Early neglect and abuse predict diurnal cortisol patterns in adults
A study of international adoptees

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1. Introduction

Children who experience neglect or abuse in early childhood are at increased risk for psychiatric problems in
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2. Methods

2.1. Sample and procedure

The sample was derived from a study on international adoptees who were born outside The Netherlands and had been legally adopted by non-relatives in The Netherlands between January 1972 and December 1975. Before adoption, many of the participants in our study had lived under dreadful circumstances. For example, several of them had been extremely malnourished, had suffered from severe physical diseases, or had received hardly any emotional warmth. Half of our sample of international adoptees had come from Korea, Colombia and India; the others came from countries including Indonesia, Bangladesh, Lebanon and Austria.

The adoptive parents of these international adoptees had been approached for participation in research in 1986 (baseline) and 1989–1990 (Time 2). The adopted children of the parents who had participated at baseline were contacted between 1999 and 2002 (Time 3). The details of the sampling procedures are reported elsewhere (Verhulst et al., 1990a; Tieman et al., 2005).

Between January 2004 and February 2006, we sought contact with the 1521 adult adoptees who had participated in the third assessment, except for five individuals who had died, 50 who had emigrated, 10 who had requested at an earlier stage to be removed from the sample, and 77 who were untraceable. Of the 1379 subjects approached, 365 refused to participate and 133 did not respond, leaving 881 who participated (60.1% corrected response rate).

Participants were asked to provide four saliva samples; 831 of them eventually providing saliva (at one or more time point) sufficient for analyses. Because reported information on both forms of early maltreatment was uncertain or missing for 130 of these participants, the people concerned were not included in the sample. This left 701 participants.

Of these 701 participants, 31 used corticosteroid-containing medication, 32 were pregnant, and 13 had extreme outliers in cortisol values (above four standard deviations (SDs) of the mean cortisol levels). Furthermore, the cortisol diurnal rhythms of two participants were reversed; the saliva samples had probably been swapped. These 78 subjects were excluded from analyses, leaving 623 participants. Furthermore, five cortisol samples were excluded because of extreme non-compliance in the time of sampling. Two of these were from people whose daily rhythm had shifted due to breastfeeding, and three were from people who were not compliant with the timing of one of the morning values (more than 50 min between the two cortisol assessments).

This left 623 participants for analyses, and between 601 and 608 valid measurements per sampling moment. Of these 623 adoptees, 345 were women (55.4%). Participants were on average 30.8 years old, and had been adopted at a mean age of 27.0 months. A large group had experienced early maltreatment: 104 had experienced severe neglect, 173 some neglect, and 298 no neglect. Fifteen had experienced severe abuse, 39 some abuse, and 436 no abuse. No information was available on neglect for 48 participants or on abuse for 133 participants; in most cases this was due to uncertainty about maltreatment.
2.2. Measurements

2.2.1. Demographic variables
At baseline, questionnaires had been used to establish the child’s gender, birth date, and age at placement (in months) in the adoptive family.

2.2.2. Early neglect and abuse
At baseline, adoptive parents had been asked about any neglect and abuse of their children before adoption using one question for each form of maltreatment. Because the Dutch term used in the question on abuse did not cover sexual or emotional abuse as well as it covered physical abuse, most abuse was physical. Neglect was specified as physical neglect; typically, it included a failure to provide basic needs, and manifested itself in results such as malnourishment. These questions at baseline referred to neglect or abuse prior to adoption; adoption was therefore not equal to neglect or abuse. Neglect and abuse were both measured using a three-point scale indicating “no”, “somewhat”, or “severe” neglect or abuse. The described definition and classification of the severity of maltreatment was applied in previous studies. In these studies, a relationship was found between the level of early maltreatment and the level of later maladjustment (Verhulst et al., 1992; Van der Vegt et al., in press).

Because information on early adverse experiences is often missing or uncertain (Verhulst et al., 1992; Fensbo, 2004), we asked adoptive parents if they were certain of their answer after each question about maltreatment. Parents had based their information about maltreatment on official documents provided by the adoption organization, on their own observations of the circumstances in the land of origin, or on the state of the child directly after adoption. In our analyses, we used only information about which the adoptive parents were certain.

2.2.3. Adult psychiatric problems
At the third assessment, at an average age of 26.3 years, 2.2.4. Parental rearing after adoption
In the third assessment round, adoptees filled out the short version of the Egna Minnen Betravande Uppfostran (s-EMBU; Perris et al., 1980; s-EMBU; Arrindell et al., 1999), a standard questionnaire to measure parental rearing. Its 23 items can be scored on a four-point scale and can be summarized in three reliable and valid scales: Rejection, Emotional Warmth and Protection or Overprotection (Arrindell et al., 1999). Items and scales are determined for mothers and fathers separately. s-EMBU scores relevant to this study were available for 591 of the participants included.

2.2.5. Cortisol
Cortisol levels were assessed in saliva. Salivary cortisol levels reflect the biologically active or unbound fraction of cortisol and can be collected in a noninvasive, stress-free manner in the natural environment (Kirschbaum and Hellhammer, 1994). We sent participants “Salivette” sampling devices (Sarstedt BV, Etten-Leur, The Netherlands) to their homes, accompanied by a written instruction. The Salivette sampling device consists of a standard centrifugation tube with a suspended insert containing a sterile neutral cotton-wool swab; to obtain a sufficient amount of saliva, the swab has to be chewed for 45 s.

To account for the typical diurnal rhythm of cortisol secretion, participants were instructed to collect four saliva samples at specific time points over the day. Times of collection were as follows: Cortisol 1: shortly after waking up (still lying in bed; mean time of 8.10 h (interquartile range: 7.03–9.03 h)), Cortisol 2: 30 min later, Cortisol 3: at 3:00 PM, and Cortisol 4: just before going to bed (mean time of 23.23 h (interquartile range: 22.30–00.05 h)).

Participants were instructed not to eat or brush their teeth 15 min before sampling, and to note the date and time of collection, the use of corticosteroids, and whether they were pregnant. They were asked to mail their used Salivette sampling devices to the institute as soon as possible, where the samples were centrifuged and stored at −80 °C. For analysis, all samples were sent in a single batch (frozen, by courier) to the laboratory (Biopsychology, TU Dresden, Germany), where cortisol concentration was determined by luminescence immunoassay. The intra-assay and inter-assay coefficients of variation were under 8%.

2.3. Attrition
Selective attrition was investigated by comparing the 701 participants who had provided saliva samples with the non-responders who had not collected these data. The non-responders were the remaining adoptees who had participated in the third assessment (N = 820), with the exception of the participants who had died (N = 5), had emigrated (N = 50), or had missing data on early maltreatment, mostly due uncertainty of the information (N = 181), and were thus not eligible for the present study. The only characteristic to differ between participants and non-responders was that of reported moderate and severe neglect; this difference was marginal (participants versus non-responders: no neglect: 52.2% versus 56.2%; some neglect: 29.4% versus 22.9%; and severe neglect: 18.4% versus 20.9%; $\chi^2 = 6.08, df = 2, p = 0.048$). Non-participants did not differ significantly from the participants with respect to gender, age, age of placement in the adoptive family, parental socioeconomic status, the abuse experienced, or the psychiatric problems as measured by the YASR.

2.4. Statistical analyses
A large group of the adoptees experienced early maltreatment; the different forms of early maltreatment frequently
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Co-occur (Paz et al., 2005). In our sample, all but four abused participants were also neglected to some extent, whereas many neglected adoptees had not been abused. We therefore studied the independent effect of neglect and the effect of abuse in addition to neglect (termed "abuse") in two mutually exclusive groups.

Due to the nature of our sample, and also because we wanted to study the specific contribution of early maltreatment, we made several adjustments in our analyses. We selected covariates on the basis of theoretical criteria. For example, because children who were older at placement were more likely to have been maltreated (Verhulst et al., 1990b), we included age at placement as a covariate. We also included actual time in addition to time from wake-up, because daylight is known to influence cortisol levels (Gunnar and Vazquez, 2006). Furthermore, associations have been found between gender and cortisol secretion, and age and cortisol secretion, although results are sometimes inconsistent (see for a review Gunnar and Vazquez, 2006).

Because there was only a very modest association between age at sampling and age at placement (r = 0.24) we were able to adjust for both. Because we wanted to examine whether early maltreatment has a direct effect on cortisol levels, and to rule out the possibility that this relationship is mediated by the impact of maltreatment on mental health, we corrected for YASR Total Problems scores. Covariates were entered simultaneously.

Because cortisol levels were not normally distributed, all values were square root-transformed to achieve a more normal distribution.

For descriptive purposes only, we performed analyses of covariance (ANCOVs), entering early neglect or abuse as a predictive variable and the four untransformed cortisol values separately as dependent variables. These data are presented in the figures. We adjusted for actual time of assessment, gender, age, age of placement and YASR Total Problems scores.

We used a formula to calculate the area under the curve (AUC) with respect to the first two cortisol assessments: CARAUC = [(C2 + C1) * (T2 - T1)]/2 with C = cortisol and T = actual time in minutes of the two time points. This formula is widely used in the literature to assess the cortisol awakening response (e.g. Sondeijker et al., 2007).

To study the level and slope of the cortisol secretion, we used multilevel analyses (Boyle and Willms, 2001; Blackwell et al., 2006). Within the multilevel models, repeated cortisol measurements (level 1) are nested within the individual (level 2), which accounts for both intra-individual and inter-individual variability in cortisol levels. Subsequently, cortisol day-curves of participants can be summarized for groups of individuals who have experienced a certain degree of early maltreatment. A benefit of the multilevel analyses is the scope it provides for using information on adoptees with missing data at one or more time point, which enhances the power of the analyses. Multilevel analyses were performed using the MIXED procedure in SPSS 12.0. Following the same procedure, we generated two multilevel models with neglect or abuse as predictor and the cortisol levels (first, third, and fourth measurement) as the outcome. Next to intercepts at the fixed and the random level, we included several other parameters in the models: severity of early maltreatment, time, the interaction between severity of early maltreatment and time, time², actual time at the measurements, age, gender, age of placement, and YASR Total Problems score.

The parameter "time" was defined as the relative time in hours from wake-up. Custom Hypotheses Tests were used to determine differences in level and shape of the cortisol rhythms between different categories of early childhood maltreatment.

Because YASR Total Problems scores were available for only 598 participants, we re-ran analyses including all 623 participants without adjusting for this covariate. To control for the effect of parental rearing after adoption, we additionally included the s-EMBU scores as confounders.

Post hoc, we compared the effects of abuse and neglect with regard to the cortisol awakening response, and the level and slope of the cortisol diurnal rhythm.

3. Results

Table 1 presents participants’ characteristics with respect to the two forms of early maltreatment. To provide greater insight into the results, we present these characteristics separately for the categories defined by the severity of neglect or abuse, and compare them according to these categories. Whereas characteristics of study participants did not differ with regard to the categories of neglect, various characteristics of participants who had been abused varied from those of participants who had not. In particular, children who had been abused were older at the time of adoption. Possibly, the older a child had been at placement, the longer he or she had been subjected to negative environmental influences, and the higher the risk is that he or she had experienced moderate or severe maltreatment. The characteristics were controlled for in analyses.

Figs. 1 and 2 show the mean untransformed cortisol levels at the four assessment times according to the categories of severity of the reported neglect and abuse in addition to neglect. The results for the cortisol awakening response, after transformation, are shown in Table 2. The cortisol secretion in participants who were reported to be severely maltreated early in life showed a smaller cortisol awakening response than in non-maltreated participants (CARAUC: severe neglect: B = -0.18; 95% CI = -0.35; -0.02; p = 0.03; severe abuse: B = -0.45; 95% CI = -0.81; -0.09; p = 0.02; B represents the difference between groups).

Table 3 presents the final models of multilevel analyses. Basal cortisol levels in participants who had allegedly experienced severe neglect were lower than in controls (p = 0.0002). Severely neglected participants had a flatter diurnal slope than those who had not been neglected; this was indicated by the significant interaction term between severe neglect and time of day (p = 0.002).

In participants who had allegedly experienced severe abuse, basal cortisol levels were lower than in controls (p = 0.002). The relationship between reported severe abuse and a flatter diurnal slope just fell short of significance (p = 0.08). However, the levels of the cortisol day-curve were higher in moderately abused participants than in adoptees who had not experienced abuse (p = 0.003). The diurnal slope was also steeper in moderately abused adoptees than in non-abused adoptees (p = 0.01).
Next, we compared the effects of abuse and neglect on the cortisol measures. Adoptees who experienced abuse did not differ from adoptees who experienced neglect with respect to the cortisol awakening response. However, alleged childhood abuse had a stronger impact than neglect on the cortisol diurnal rhythm. Adoptees who experienced some abuse had higher cortisol levels than adoptees who experienced neglect (estimate (SE) and $p$-value: 0.44 (0.14), $p = 0.002$), whereas adoptees who experienced severe abuse had lower cortisol levels (estimate (SE) and $p$-value: $-0.51$ (0.21), $p = 0.01$). Furthermore, the diurnal slope of somewhat abused adoptees was steeper than in neglected adoptees (estimate (SE) and $p$-value: $-0.04$ (0.01), $p = 0.001$). Thus, as compared to non-maltreated adoptees, abuse together with neglect consistently had a more marked effect on cortisol secretion than neglect only.

![Figure 1](image-url)  
Figure 1  Early neglect and the mean cortisol levels across the day. Note. Participants who had experienced abuse were excluded. Cortisol levels (in nanomoles per liter) are untransformed and were derived by separate ANCOVAs for each of the four instructed sampling times: $C_1$: cortisol directly after awakening; $C_2$: cortisol half an hour after awakening; $C_3$: cortisol at 3:00 PM; $C_4$: cortisol before going to bed. Results were corrected for actual time of assessment, gender, age, age of placement and YASR Total Problems score. Number of participants: no neglect, $N = 294$; some neglect, $N = 149$; severe neglect, $N = 86$. 

### Table 1a  Characteristics according to the severity of neglect.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>No neglect ($N = 294$; 51.7%)</th>
<th>Some neglect ($N = 149$; 26.2%)</th>
<th>Severe neglect ($N = 86$; 15.1%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Demographics</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gender, female</td>
<td>53</td>
<td>60</td>
<td>62</td>
</tr>
<tr>
<td>Age, in years $\pm$ SD (range)</td>
<td>30.8 $\pm$ 1.2 (28–34)</td>
<td>30.8 $\pm$ 1.2 (28–34)</td>
<td>31.0 $\pm$ 1.3 (28–34)</td>
</tr>
<tr>
<td>Age at placement, in months $\pm$ SD (range)</td>
<td>22.3 $\pm$ 24.8 (1–111)</td>
<td>25.1 $\pm$ 21.0 (1–114)</td>
<td>29.9 $\pm$ 19.9 (2–90)</td>
</tr>
<tr>
<td><strong>Adult psychiatric problems</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total Problems score $\pm$ SD (range)</td>
<td>35.8 $\pm$ 23.6 (2–117)</td>
<td>38.3 $\pm$ 25.0 (1–116)</td>
<td>36.9 $\pm$ 23.5 (5–102)</td>
</tr>
<tr>
<td><strong>Parental rearing after adoption</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rejection, mean $\pm$ SD, by mother; father</td>
<td>9.6 $\pm$ 3.7; 9.1 $\pm$ 2.8</td>
<td>10.1 $\pm$ 3.4; 9.4 $\pm$ 2.7</td>
<td>11.0 $\pm$ 5.6; 9.5 $\pm$ 3.5</td>
</tr>
<tr>
<td>Emotional Warmth, mean $\pm$ SD, from mother; father</td>
<td>18.9 $\pm$ 3.9; 18.5 $\pm$ 3.7</td>
<td>18.3 $\pm$ 4.1; 18.0 $\pm$ 4.1</td>
<td>17.8 $\pm$ 4.2; 17.9 $\pm$ 3.6</td>
</tr>
<tr>
<td>(Over)Protection, mean $\pm$ SD, by mother; father</td>
<td>20.1 $\pm$ 5.1; 18.4 $\pm$ 4.4</td>
<td>20.1 $\pm$ 4.6; 18.3 $\pm$ 4.4</td>
<td>20.4 $\pm$ 5.7; 18.3 $\pm$ 4.8</td>
</tr>
<tr>
<td><strong>Basal cortisol levels (no comparisons between groups were made)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cortisol 1, in nmol/L $\pm$ SD</td>
<td>11.6 $\pm$ 6.2</td>
<td>12.3 $\pm$ 6.9</td>
<td>9.6 $\pm$ 5.5</td>
</tr>
<tr>
<td>Cortisol 2, in nmol/L $\pm$ SD</td>
<td>15.1 $\pm$ 7.9</td>
<td>16.9 $\pm$ 9.7</td>
<td>14.1 $\pm$ 8.6</td>
</tr>
<tr>
<td>Cortisol 3, in nmol/L $\pm$ SD</td>
<td>5.1 $\pm$ 3.4</td>
<td>4.7 $\pm$ 3.4</td>
<td>4.6 $\pm$ 3.2</td>
</tr>
<tr>
<td>Cortisol 4, in nmol/L $\pm$ SD</td>
<td>1.6 $\pm$ 2.0</td>
<td>1.6 $\pm$ 2.2</td>
<td>2.2 $\pm$ 2.9</td>
</tr>
<tr>
<td>CAR, increase of at least 2.5 nmol/L, $N$ (%)</td>
<td>147 (50.0)</td>
<td>85 (46.4)</td>
<td>36 (41.9)</td>
</tr>
<tr>
<td>CAR, any increase, $N$ (%)</td>
<td>187 (63.6)</td>
<td>112 (61.2)</td>
<td>57 (66.3)</td>
</tr>
</tbody>
</table>

*Note. Participants who had experienced abuse were excluded. SD: standard deviation; Cortisol 1: cortisol directly after awakening; nmol/L: nanomoles per liter; Cortisol 2: cortisol half an hour after awakening; Cortisol 3: cortisol at 3:00 PM; Cortisol 4: cortisol before going to bed; CAR: cortisol awakening response.*
4. Discussion

The present study used a large adult sample to demonstrate that reported maltreatment is associated with levels of cortisol under basal conditions. The nature of this relationship is determined by the level of severity of early maltreatment: whereas allegedly moderate maltreatment was associated with higher basal cortisol levels and a steeper diurnal slope, allegedly severe maltreatment was associated with lower levels and a flatter slope. As many participants

![Figure 2](image-url)  
Figure 2 Early abuse and the mean cortisol levels across the day. Note. All participants experienced abuse in addition to neglect. We excluded four participants who were allegedly abused but not neglected. Cortisol levels (in nanomoles per liter) are untransformed and were derived by separate ANCOVAs for each of the four instructed sampling times: C1: cortisol directly after awakening; C2: cortisol half an hour after awakening; C3: cortisol at 3:00 PM; C4: cortisol before going to bed. Results were corrected for actual time of assessment, gender, age, age of placement and YASR Total Problems score. Number of participants: no abuse, N = 436; some abuse, N = 35; severe abuse, N = 15.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>No abuse (N = 436; 70.4%)</th>
<th>Some abuse (N = 35; 5.7%)</th>
<th>Severe abuse (N = 15; 2.4%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Demographics</td>
<td></td>
<td></td>
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<tr>
<td>Gender, female (%)</td>
<td>57</td>
<td>31**</td>
<td>60</td>
</tr>
<tr>
<td>Age, in years ± SD (range)</td>
<td>30.7 ± 1.3 (28–35)</td>
<td>31.5 ± 1.5 (28–33)*</td>
<td>31.3 ± 1.3 (28–34)*</td>
</tr>
<tr>
<td>Age at placement, in months ± SD (range)</td>
<td>22.7 ± 23.3 (1–111)</td>
<td>53.1 ± 22.9 (4–92)***</td>
<td>49.2 ± 16.2 (24–73)***</td>
</tr>
<tr>
<td>Adult psychiatric problems</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total Problems score ± SD (range)</td>
<td>36.4 ± 24.1 (1–117)</td>
<td>32.9 ± 25.7 (0–121)</td>
<td>40.9 ± 32.0 (9–110)</td>
</tr>
<tr>
<td>Parental rearing</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rejection, mean ± SD regarding to mother; father</td>
<td>9.6 ± 3.7; 9.1 ± 3.7</td>
<td>10.5 ± 3.7; 9.6 ± 2.8</td>
<td>11.1 ± 5.0; 9.9 ± 3.8*</td>
</tr>
<tr>
<td>Emotional Warmth, mean ± SD regarding to mother; father</td>
<td>18.9 ± 3.9; 18.5 ± 3.9</td>
<td>18.0 ± 4.1; 17.6 ± 4.1</td>
<td>17.6 ± 4.1; 17.4 ± 4.1*</td>
</tr>
<tr>
<td>(Over)Protection, mean ± SD regarding to mother; father</td>
<td>20.1 ± 5.1; 18.4 ± 4.4</td>
<td>20.5 ± 4.6*; 18.6 ± 4.1</td>
<td>21.0 ± 5.8*; 18.9 ± 5.1*</td>
</tr>
<tr>
<td>Basal cortisol levels (no comparisons between groups were made)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cortisol 1, in nmol/L ± SD</td>
<td>11.7 ± 6.5</td>
<td>14.2 ± 6.8</td>
<td>8.2 ± 5.1</td>
</tr>
<tr>
<td>Cortisol 2, in nmol/L ± SD</td>
<td>15.3 ± 8.6</td>
<td>16.6 ± 11.5</td>
<td>11.5 ± 8.2</td>
</tr>
<tr>
<td>Cortisol 3, in nmol/L ± SD</td>
<td>5.0 ± 3.5</td>
<td>4.5 ± 2.2</td>
<td>4.1 ± 3.4</td>
</tr>
<tr>
<td>Cortisol 4, in nmol/L ± SD</td>
<td>1.7 ± 2.1</td>
<td>1.1 ± 1.4</td>
<td>1.3 ± 0.8</td>
</tr>
<tr>
<td>CAR, increase of at least 2.5 nmol/L, N (%)</td>
<td>212 (48.6)</td>
<td>14 (40.0)</td>
<td>6 (40.0)</td>
</tr>
<tr>
<td>CAR, any increase, N (%)</td>
<td>267 (61.2)</td>
<td>20 (57.1)</td>
<td>10 (66.7)</td>
</tr>
</tbody>
</table>

Note. All participants experienced abuse in addition to neglect. Four participants, allegedly abused but not neglected, were excluded. SD: standard deviation; Cortisol 1: cortisol directly after awakening; nmol/L: nanomoles per liter; Cortisol 2: cortisol half an hour after awakening; Cortisol 3: cortisol at 3:00 PM; Cortisol 4: cortisol before going to bed; CAR: cortisol awakening response.

* Because of missing information about neglect, the categories of no, some and severe neglect do not add up to 100%; this information was missing for 113 participants, due especially to uncertainty. Characteristics differ significantly compared to the characteristics of no abuse at *p < .05; **p < .01; ***p < .001.
had experienced neglect or the combination of abuse and neglect, but all had later been raised in another environment, the data suggest that these effects on cortisol were lasting effects of maltreatment that had taken place in early life. No meaningful change to these results was produced by adjusting for parental rearing after adoption.

Research to date has focused mainly on the effects of abuse on basal cortisol level; the results of few studies on neglected participants have been inconsistent. Whereas severely deprived institutionalized children are reported to have low early-morning cortisol levels and a general lack of diurnal variation, there is an indication that, after adoption, their cortisol day-curves can normalize (Gunnar and Vazquez, 2001, 2006) or even become slightly elevated (Gunnar and Vazquez, 2001, 2006). It has therefore been suggested that basal cortisol levels may be less strongly affected by early neglect than by early abuse (Gunnar and Vazquez, 2006). In the present study, however, we found a clear relationship of early neglect with cortisol levels in adulthood.

In participants whose adoptive parents had reported a combination of severe abuse and neglect, basal cortisol levels were lower than in participants whose adoptive parents were certain that no abuse or neglect had occurred. This is in line with the literature on adults who were abused as children; for example, Roy (2002) reported low 24-h urinary free cortisol (UFC) production in abstinent cocaine-dependent adults who had experienced emotional neglect or were sexually abused as children. Similarly, Yehuda et al. (2001) observed low 24-h UFC secretion in adults who were offspring of Holocaust survivors and had been emotionally abused in childhood. Furthermore, in accordance with some previous studies in maltreated children, a flat diurnal rhythm was seen in participants with reported severe neglect (Cicchetti and Rogosch, 2001a; Gunnar et al., 2001; Weissbecker et al., 2006). However, a different pattern emerged from our own investigation of moderately severe early maltreatment, the adults in our study showing hypercortisolism in the morning and a steeper diurnal incline than non-abused or non-neglected persons. If these are not chance findings and they are consistent for neglect and abuse, they strongly suggest that the level and slope of cortisol secretion we observed are related to the severity of the early neglect or abuse.

We can only speculate on the determinant of this differential effect of maltreatment severity. One possibility is that the development of the HPA axis after maltreatment is similar to that in the pancreas of obese persons during progression to type 2 diabetes. Obesity typically co-occurs with insulin resistance that is compensated by insulin hypersecretion by the pancreatic β cells. However, in severely

### Table 2 Early maltreatment and the cortisol awakening response.

<table>
<thead>
<tr>
<th>Neglect only</th>
<th>N</th>
<th>CARAUC Means (SE)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>277</td>
<td>2.15 (0.04)</td>
</tr>
<tr>
<td>Some</td>
<td>134</td>
<td>2.25 (0.06)</td>
</tr>
<tr>
<td>Severe</td>
<td>75</td>
<td>1.96* (0.07)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Abuse with neglect</th>
<th>N</th>
<th>CARAUC Means (SE)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>408</td>
<td>2.17 (0.03)</td>
</tr>
<tr>
<td>Some</td>
<td>31</td>
<td>2.28 (0.12)</td>
</tr>
<tr>
<td>Severe</td>
<td>13</td>
<td>1.72* (0.18)</td>
</tr>
</tbody>
</table>

Significantly different from ‘No’ at *p < .05.

Note. Neglect signifies neglect only, i.e., without abuse. Participants whose parents had reported both abuse and neglect were excluded from these analyses. Abuse signifies abuse in addition to neglect. We excluded four participants who were allegedly abused but not neglected.

We performed separate ANCOVAs corrected for actual time of assessment(s), gender, age, age of placement, YASR Total Problems score. CARAUC values are based on square root-transformed cortisol values. SE: standard error; CARAUC: cortisol awakening response area under the curve.

### Table 3 Final multilevel models: early maltreatment as a predictor of diurnal cortisol level and slope.

<table>
<thead>
<tr>
<th></th>
<th>Neglect only Estimates (SE)</th>
<th>Abuse with neglect Estimates (SE)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intercept</td>
<td>1.28 (0.87)</td>
<td>0.96 (0.90)</td>
</tr>
<tr>
<td>Early maltreatment</td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>Ref.</td>
<td>Ref.</td>
</tr>
<tr>
<td>Some</td>
<td>0.05 (0.073)</td>
<td>0.29* (0.13)</td>
</tr>
<tr>
<td>Severe</td>
<td>−0.33** (0.090)</td>
<td>−0.63** (0.20)</td>
</tr>
<tr>
<td>Early maltreatment × time</td>
<td></td>
<td></td>
</tr>
<tr>
<td>None × time</td>
<td>Ref.</td>
<td>Ref.</td>
</tr>
<tr>
<td>Some × time</td>
<td>−0.0092 (0.0073)</td>
<td>−0.039* (0.012)</td>
</tr>
<tr>
<td>Severe × time</td>
<td>0.028** (0.0088)</td>
<td>0.033 (0.019)</td>
</tr>
<tr>
<td>Time</td>
<td>−0.21*** (0.011)</td>
<td>−0.20*** (0.011)</td>
</tr>
<tr>
<td>Time^2</td>
<td>0.0041*** (0.00068)</td>
<td>0.0041*** (0.00069)</td>
</tr>
</tbody>
</table>

Neglect signifies neglect only, i.e., without abuse. Participants whose parents had reported both abuse and neglect were excluded from these analyses. Abuse signifies abuse in addition to neglect. We excluded four participants who were allegedly abused but not neglected. SE: standard error; time is the interval in minutes from reported time of awakening sample (C₁) to the current sample. The parameters that are shown are those of the fixed model. The final models further included the following covariates: actual time of assessments, gender, age, age of placement, YASR Total Problems score.

Cortisol values were square root-transformed.

* p < .05.

** p < .01.

*** p < .001.
obese persons, insulin compensation is insufficient and, in
time, is followed by β-cell failure and diabetic hyposecretion
of insulin (Kasuga, 2006; Prentki and Nolan, 2006). By ana-
logy, early maltreatment might stimulate the HPA axis, lead-
ing to hypersecretion of cortisol and, possibly, to a steeper
diurnal incline. However, the experience of profound mal-
treatment may result in the downregulation of the HPA axis,
leading to a lower set point of cortisol secretion and a flatter
day-curve, as seen in many adults who were severely abused
as children (Heim et al., 2001; Yehuda et al., 2001; Roy, 2002;
Weissbecker et al., 2006). To investigate this possibility and
the mechanism behind it, a longitudinally study is necessary
with reported measures. The consequences of hypocortiso-
lism to the individual should also be investigated; the litera-
ture has not only reported the well-known negative
symptoms such as high stress-sensitivity, pain and fatigue,
but has also suggested that moderate hypocortisolism may
have some protective effects (Fries et al., 2005).

There are several possible reasons that previous studies
did not find an effect of severity of early maltreatment on
cortisol secretion. The first is that because these studies did
not differentiate according to the severity of early maltreat-
ment, the effects of moderately severe abuse might not have
been noticed. Second, many studies in adults relied on retro-
spective self-reports of maltreatment in childhood (Heim
et al., 2000; Yehuda et al., 2001; Roy, 2002; Weissbecker
et al., 2006) and severe abuse is generally the best remem-
bered. It is also the case that the severity of early maltreat-
tment typically reflects the frequency and duration of the
experiences; because most maltreatment occurs within the
family environment (Cicchetti and Rogosch, 2001a), most
abused children generally stay in risk-increasing circum-
stances for much longer. In these previous studies, the
duration, frequency, and thus severity of maltreatment
may all have been higher. The third possible reason that
studies did not find an effect of severity of early maltreat-
ment on cortisol secretion involves the fact that early mal-
treatment in international adoptees is associated with
malnutrition and stunted growth, and that the degree of
growth retardation may be associated with diurnal cortisol
patterns (Gunnar and Vazquez, 2001; Rutter and O’Connor,
2004; Van Uzendoorn et al., 2007). Although the low cortisol
levels and flattened diurnal slopes have been found to
recover after adoption, it is not yet known whether adult
cortisol patterns normalize completely after severe malnu-
trition and stunted growth (Gunnar and Vazquez, 2001).
Because we do not have growth data, we are unable to
consider this possibility in more detail.

Any of these three processes might explain why our study
found a clearer effect of reported early maltreatment on
cortisol patterns than other studies. However, these possible
explanations do not rule out the importance of other factors
put forward in previous research, such as the age at cortisol
assessment, or the duration between early maltreatment and
the measurement of basal cortisol levels.

4.1. Limitations

The data presented here have five main limitations. The first
concerns the lack of precision in the assessment of early
maltreatment: to obtain information on the possibility of
early adverse experiences before adoption, we asked adop-
tive parents a single question per form of maltreatment at
baseline. Our results would have been more complete if we
had been able to obtain information that covered not just the
severity of maltreatment, but was also more specific, includ-
ing factors such as the frequency, duration, age of onset, or
perpetrator type. And even though his information was
recorded almost 20 years before the cortisol assessments,
the retrospective nature of the questions may have intro-
duced reporting bias (Horwitz et al., 2001).

The second limitation is that we had no information on
other stressful events and trauma exposure throughout life.
Similarly, the discontinuity of maltreatment in the adoptees
was assumed, and only partly examined. However, it is very
likely that the dreadful circumstances under which many
maltreated participants had lived were dramatically
improved by adoption into different environment. The
results were not significantly changed by our correction for
parental rearing after adoption, but this only partially
controls for circumstances and events after adoption.

The third limitation is the substantial attrition. Consider-
ing the nature of the sample, however, such attrition is not
unusual. The prevalence of reported moderate and severe
neglect differed marginally between participants and non-
responders, with more severe neglect in the non-responder
group. If the cortisol patterns in severely neglected non-
participants were different from those in severely neglected
participants, which we cannot verify, this might have
affected our results, leading us to underestimate the asso-
ciation between severity of neglect and cortisol secretion.

The fourth possible limitation is that saliva samples were
obtained at home. Although this provided an opportunity
to measure basal cortisol levels in a natural environment,
without stresses from a visit to the laboratory, the home
assessment meant that we could not control the sampling
procedure. Even though specific instructions were supplied,
compliance in collecting saliva samples at specific times at
home can be poor (Kudielka et al., 2003). And even though
more reliable measurements can be obtained by collecting
salivary diurnal cortisol over several days (ideally 3–4 days;
Kraemer et al., 2006), we were able to collect salivary
cortisol on only one day. This probably made our estimates
less precise. If intra-individual variance is related to mal-
treatment, it might introduce bias. Our statistical control
for the effect of daylight on cortisol levels was limited
because the season of measurement, which determines
the amount of daylight was not controlled for. However,
itis unlikely that the effect of daylight is related to the level
of early maltreatment and therefore it is not likely to bias
results.

Finally, the extent to which results can be generalized is
debatable. All analyses were performed within a group of
international adoptees, because in this group severe adverse
experiences are common in early childhood and presumably
less common later in life. Furthermore, non-maltreated and
non-adopted persons would be no suitable reference group
for maltreated adoptees. To judge whether the results are
generalizable, it is not important whether or not adoption
has an effect on cortisol levels, but whether or not adoption
and maltreatment interact to determine cortisol levels.
Indeed, if factors such as malnutrition and stunted growth
play an important role in the relationship between early
maltreatment and cortisol secretion, the nature of the sam-
ple might have influenced the effect of maltreatment, thus limiting the generalizability.

5. Conclusions

Investigating the long-term relationship between reported early maltreatment and the stress-system in a large adult sample of international adoptees, the present study found that neglect and abuse together with neglect early in life predicted alterations of the HPA axis, even if another environment was experienced after the early maltreatment. Profound maltreatment was related to lower cortisol levels and a flatter day-curve, whereas less severe early maltreatment was associated with higher levels of cortisol and a steeper diurnal decline.

Role of the funding source

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Conflict of interest

All authors declare that they have no conflicts of interest.

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