the PBI and the telephone interview, each participant attended 3 sessions at the laboratory. During the first session, the Mini Structured Clinical Interview²² was performed to confirm the absence of psychological disorders. Participants also completed a set of psychological questionnaires and a checklist of the most common intra- and extra-familial stressors during childhood and adolescence. Since cortisol secretion is characterized by a strong circadian rhythm with peak levels after awakening,²³ the subsequent 2 stress testing sessions took place between 1 pm and 5 pm. For each participant, the 2 TSSTs occurred at the same time of day, separated by a minimum of 1 and a maximum of 7 days. The experimental setup was identical on both testing days.

Measures

Early-life experiences

The PBI¹⁹ was administered to retrospectively assess maternal care. Using 2 times 25 items, this questionnaire measures care and overprotection received independently from mother and father during the first 16 years of life. To avoid confounding effects of maternal care and childhood trauma, we assessed traumatic stress experiences during childhood and adolescence using a checklist of the most common intra- (e.g., sexual abuse, physical or emotional abuse or neglect, death of a family member, separation of parents, financial difficulties) and extrafamilial (e.g., being victim of a violent act or rape, being robbed, involvement in an accident, immigration) stressors.

Psychological variables

The Mini Structured Clinical Interview,²² a semistructured diagnostic interview based on the DSM-III, was performed to verify the absence of psychiatric disorders. Next to the PBI, we administered a set of psychological questionnaires to assess further potential determinants of interindividual variability in the cortisol stress response. The Beck Depression Inventory (BDI)²⁴ measured characteristic attitudes and symptoms

of depression, the State-Trait Anxiety Inventory (STAI)²⁵ measured symptoms of anxiety and the Rosenberg Self-Esteem Scale (RSES)²⁶ measured self-esteem. We calculated all questionnaire scores following the guidelines of the respective authors.

Cardiovascular and subjective psychological stress responses

For the assessment of the cardiovascular stress response, we monitored heart rate using a finger clip pulse oximeter (Nonin Medical, Inc.). Heart rate measures were recorded 1 minute before (−1 min), in 1-minute intervals during (at +1, +2, +3, +4, +5, +6, +7, +8, +9, +10 min) and 1 minute after (+11 min) the TSST. We assessed subjective psychological stress responses using the Profile of Mood States (POMS),²⁷ which measured tension, depression, anger, confusion, vigour and fatigue. Participants completed the POMS 20 minutes before and immediately after the TSST.

Cortisol stress response

We focused on cortisol, a validated biomarker of stress, as an endocrine indicator of the perceived stressfulness of the situation. Cortisol was sampled using the salivette collection device (Sarstedt Inc.) and stored at −20°C until analysis. Saliva samples were taken in 10-minute intervals before and after the TSST (at −20, −10, 0, +10, +20, +30, +40, +50 and +60 min). Cortisol (nmol/L) activity was determined using a time-resolved fluorescence immunoassay,²⁸ with intra- and inter-assay variabilities of less than 10% and 12%, respectively.

Trier Social Stress Test

Participants were exposed to a modification of the Trier Social Stress Test (TSST), a social evaluative and mentally challenging laboratory stressor.⁶ To control for the pretesting stress exposure, participants rested for an hour before being introduced to the stressor. Participants were then informed that they were to give a 10-minute free speech for a simulated job interview. The free speech would have to be held in front of a panel of 2 trained behavioural analysts who would evaluate the participants' tone of voice, mimic, body posture and verbal skills. Additionally, the free speech would be videotaped for a later in-depth behavioural assessment. Participants were given 10 minutes of preparation time (stress anticipation phase). For the stress testing phase, participants were brought to a separate room, in which they gave their speech while standing up in front of a microphone. The 10-minute stress test was followed by a 50-minute recovery phase. Unbeknownst to the participants, panelists were regular students instructed to maintain neutral facial expressions and not to give feedback. Also, no video recording took place. Participants were debriefed about the true nature of the TSST only after finishing the second testing session (except if they decided to discontinue the study beforehand). The modification of a 10-minute speech instead of a 5-minute speech and 5-minute mental arithmetic was implemented to allow for the possibility of follow-up testing with a subgroup of participants employing a complimentary stress task, the MIST.¹⁵

Statistical analysis

The prescreened participant sample (with homogeneous care scores for mothers and fathers) was clustered into 3 sub-groups based on their maternal care scores (low, medium and high care) using a k-means cluster analysis.²⁹ To compare the between-group distributions of potential confounding factors (age, sex, hormonal contraceptive use in women and the occurrence of traumatic stress experiences), we performed 1-way independent analyses of variance (ANOVAs) and χ^2 tests. Log transformations were applied to correct the moderate positive skew in the cortisol data, and reciprocal transformations were applied to correct the severe positive skew in the subjective psychological stress data. We used original data for display in the figures.

To examine the initial (day 1) cortisol and heart rate stress responses among the 3 maternal care groups while controlling for the influence of sex, we performed 2-way mixed analyses of covariance (ANCOVAs) with the within-subject factor measurement time point (−10, 0, +10, +20, +30, +40, +50, +60 min for cortisol; −1, 0, +1, +2, +3, +4, +5, +6, +7, +8, +9, +10 min for heart rate), the between-subject factor group and the covariate sex. To test for possible sex effects in the cortisol stress response, the analysis was repeated as a 2-way mixed ANOVA in women only (with too few men not allowing a separate analysis). Regarding the subjective psychological stress response, we performed univariate ANCOVAs with the between-subject factor group, the covariate sex and the difference between −20 minutes pre- and post-TSST scores of the respective POMS scale as dependent variables.

To examine the repeated cortisol and heart rate stress responses among maternal care groups while controlling for the influence of sex, we performed 3-way mixed ANCOVAs with the within-subject factors day and measurement time point, the between-subject factor group and the covariate sex. Here again, the cortisol analysis was repeated as a 3-way mixed ANOVA in women only. Regarding the subjective psychological stress response, we performed 2-way mixed ANCOVAs with the within-subject factor day, the between-subject factor group, the covariate sex and the difference between −20 minutes pre- and post-TSST scores of the respective POMS scale as dependent variables.

Using univariate ANCOVAs, we compared BDI depression, STAI anxiety and RSES self-esteem scores among maternal care groups while controlling for the influence of sex.

Throughout these analyses, violations of the assumption of sphericity were adjusted using the Greenhouse–Geisser correction. We further investigated significant effects using Bonferroni post-hoc tests. The level of significance was set at 0.05 for all analyses. We performed Kolmogorov–Smirnov tests to verify that, within each maternal care group, the log-transformed cortisol data, the heart rate data, the reciprocally transformed subjective psychological stress data and the psychological questionnaire data were normally distributed. We performed Levene tests of sphericity to verify that homogeneity of variance was given for the dependent variables across all maternal care groups. For each ANCOVA, a model including the interaction between maternal care and sex was

customized to test the ANCOVA-specific assumption of homogeneity of regression slopes. We used the Predictive Analytics Software (PASW) version 17 to compute all analyses.

Results

Participants

Overall, with respect to the care scale, 110 (22.3%) of the 495 individuals screened scored below, whereas 195 (39.4%) scored above the normative data for both their parents; 183 (36.9%) had mixed scores for mothers and fathers and 7 (1.4%) were raised by their mothers alone. We contacted 305 (61.6%) potential participants for a follow-up. Following the telephone interview, we included 63 participants (19 men, 44 women; mean age 21.08, standard deviation [SD] 2.55 yr) in the study.

Descriptive statistics

The cluster analysis identified low ($n = 15$; mean care 16.33, SD 2.72, range 11–20), medium ($n = 19$; mean care 24.74, SD 2.10, range 22–28) and high ($n = 29$; mean care 32.52, SD 2.21, range 29–36) maternal care groups. Two of the 63 participants (both from the low maternal care group) reported separation of their parents. We found no significant between-group differences regarding the distribution of age ($F_{2,58} = 1.97, p > 0.10$), hormonal contraceptive use in women

($\chi^2_2 = 1.31, p > 0.50$) and the occurrence of intra- ($F_{2,41} = 2.76, p = 0.075$) and extrafamilial ($F_{2,54} = 0.15, p > 0.80$) traumatic stress experiences in childhood and adolescence. The distribution of sex among the maternal care groups was unequal (whereby the number of men with low care was too small to allow performing a χ^2 test; Table 1 shows the number of participants per cell). We included sex as a covariate in all the between-group analyses. Data were normally distributed and homogeneity of variance was given for the dependent variables across the maternal care groups. All interactions between maternal care and sex were nonsignificant, indicating that the assumption of homogeneity of regression slopes was met for the calculated ANCOVAs.

Initial stress responses among maternal care groups

The 2-way mixed ANCOVA for the cortisol stress response on testing day 1 revealed a time effect ($F_{2,67,152.42} = 3.18, p = 0.003$), a group effect ($F_{2,57} = 5.47, p = 0.007$) and a time by group interaction ($F_{5,35,152.42} = 3.36, p = 0.005$; Fig. 1a). Post-hoc tests showed that the medium maternal care group exhibited higher overall cortisol levels than both the low (mean difference = 0.24, $p = 0.002$) and the high (mean difference = 0.17, $p = 0.013$) care groups, which did not differ from each other (mean difference = 0.07, $p > 0.70$). In women only, a 2-way mixed ANOVA showed the same pattern of results, suggesting that this finding was independent of sex (Table 2). A 2-way mixed ANCOVA revealed no between-group differences in heart rate (all $F < 1.00$, all $p > 0.60$). With respect to the subjective psychological stress response, univariate ANCOVAs revealed marginal group effects for the POMS scales tension ($F_{2,53} = 1.87, p = 0.15$) and anger ($F_{2,50} = 2.12, p = 0.13$). Figure 2 illustrates that the low maternal care group exhibited the highest overall levels of tension both pre- and post-TSST (Fig. 2a), and equally high levels of poststress anger than the

Table 1: Number of male and female participants in low, medium and high maternal care groups on testing days 1 and 2

Testing day	Low maternal care		Medium maternal care		High maternal care	
	Male	Female	Male	Female	Male	Female
Day 1	2	13	11	8	6	23
Day 2	1	13	10	5	6	18

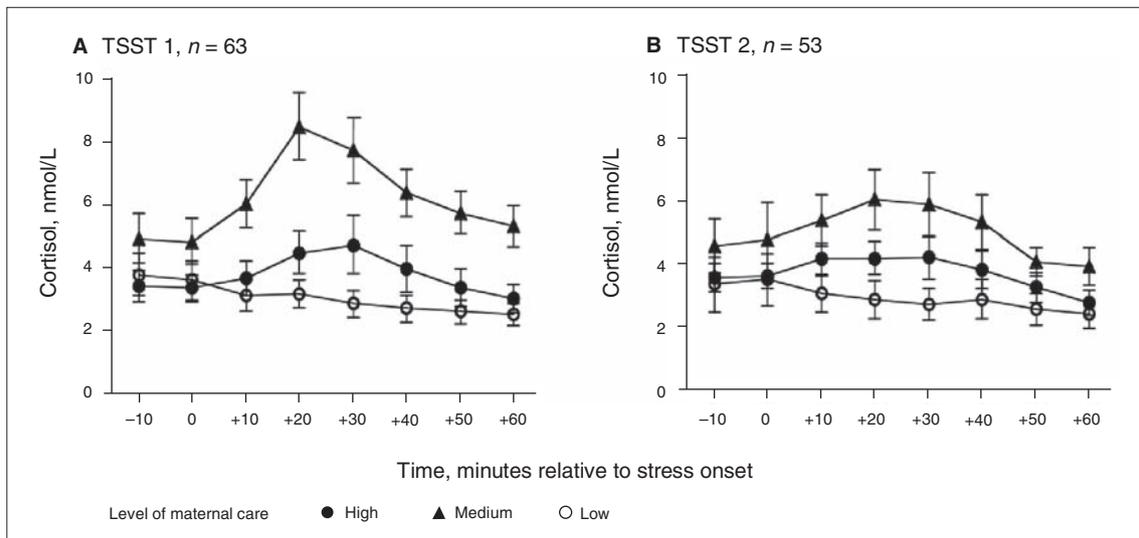


Fig. 1: Means and standard errors for cortisol levels in high ($n = 29$), medium ($n = 19$) and low ($n = 15$) maternal care groups on (A) testing day 1 and (B) testing day 2 (high $n = 24$, medium $n = 15$, low $n = 14$ maternal care groups). On both testing days, the medium maternal care group displayed the highest cortisol levels. Low and high maternal care groups did not differ from each other. TSST = Trier Social Stress Test.⁶

medium care group who, other than the low care group, exhibited a significant increase in the cortisol stress response (Fig. 2b).

Repeated stress responses among maternal care groups

Ten participants decided to discontinue the study after the initial stress testing session (see Table 1 for the distribution among the care groups). One-way independent and 2-way mixed ANOVAs showed that these 10 participants did not differ from the rest of the sample with respect to their maternal care scores ($F_{1,61} < 0.40, p > 0.50$), scores on the assessed psychological questionnaires (all $F < 1.0$, all $p > 0.30$) and their heart rate stress responses ($F_{6,52,228,30} < 0.90, p > 0.55$). They differed from the rest of the sample in that they exhibited a trend for higher cortisol stress responses in the initial testing ($F_{2,44,149,11} = 2.71, p = 0.06$) and higher stress-induced levels of depression on the POMS ($F_{1,55} = 4.22, p = 0.045$).

When considering both testing days, analyses revealed a

Table 2: Summary of results for the cortisol stress response in the maternal care groups

Test; effect	Statistic	<i>p</i> value
Day 1, women only, <i>n</i> = 44*		
Time main effect	$F_{2,81,115,34} = 3.35$	0.024
Maternal care main effect	$F_{2,41} = 6.28$	0.004
Time by maternal care interaction	$F_{5,63,115,34} = 3.55$	0.004
Days 1 and 2, total group, <i>n</i> = 53†		
Day main effect	$F_{1,33} = 0.24$	> 0.60
Time main effect	$F_{2,34,77,16} = 3.89$	0.019
Maternal care main effect	$F_{2,33} = 3.97$	0.029
Time by maternal care interaction	$F_{4,68,77,16} = 2.92$	0.020

*2-way mixed analysis of variance.

†3-way mixed analysis of variance.

time effect ($F_{2,44,114,74} = 3.40, p = 0.028$), a group effect ($F_{2,47} = 3.77, p = 0.030$) and a time by group interaction ($F_{4,88,114,74} = 2.55, p = 0.033$; Fig. 1). There was no effect of day ($F_{1,47} = 0.23, p > 0.60$). The medium maternal care group exhibited higher overall cortisol levels than the low care group (mean difference = 0.22, $p = 0.015$). The medium and the high (mean difference = 0.13, $p > 0.10$), and the low and the high (mean difference = 0.07, $p > 0.40$) maternal care groups did not differ from each other. Calculations in women only revealed the same pattern of results (Table 2). There were no significant differences in heart rate (all $F < 2.00$, all $p > 0.10$) and subjective psychological stress responses (all $F < 2.0$, all $p > 0.10$) among the 3 maternal care groups.

Psychological profile among maternal care groups

Univariate ANCOVAs for the psychological profiles revealed group effects for scores of BDI depression ($F_{2,57} = 8.03, p = 0.001$), STAI trait ($F_{2,52} = 10.83, p < 0.001$) and state ($F_{2,51} = 7.57, p = 0.001$) anxiety and RSES self-esteem ($F_{2,57} = 6.83, p = 0.002$; Fig. 3a–c). Post-hoc tests showed that the low maternal care group exhibited higher depression and trait anxiety scores than both the medium and the high care groups. Also, the low maternal care group exhibited higher state anxiety and lower self-esteem scores than the high care group. The self-esteem difference between low and medium maternal care groups was only marginal. There were no differences between low and medium maternal care groups for state anxiety, and between medium and high care groups for any of the psychological variables (Table 3).

Discussion

We compared the responses to psychosocial stress in 3 groups

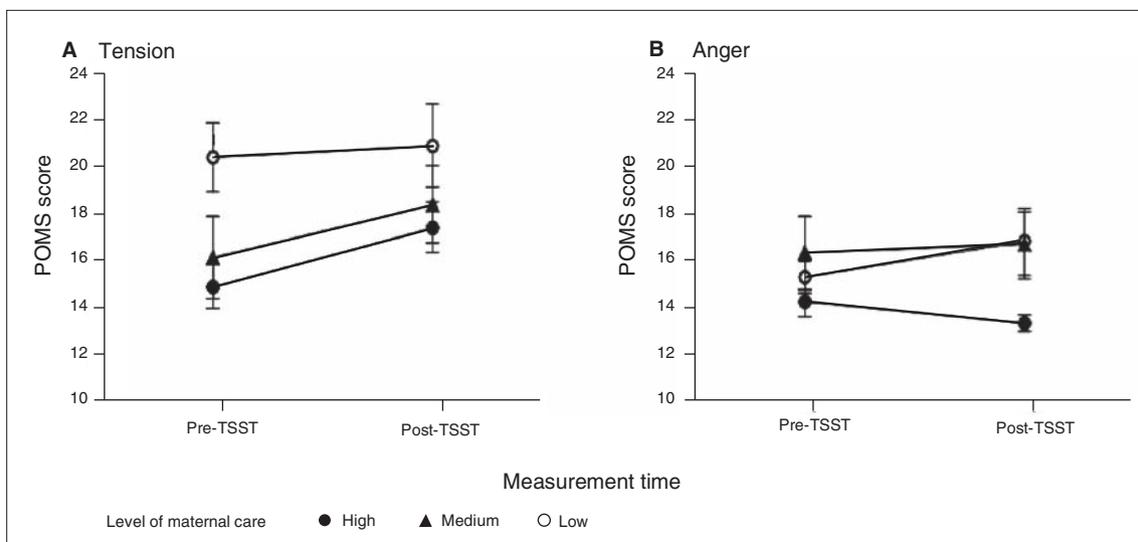


Fig. 2: Means and standard errors in high, medium and low maternal care groups for the Profile of Mood States (POMS)²⁷ scales (A) tension (high $n = 29$, medium $n = 16$, low $n = 15$ maternal care groups) and (B) anger (high $n = 27$, medium $n = 16$, low $n = 15$ maternal care groups) before and after attending the Trier Social Stress Test (TSST)⁶ on testing day 1. The low maternal care group displayed the numerically highest overall level of tension and equally high poststress levels of anger as the medium maternal care group.

of participants with retrospectively self-reported low, medium and high maternal care experiences, and observed an inverted u-shaped relation between levels of early-life maternal care and cortisol stress responsivity. In detail, whereas low and high maternal care groups were associated with blunted or reduced cortisol stress responses, respectively, the medium care group exhibited a significant stress-induced cortisol increase on the first testing day, which was reduced on testing day 2.

Previous TSST studies on the association between severe early-life adversity and HPA axis responsivity have yielded conflicting results.¹⁰⁻¹³ In view of results from animal research^{30,31} and our own earlier studies using the MIST,¹⁴ we had expected to find an increased cortisol stress response in participants with low maternal care. The main question arising from the current findings is what an inverted u-shaped relation could mean in terms of stress vulnerability and resistance for each maternal care group, especially since the blunted cortisol stress response in the low care group is clearly incompatible with our hypothesis. Here, we offer several possible interpretations.

It has been proposed by Fries and colleagues³² that the phenomenon of “hypocortisolism,” which is linked to a number of stress-related states, might develop following a period of chronic stress with accompanying HPA axis hyperactivity. As potential physiologic mechanisms, Fries and colleagues suggested the downregulation of specific receptors on different levels of the HPA axis (hypothalamus, pituitary, adrenals, target cells), reduced biosynthesis or depletion at different levels of the HPA axis, combined with increased negative feedback sensitivity to glucocorticoids. Following this line of reasoning, the hypocortisolemic stress responsivity observed in our low maternal care group might represent the long-term developmental adaptation to an initially hyperresponsive system. In other words, the low maternal care group might have initially presented with a hyperactive stress response system after sensitization through a more stressful en-

vironment as a consequence of low maternal care. With chronically high cortisol levels, downregulatory mechanisms might have occurred at key sites of the HPA axis over time. If these counteractive mechanisms occurred during critical development periods, they might have “locked” the HPA axis into a state of hyporesponsiveness, with all the adverse consequences for the ability to cope with stress. Blunted cortisol levels might thus be a sign of exhaustion: low care participants might be in the maladaptive state of subjectively experiencing stress without being able to mount the appropriate endocrine stress response. This would impair their ability to cope with the increased energy demand and restore the body’s homeostasis after a stress experience. The subjective psychological measures we took alongside the endocrine

Table 3: Summary of results from Bonferroni post-hoc tests for the psychological profiles in the maternal care groups while controlling for the effect of sex

Test; comparison	Mean difference	p value
Beck Depression Inventory²⁴		
Low v. medium maternal care	5.34	0.009
Low v. high maternal care	5.60	0.002
Medium v. high maternal care	0.26	> 0.95
State-Trait Anxiety Inventory²⁵		
Trait anxiety		
Low v. medium maternal care	11.72	0.007
Low v. high maternal care	13.62	< 0.001
Medium v. high maternal care	1.90	> 0.95
State anxiety		
Low v. medium maternal care	7.09	> 0.20
Low v. high maternal care	10.57	0.007
Medium v. high maternal care	3.49	> 0.95
Rosenberg Self-Esteem Scale²⁶		
Low v. medium maternal care	4.26	0.054
Low v. high maternal care	5.76	0.001
Medium v. high maternal care	1.50	> 0.90

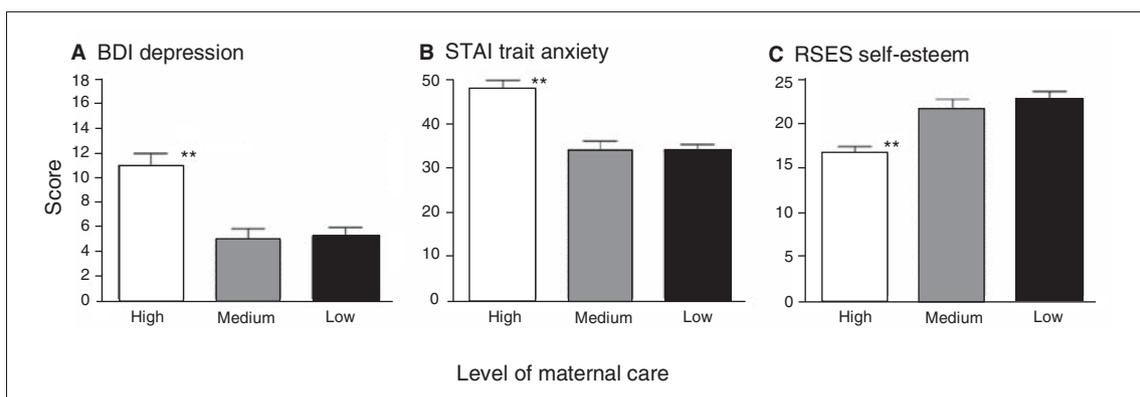


Fig. 3: Means and standard errors in high, medium and low maternal care groups for scores on the (A) Beck Depression Inventory (BDI;²⁴ high *n* = 29, medium *n* = 19, low *n* = 15 maternal care groups), (B) trait scale of the State Trait Anxiety Inventory (STAI;²⁵ high *n* = 28, medium *n* = 16, low *n* = 14 maternal care groups) and (C) Rosenberg Self-Esteem Scale (RSES;²⁶ high *n* = 29, medium *n* = 19, low *n* = 15 maternal care groups). **All *p* < 0.01. The low maternal care group exhibited higher depression and trait anxiety scores than both the medium and the high care groups. Also, the low maternal care group exhibited higher state anxiety and lower self-esteem scores than the high care group. There were no differences between low and medium maternal care groups for state anxiety, and between medium and high maternal care groups for any of the psychological variables.

measures offer partial support for this view: the low maternal care group exhibited the highest overall levels of tension, and equally high levels of poststress anger on the POMS as the medium care group. Unfortunately, when compared with the other 2 groups, these differences only showed a trend for statistical significance, likely owing to a lack of statistical power.

In terms of subjective trait measures, a clearer picture emerged: next to elevated depression levels, the low maternal care group reported elevated levels of trait anxiety and decreased levels of self-esteem when compared with the medium and high care groups. We have repeatedly found similar associations in earlier studies comparing low and high parental care groups.^{14,18}

When comparing the medium with the high maternal care group (whereby the mean maternal care score of the medium care group lay below Parker's²⁰ cut-off score for high care), the expected negative linear relation between care and cortisol stress responsivity did become apparent. It could thus be argued that our initial hypothesis was not completely falsified, and that the relatively increased cortisol stress response in the medium maternal care group indicates a higher probability to process everyday stressors as a threat to the self. At the same time, the psychological profile (scores of self-esteem, depression and anxiety) of the medium care participants points to a psychologically normal, stable group. We thus suggest that the medium maternal care group displayed what would be considered an average and adaptive cortisol response to the TSST. This view is supported by a comparison with earlier work from our laboratory using the same TSST modification. Andrews and colleagues³³ showed a maximum saliva cortisol increase of 4.5 nmol/L in a 10-minute free speech TSST. Our medium maternal care group displayed a quite similar maximum cortisol increase of 3.6 nmol/L.

Finally, we observed reduced endocrine stress responsivity in the high maternal care group. We hypothesize that this reduced cortisol stress response might indicate resilience against perceiving everyday challenges as stressors. This view is supported by the fact that the high maternal care group exhibited relatively high levels of self-esteem, and low levels of depression and trait anxiety. Our group has shown in previous studies that high levels of self-esteem are associated with lower cortisol stress responsivity and quicker stress habituation.^{7,9,34,35} Subjective psychological stress measures again provide partial support for the above reasoning, since the high maternal care group exhibited the numerically lowest levels of poststress tension and anger on the POMS. As a guiding hypothesis for future studies, we suggest that the high maternal care group participants formed an optimally adapted group with the necessary psychological resources to buffer the potentially threatening social evaluation induced by the TSST.

We found no group differences with respect to heart rate and subjective psychological stress measures. However, given the unspecific nature of cardiovascular responses and the recurrent difficulty of TSST studies to establish stable associations between endocrine, cardiovascular and subjective psychological stress parameters,^{7,8,36-38} it is not surprising that group differences in the cortisol stress response were not confirmed by heart rate and POMS data.

The TSST repetition revealed almost identical between-group patterns of cortisol, heart rate and subjective psychological stress responsivity as found on the initial testing day. However, owing to habituation and the lack of 10 participants with relatively increased cortisol stress responses on the initial testing day, the maximum cortisol increase in the medium maternal care group was reduced from 3.6 to 1.5 nmol/L in response to the second TSST.

Limitations

There are several limitations to the current study. First, the question arises whether the self-perception of early-life maternal care reflects the actual perception of maternal care or whether this perception is influenced by the current state of the participant. In this context, long-term test-retest stability of PBI scores over intervals as long as 90 months was demonstrated (intraclass correlations ranged from 0.64 to 0.88, with a median of 0.77).³⁹ Also, PBI scores were shown to be stable despite significant changes in the level of depressed mood reported by depressed outpatients.³⁹ Congruent validity of PBI scores can be concluded from high agreement between care and overprotection scores obtained at the interview and determined by the PBI (Pearson correlations ranging between 0.77 and 0.78 for 2 different raters).¹⁹ Second, the factor sex was unequally distributed among maternal care groups, whereby the number of men with low maternal care was too small to allow introducing sex as a second between-group variable. With respect to cortisol stress responsivity, we could, however, confirm the pattern of results found in the whole group in the women only. Given the influence of gonadal steroids on HPA axis stress responsiveness,²¹ future studies will need to pay closer attention to potential sex differences among maternal care groups. Third, several participants did not provide information on intra- and extrafamilial traumatic stress experiences in childhood and adolescence. Thus, although the occurrence of traumatic stress experiences did not differ significantly among maternal care groups, we cannot say with certainty that the effect of maternal care was independent of early-life trauma. Finally, our interpretation of the observed endocrine patterns in the 3 maternal care groups is speculative. A more thorough assessment of the HPA axis (by measuring endocrine markers apart from cortisol and employing stimulation tests other than the TSST) in future studies will allow a more critical examination of the present interpretations. Also, longitudinal studies starting in childhood or adolescence will have to provide evidence for the hypothesis that individuals with low maternal care experiences initially demonstrate a hyperresponsive HPA axis, which becomes hyporesponsive over time.

Conclusion

Taken together, this study presents novel data by showing an inverted u-shaped relation between early-life maternal care and cortisol stress responsivity. We suggest that these findings can be interpreted as signs of long-term HPA axis regulation changes in response to early-life experiences. Altogether, a

dissociation between endocrine and psychological parameters within 3 maternal care groups became apparent. Whereas low and high maternal care group participants exhibited similar endocrine stress responses, their psychological profiles were opposed. Medium and high maternal care group participants, on the other hand, exhibited similar psychological profiles, whereas their endocrine stress responses were opposed. We suggest that in the future, screening for a blunted cortisol stress response in combination with psychological assessment might contribute to the identification of vulnerable individuals before the manifestation of stress-related psychopathology.

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