Early childhood aggression

Alink, L.R.A.

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Cortisol and aggression in children and adolescents: Review and meta-analyses of the inverse relation of basal cortisol and cortisol reactivity with aggression

Alink, L.R.A., Van IJzendoorn, M.H., Mesman, J., Bakermans-Kranenburg, M.,J., Juffer, F., Stolk, M.N., Van Zeijl, J., & Koot, H.M.

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Abstract

An inverse relation between cortisol (reactivity) and aggression has been hypothesized, but research findings seem equivocal. We reviewed the literature concerning cortisol and aggression in children and adolescents, and tested the hypo(re-)activity hypothesis in two meta-analyses, one for basal cortisol level (k = 28 studies, N = 1,658) and one for cortisol reactivity to a stressor (k = 12 studies, N = 671). No evidence for the hypothesized association between cortisol reactivity and aggression was found. Aggression was however associated with high basal cortisol (hyperactivity) in preschoolers, and with low basal cortisol (hypoactivity) in both school-aged children and children with clinical levels of problem behavior, which points to changes in functioning of the HPA axis in specific groups of children.

Introduction

In the past two decades, an increasing number of studies have investigated biological correlates of aggressive behavior. The hypothalamic-pituitary-adrenal (HPA) axis - with cortisol as its primary hormonal product in humans - is one of the biological systems that have been the focus of these studies. Researchers have investigated aggression in relation to basal levels of cortisol as well as to the change in cortisol levels in reaction to a stressor. Leading hypothesis is the hypo(re-)activity of the HPA axis in children and adolescents with elevated levels of aggression (e.g., Lahey, McBurnett, Loeber, & Hart, 1995; Van Goozen, 2005). A large number of studies proposed an inverse relation between basal cortisol levels and aggression, but findings so far have been equivocal. Results of studies associating cortisol reactivity with aggressive behavior are even more diffuse. Aims of the present study are (1) to review the literature concerning basal cortisol levels and cortisol reactivity in relation to aggressive behavior in children and adolescents, and (2) to test the hypo(re-)activity hypothesis in two separate meta-analyses, one for basal cortisol level and one for cortisol reactivity.

Several studies hypothesized that lower basal cortisol levels and lower cortisol reactivity are associated with higher rates of aggression (e.g., McBurnett, Lahey, Capasso, & Loeber, 1996; Oosterlaan, Geurts, Knol, & Sergeant, 2005; Pajer, Gardner, Rubin, Perel, & Neal, 2001; Scerbo & Kolko, 1994; Schulz, Halperin, Newcorn, Sharma, & Gabriel, 1997; Van Bokhoven et al., 2005; Van de Wiel, Van Goozen, Matthys, Snoek, & Van Engeland, 2004; Wright, 2000). There are a number of theories that may explain this hypothesized inverse relation. Raine (1996) proposed several mechanisms underlying the association between reduced autonomic activity and aggressive behavior that may also be helpful in explaining low HPA activity in aggressive children. One mechanism may be that people who are characterized by low autonomic arousal, are predisposed to seek stimulation to compensate for the low levels of arousal. People with lower basal levels of cortisol may also be inclined to seek sensation or act aggressively in order to elevate their levels of cortisol and to get the pleasant feeling of arousal. The inverse relation between cortisol levels and aggression is also in line with the fearlessness theory formulated by Raine (1996). This theory claims that some children are more aggressive than others because they are less sensitive to stress and are less easily physiologically aroused, and therefore they have lower levels of anxiety. Because of these lower anxiety levels, these children engage more often in outgoing, aggressive behavior. It has also been hypothesized that cortisol is involved in processes involving the Behavioral Inhibition System (BIS) and the Behavioral Activating System (BAS) proposed by Gray (1975). Hypoactivity of the HPA axis may be an indication that the BIS is deficient (McBurnett et al., 1996). In case of a less active BIS compared to BAS, behavior is less likely to be inhibited in response to punishment, which may result in aggressive and antisocial behavior.

A theory concerning the relation between cortisol and aggressive behavior in general has been proposed by McBurnett, King, and Scarpa (2003). They argued that children with (aggressive) conduct problems are likely to have been exposed to prenatal and postnatal stress as a result of family circumstances, parenting, and parental characteristics (such as domestic violence, substance abuse, low socioeconomic status, or parental depression). These early stressors may cause

permanent alteration of the HPA axis and at the same time may be risk factors for the development of (aggressive) behavioral disorders.

There are several models considering the direction of the relation between cortisol and aggression. The functioning of the HPA axis can be viewed both as cause and consequence of behavior. Illustrative of modern biological perspectives on development is the perspective that hormones and behavior are mutually influencing each other and that this interaction can be both moderated and mediated by environmental factors (Susman & Ponirakis, 1997).

Not all empirical evidence regarding basal cortisol levels and reactivity in relation to aggressive behavior confirms the hypo(re-)activity hypothesis. For example, Van Bokhoven et al. (2005) concluded that basal levels of cortisol are *positively* related to aggression, and Granger, Weisz, and Kauneckis (1994) reported that *enhanced* cortisol reactivity to a stressor was associated with elevated levels of aggressive behavior. In addition, many studies presented nonsignificant relations between cortisol (reactivity) and aggression. In the first part of this paper, we review the literature on the relation between basal cortisol and cortisol reactivity on the one hand, and aggression on the other. In the second part, we test the hypothesized inverse relation of cortisol and cortisol reactivity with aggression in two separate meta-analyses, one for basal cortisol level and one for cortisol reactivity, and focus on various factors (characteristics of study sample and design) that may moderate this relation.

LITERATURE REVIEW

Method

Literature search

For the review and meta-analyses we systematically searched the electronic databases EconLit, ERIC, PAIS, PsychInfo, Science Citation Index Expanded, Social Sciences Citation Index, and Art & Humanities Citation Index with the key words *cortisol, adrenocortical, neuroendocrine, HPA,* combined with *aggress** (the asterisk indicates that the search contained, but was not limited to the word or word fragment). Second, the reference lists of the collected papers and dissertations were searched for relevant studies.

Studies were included if they reported adequate statistics on the relation between cortisol (reactivity) and aggression in children and adolescents (age range 0 to 19 years). Based on the definition proposed by Loeber and Hay (1997), we defined aggression as aversive behavior that may cause harm to people, objects, or animals, or threaten to do so. Thus, aggression only partly overlaps with the broader category of externalizing behaviors (Campbell, Shaw, & Gilliom, 2000). When studies reported on aggression, the measure that was used was carefully examined in order to assess whether it fitted our definition. Studies using a factor labeled *aggression* that consisted of scales or items inconsistent with this definition

were not included (e.g., Gunnar, Tout, De Haan, Pierce, & Stansbury, 1997), since it was not clear whether cortisol levels were related to aggression or to other types of aversive behaviors. Studies that compared groups that were selected on the basis of a variable that was only indirectly related to aggression were also excluded. For example, Blair, Peters, and Granger (2004) compared cortisol levels of children with a high/low activity of the Behavioral Activation System (BAS) and a high/low activity of the Behavioral Inhibition System (BIS), with BIS/BAS related to aggressive behavior. Another illustration is the comparison of cortisol levels of boys and girls, showing different levels of aggression (see Alink et al., 2006b [chapter 2]). This comparison does not provide information on the direct relation between cortisol and aggression. Including results of these types of studies, with ambiguous measures or indirect indications of aggression, would complicate interpretation of the results of the meta-analyses.

Regarding studies on cortisol reactivity, we included studies using different kinds of psychological stressors, such as a public speaking task, a test, or playgroup sessions with unfamiliar teachers and peers. We did not include studies that reported on HPA-reactivity to a chemical challenge (e.g., dexamethasone).

We found 34 studies with 40 outcomes that were relevant to our review and meta-analyses (24 studies with 28 outcomes concerning basal cortisol and 10 studies with 12 outcomes regarding cortisol reactivity, see Table 5.1). First, we review studies addressing basal cortisol and aggression. Next, specifics of the studies reporting on cortisol reactivity and aggression are presented.

Results

Basal cortisol

An inverse relation between basal cortisol values and aggressive behavior was reported in five studies. In these studies, lower cortisol values were related to higher levels of aggression. Within two studies, different measures of aggression were used that yielded different results. In both studies an inverse as well as a nonsignificant relation were reported, depending on the measure that was used. Three papers showed a positive relation between basal cortisol levels and aggression and in 14 studies no significant relation was found. Four of these reported (nonsignificant) statistics separately for boys and girls.

Most studies involved only boys. For example, Van Bokhoven et al. (2005) compared basal cortisol levels of boys showing at least one aggressive Conduct Disorder (CD) symptom (n = 39) to those of boys showing one or more covert CD symptoms (n = 22) between the ages of 14 to 16 years. A single saliva sample was assessed in the morning upon arrival at the laboratory when the boys were 13 years of age. Cortisol levels in the aggressive CD group were significantly higher than in the covert CD group.

One of the few studies that focused only on girls was conducted by Azar et al. (2004). They investigated salivary cortisol levels in 228 adolescent mothers (mean age = 17.2 years), 4 and 9 months after the birth of their child. A self report measure, obtained in the 7th month of pregnancy, was used to assess aggressive

CD symptoms. The relation between basal cortisol and aggressive CD was not significant.

Clinic-referred children were investigated by McBurnett and colleagues (McBurnett et al., 1996). These researchers assessed basal salivary cortisol and aggressive CD symptoms in a 4-year longitudinal study. Participants were boys diagnosed with CD, who were between 7 and 12 years of age at the outset of the study. Saliva for cortisol determination was collected in year 2 ($n = 63$) and year 4 of the study ($n = 42$). Every year, parents, teachers, and the children themselves rated the number of (aggressive) CD symptoms. Whereas the total number of covert CD symptoms was not related to cortisol level, the total number of aggressive CD symptoms was inversely related to the level of cortisol in both years.

In contrast to McBurnett et al. (1996), Shoal, Giancola, and Kirillova (2003) investigated cortisol levels of boys with *average* levels of problem behavior. Saliva was collected in the laboratory at ages 10 to 12 years and aggressive behavior was assessed at ages 15 to 17 years. Two self reports were used to assess aggressive behavior. The authors reported a significant negative association of resting cortisol with only one of these self reports.

The studies on basal levels of cortisol described thus far all had a longitudinal research design. However, the majority of the collected studies assessed cortisol levels and aggression concurrently. For example, Grayson (2001) investigated cortisol levels in a sample of 26 normally developing boys using a cross-sectional research design. The boys, aged 9 to 11 years, were divided into an aggressive and a nonaggressive group based on parent and teacher reports. The saliva samples obtained before watching a video were considered baseline samples. These cortisol values did not differ between the two groups.

In contrast to the aforementioned studies that all focused on the relation between cortisol levels and aggression in school-aged children or adolescents, Granger, Stansbury, and Henker (1994) investigated preschoolers. They examined salivary cortisol levels of 29 children who were 3 to 6 years of age, before (baseline) and after participation in an activity with unfamiliar peers and teachers. Global summary impressions of aggressive behavior were obtained from the research staff. No significant associations between baseline cortisol values and aggressive behavior were found.

Salivary cortisol measurement is a relatively easy, noninvasive technique. Most studies used this method to assess cortisol levels. However, some researchers collected blood samples in order to obtain levels of cortisol (Gerra et al., 1997, 1998; Pajer et al., 2001). Results from these studies concerning the relation between plasma cortisol levels and aggression were nonsignificant. In one of the studies of Gerra et al. (1997), 18- and 19-year-old boys were investigated. Based on several measures of aggression completed by the school teachers, a psychiatrist, and the adolescents themselves, the participants were divided into a group consisting of 15 boys with high to normal levels of aggression and a group of 15 boys with low to normal levels of aggression. No differences regarding pretask cortisol levels were found between the two groups. In another study, Gerra and colleagues (1998) focused on younger adolescents. Plasma cortisol levels of 30 highly aggressive 12-year-old boys before and after a stressor were compared to cortisol levels of boys showing low/medium levels of aggression. As was the case in the first study, several measures were used to assess aggressive behavior.

Again, baseline cortisol levels of these groups did not differ significantly.

In three papers, the relation between urine cortisol levels and aggressive behavior was reported (Granda, 1982; Montagner et al., 1978; Tennes & Kreye, 1985). In contrast to salivary or plasma cortisol, urinary free cortisol (UFC) is not an indication of the hormone level at a certain time point, but it reflects the integrated activity of the HPA axis over a period of time. As far as we know, Montagner et al. (1978) were the first authors who presented results on the relation between cortisol and aggression. They investigated behavioral profiles and levels of UFC in 147 children between 2 and 5 years of age. Behavioral profiles were based on extensive observations of interactions among the children. Cortisol levels of dominant-aggressive children were compared to those of leaders (children who were dominant but rarely showed spontaneous aggression). Children who had dominant aggressive behavior profiles had higher basal cortisol levels than children who were characterized as leaders.

Most studies assessed basal level of cortisol in a nonsocial situation at a laboratory or research center. Some researchers however, obtained samples for basal cortisol when the child had been in a situation with peers present. For example, Gunnar, Sebanc, Tout, Donzella, and Van Dulmen (2003) assessed morning and afternoon salivary cortisol levels of 76 children aged 3 to 5 years in a peer-group setting. The authors found an indirect path from teacher-rated aggression to cortisol via peer rejection. Children who had higher levels of aggression were more often rejected by peers and children who were rejected by peers had higher cortisol levels. Nevertheless, no significant direct relations between cortisol and aggression were found for either boys or girls. Another example of cortisol assessment in a peer-group setting is the study of Tout, De Haan, Campbell, and Gunnar (1998). HPA-functioning in 75 preschoolers attending child-care was examined. Saliva was collected during several days in the mornings and afternoons and behavior problems were rated by teachers. Daily average median cortisol levels were not significantly related to teacher-rated angry/aggressive behavior. This result was also obtained when data were analyzed separately for boys (n = 38) and girls (n = 37).

Our own research group investigated the relation between aggression and three basal levels of cortisol (morning, noon, evening), collected at home (Alink et al., 2006c). Aggressive behavior of 2-, 3-, and 4-year-old children (N = 130) was rated by independent observers (for the coding scheme, see Mesman et al., 2006). In addition, mothers completed a questionnaire regarding physical aggression of their child (see Alink et al., 2006b [chapter 2]). Log-transformed cortisol levels at all three times of the day were not significantly related to aggressive behavior for both boys (n = 70; observed aggression: r = -.04, r = -.04, r = .05; mother-rated aggression: r = .03, r = .09, r = .04, for the three time points, respectively) and girls (n = 60; observed aggression: r = .06, r = -.12, r = .14; mother-rated aggression: r = .22, r = .10, r = .08, for the three time points, respectively). The same analyses were also performed with possibly relevant covariates. Mothers in half of the sample had received an intervention in order to decrease the level of externalizing problem behavior of the child. In addition, level of cortisol was related to the time of day of the assessment. Adding condition (intervention or control) and time of day of assessment (and time difference between waking up and saliva collection for the morning samples) as covariates did not change our results.

Table 5.1

Studies included in the meta-analyses

Study	Sample size		Age (years) at cortisol assessment		Clinical sample	Aggression		Cortisol assessment			
	Total	Meta	*M*	Range		Informant	Instrument	Time	Measure (flow stim)	Setting baseline	Stressor
Alink et al., 2006[a e]	130	70 boys 60 girls	3.4 3.5	2.1-4.4 2.1-4.6	No	Mother, observer	PASEC, observation of physical aggr.	After wake-up, noon, around 7 pm	Saliva	Home	-
Alink et al., 2006[b e]	155	79 boys 76 girls	3.4 3.5	2.1-4.7 2.1-4.6	No	Mother, observer	PASEC, observation of physical aggr.	9.00 am, 12.00, or 3.00 pm	Saliva	University laboratory	Strange Situation Procedure
Azar et al., 2004[a]	228	170	17.2		No	Child	C-DIS aggr. items	10.00 and 10.30 am	Saliva	Laboratory	-
Blair et al., 2005[c]	169	169	5.1	3.8-5.7	No	Teacher	TOCA-R aggr. scale	9.00 a.m. or 3.30 pm	Saliva	Quiet testing area, Head Start center	Testing session
Fulgham, 2003[a]	75	67		5-7	No	Observers	Free-play coding sheet for aggr. behavior	Between 12.00 and 4.00 pm	Saliva (Kool-Aid)	University laboratory	-
Gerra et al., 1997[c]	30	30	18.7	18-19	No	Teacher, psychiatrist, adolescent	BDHI, clinical impression psychiatrist, VAS, teacher interview, MMPI, PDQ-R	Not reported	Plasma	Research center	Free-operant procedure to induce aggression
Gerra et al., 1998[c d]	30	30	12.7		No	Psychologist, child	Interview by psychologist, CPQ factor E	Between 4.00 and 6.00 pm	Plasma	Separate room at laboratory	Stroop Color-Word Interference Task, mental arithmetic, public speaking task
Granda, 1982[a e]	38	21 boys 17 girls	5	3-6	No	Observers: two high school students	PAVAR	8.30-11.30 am, 11.30 am-2.30 pm, and 2.30-5.30 pm	Urine	Preschool	-
Granger, Stansbury, et al., 1994[c]	29	29	4.7	3.4-6.7	No	Research staff	Staff dispositional impressions of aggr.	Between 4.00 and 7.30 pm	Saliva (Kool-Aid)	Research center, playing computer game	Playgroup sessions with unfamiliar teachers and peers

Granger, Weisz, et al., 1994[b]	102	102	12.1	7.0-17.8	Intern. and/or extern.	Parent, child	CBCL, YSR aggr. scales	4.26 ± 3hr 10min and 5.27 pm ± 3hr 15min	Saliva (Kool-Aid)	Outpatient clinic	Parent-child conflict discussion task
Granger et al., 1998[c]	62	62	6.7	5-11	No	Mother	CBCL aggr. scale	2.47 pm ± 1hr 57min	Saliva	University laboratory	Social interaction with mother (including conflict discussion)
Grayson, 2001[a]	30	26		9-11	No	Parent, teacher	CBCL, CTQ aggr. scales	Afternoon	Saliva	Clinic, after playing and watching cartoons	-
Gunnar et al., 2003[a e]	82	76 (55% boys) [g]	4.0	3-5	No	Teacher	CBQ long form aggr. scale	Morning class: 10.30 am, aftern: 2.30 pm	Saliva (Kool-Aid)	Preschool, during transition points in class	-
Hruschka et al., 2005[a]	29	29		6.5-8.0	No	Teacher	BASC Teacher Report aggr. scale	30, 60, 90 min post waking, noon, 7 pm	Saliva	Orphanage/ school	-
McBurnett et al., 1996[a]	67	53	9.6	7-12	CD	Mother, teacher, child	DISC aggr. symptoms	Between morning and mid-afternoon	Saliva	Clinic	-
Montagner et al., 1978[a]	147	33		2-5	No	Observers	Assessment of dominant/aggr. behavior profiles	Several times of day	Urine	Home and daycare center	-
Oosterlaan et al., 2005[a]	25	25	9.2	6-12	ODD/ CD (*n*=18)	Parent, teacher	DSM-IV screener aggr. CD	Between 10.00 am and 2.25 pm	Saliva (citric acid)	Research center	-
Pajer et al., 2001[a]	84	47	16.3	15-17	CD (*n*=47)	Parent, child	DISC aggr. symptoms	Between 9.00 and 11.15 am	Plasma	Study office/ home/school	-
Scarpa & Kolko, 1996[b]	19	17 [f]		7-15	DBD, abused	Clinic staff	OAS	Not reported	Saliva	Not reported	Provocation task
Scerbo & Kolko, 1994[a]	40	40	11.2	7-14	CD, ADHD, ODD	Parent, teacher, clinic staff	CBCL aggr. scale, OAS	Between 9.00 and 10.00 am	Saliva	Separate office	-
Schulz et al., 1997[a]	50	50	9.0	7-11	ADHD	Parent, teacher	CBCL, CTQ aggr. scales	9.45 and 9.55 am	Plasma	Research center	-
Shoal et al., 2003[a]	314	314	11.4	10-12	No	Child	MPQ, YASR aggr. scales	9.00 am	Saliva	Research center	-
Tennes & Kreye, 1985[a]	70	30	7.7	6.9-9.0	No	Teacher	Teacher rating scale, aggr. dimension	11.00 am	Urine	School (normal school days)	-

Study	Sample size		Age (years) at cortisol assessment		Clinical sample	Aggression		Cortisol assessment			
	Total	Meta	*M*	Range		Informant	Instrument	Time	Measure (flow stim)	Setting baseline	Stressor
Tout et al., 1998[a e]	75	38 boys 37 girls	4.3	2.7-5.8	No	Teacher	SCBE, angry/ aggr. scale	10.30 am and 3.00 pm	Saliva (Kool-Aid)	Child care center	-
Van Bokhoven et al., 2005[a]	194	61	13	-	No	Parent, teacher, child	DISC aggr. symptoms	Between 8.45 and 9.55 am	Saliva	Laboratory	-
Van de Wiel et al., 2004[c]	22	22	10.3	8-13	DBD	Parent	PDR, overt aggr. factor	Between 1.00 and 4.00 pm	Saliva (citric acid)	Research center, filling out questionnaires and watching film clips	Competitive setting inducing frustration, provocation, and aggression
Van Goozen et al., 1998[a]	52	52	9.9	8-11	ODD (*n*=21)	Parent (controls), child care worker (ODD), teacher	CBCL, TRF aggr. scales	Between 9.00 and 11.00 am	Saliva	Research center, filling out questionnaires and watching film clips	-
Wright, 2000[b e]	60	26 boys 29 girls	13.4		No	Teacher	TRF aggr. scale	Between 3.30 and 6.30 pm	Saliva	Research center	Trier Social Stress Test: public speaking, mental arithmetic task

Note. Intern. = Internalizing problems; Extern. = Externalizing problems; ADHD = Attention Deficit Hyperactivity Disorder; CD = Conduct disorder; DBD = Disruptive Behavior Disorder; ODD = Oppositional Defiant Disorder; aggr. = aggression/aggressive; BASC = Behavior Assessment System for Children; BDHI = Buss-Durkee Hostility Inventory; CBCL = Child Behavior Checklist; CBQ = Children's Behavior Questionnaire; C-DIS = computerized version of the NIMH Diagnostic Interview Schedule; CPQ = Children Personality Questionnaire; CTQ = IOWA Conners Teacher Questionnaire; DISC = Diagnostic Interview Schedule for Children; MMPI = Minnesota Multiphasic Personality Inventory; MPQ = Multidimensional Personality Questionnaire; OAS = Overt Aggression Scale; PASEC = Physical Aggression Scale for Early Childhood; PAVAR = behavioral checklist for Physical Aggression, Verbal Aggression, and Retaliation; PDQ-R = Personality Diagnostic Questionnaire-Revised; PDR = Parent Daily Report; SCBE = Social Competence and Behavioral Evaluation Questionnaire; TOCA-R = Teacher Observation of Classroom Adaptation – Revised; TRF = Teacher Report Form; VAS = Visual Analog Scale; YASR = Youth Self Report. A complete list of references to these instruments can be obtained from the first author.

[a] Outcome used in meta-analysis for basal cortisol.

[b] Outcome used in meta-analysis for cortisol reactivity.

[c] Outcomes used in both meta-analyses (basal and reactivity).

[d] Mean statistics for comparison of cortisol reactivity of the high aggression group with the medium and low aggression groups were used. Half of the sample size of the high aggression group was used for both statistics.

[e] Results were presented separately for boys and girls and were used independently in the meta-analysis.

[f] This sample size is based on the degrees of freedom reported for the *t*-test for comparing abused cortisol reactors to nonreactors. However, considering the overall *N*, this sample size of the abused group seems unlikely. A *t*-test was only conducted for the abused groups. No statistics were presented for comparison of the nonabused groups regarding aggression scores.

[g] The number of boys in the final sample is not given. However, 55% of the original sample (*N* = 82) were boys. Based on this percentage, we esimated the number of boys in the final sample on 42.

Cortisol reactivity

As far as cortisol reactivity to a stressor is concerned, two studies presented a negative relation between the change in cortisol levels from pre- to poststressor and aggression. In these studies children with higher levels of cortisol showed a blunted cortisol response (or a decline) after the stressor. In one study the relation between cortisol reactivity and aggression was negative for girls and nonsignificant for boys. Additionally, six studies reported a nonsignificant relation between cortisol reactivity and aggressive behavior. One of these reported separate (nonsignificant) statistics for boys and girls. The only study reporting a positive relation between cortisol reactivity and aggression is the one by Granger, Weisz, and Kauneckis (1994). Their study concerned cortisol levels and aggressive behavior in 7- to 17-year-old children who were referred to an outpatient clinic for a variety of externalizing and internalizing problems (N = 102). Saliva samples were obtained before and after a conflict discussion task between the children and their mothers. On average, cortisol levels dropped from pretask to posttask. However, higher cortisol responses in reaction to the stressor were associated with higher levels of aggression (reported by the children and their mothers).

Van de Wiel et al. (2004) reported a nonsignificant relation between cortisol reactivity and aggression. Similar to Granger, Weisz, and Kauneckis (1994), they investigated children with clinical levels of problem behavior (Oppositional Defiant Disorder [ODD] or CD). Boys, aged 8 to 13 years, with a high (n = 11) and low (n = 11) salivary cortisol reaction to a stressor were compared regarding parent-rated level of overt aggression. Stress was induced for 80 minutes and involved frustration, provocation, and child directed aggression in a general setting of competition between the child and a videotaped opponent who competed with the child for the best performance. No significant differences on aggression scores were found between the high and low cortisol reactors.

In contrast to Granger, Weisz, and Kauneckis (1994) and Van de Wiel et al. (2004) who focused on children with clinical levels of problem behavior, normally developing children were investigated by Granger et al. (1998). They obtained salivary cortisol from 62 boys and girls, aged 5 to 11 years, prior to and after a conflict discussion task with their mothers. Overall, no differences between pre- and posttask cortisol levels were found. Aggression scores, obtained from mother, were not significantly associated with cortisol reactivity.

A different and possibly stronger stressor than the conflict discussion task reported by Granger et al. (1998) was used by Wright (2000). In her dissertation she reported on the relation between teacher-rated aggression and cortisol reactivity to a public speaking task and a mental arithmetic test (the Trier Social Stress Test) in 13-year-old children. In the group as a whole, the cortisol level increased after the stressor. The participants were divided in a group that showed an increase in cortisol levels in response to the stressor and a group that exhibited a decrease. For boys (n = 26), no differences regarding their aggression scores existed between the cortisol increasers and decreasers. However, girls (n = 29) who showed a decrease in cortisol had higher aggression levels than girls who showed an increase.

A similar stressful task was used by Gerra et al. (1998). Instead of collecting saliva samples to assess levels of cortisol, like most studies did, they investigated

plasma cortisol levels. Blood was drawn before and after a Stroop Color-Word Interference Task, a mental arithmetic test, and a public speaking task from 12-year-old boys with low-normal, medium-normal and high-normal levels of aggression. Only in the medium aggressive group, cortisol levels after the stressor were significantly higher than the baseline values. However, cortisol reactivity in the highly aggressive group did not differ significantly from reactivity in the other two groups.

Our research group is one of the few that investigated cortisol reactivity and aggression in preschoolers (Alink et al., 2006c). Saliva of 155 children aged 2, 3, and 4 years was obtained before and approximately 20 minutes after the Strange Situation Procedure (Ainsworth, Blehar, Waters, & Wall, 1978). Data were analyzed separately for boys and girls. Correlations between cortisol reactivity (difference between pre- and poststressor levels) and observed aggression were .05 for boys (n = 79) and -.17 for girls (n = 76). Both correlations were nonsignificant. Correlations between cortisol reactivity and mother-reported aggression were also nonsignificant for both boys and girls (r = .00 and r = .03, respectively). In line with our results on basal cortisol, correcting for intervention condition and time of day of cortisol assessment did not change the results.

META-ANALYSES

As is clear from the review, there are substantial differences among the outcomes of studies addressing cortisol (reactivity) and aggression. A number of differences concerning study sample and design are evident as well. Using meta-analysis it is possible to test whether these differences are related to study outcomes. In the second part of this paper, we first describe possible moderators of the relation between cortisol and aggression. Next, we test the association of aggressive behavior with both basal levels of cortisol and cortisol reactivity to a stressor in two separate meta-analyses. Finally, we test whether the hypothesized moderators actually influence the relation between cortisol and aggression.

Explaining contradictory findings: Possible moderators

Clinical versus normal samples

Cortisol levels and aggression have been assessed in children with clinical levels of problem behavior (e.g., McBurnett et al., 1996; Van de Wiel et al., 2004) and in normally developing children (e.g., Granger, Stansbury, & Henker, 1994; Tennes & Kreye, 1985). Clinical levels of problem behavior have been shown to be related to altered biological functions (Cicchetti & Walker, 2003; Goodyer, 2002; Keenan, 2000; Van Goozen et al., 2000). Since it is likely that in clinical groups a number of children show strongly elevated levels of aggression, altered functioning of the HPA axis might be particularly detected in clinical groups. Psychosocial and other biological risk factors (besides altered HPA axis functioning) are also (inherently) more often present in clinical groups than in normally developing groups of children (Cummings, Davies, & Campbell, 2000). Liu and Wuerker (2005) proposed a biopsychosocial model of aggressive and violent behavior

in which biological and psychosocial factors interact in the development of aggressive behavior. Effects of biological factors (such as low cortisol production) may be moderated by other risk factors (e.g., socio-economical problems in the family, parental psychopathology) that are more often present in clinical groups. Consequently, a relation between cortisol levels and aggression might exist particularly in clinical groups.

Age groups

Different outcomes of the studies may also be due to differences in age of the participants in the different studies. Seven studies investigated cortisol levels and aggression in preschoolers, 13 focused on school-aged children, and 7 on adolescents. Kudielka, Buske-Kirschbaum, Hellhammer, and Kirschbaum (2004) reported that the HPA response to stress declines with age. Because the HPA axis is a dynamic system, liable to change as a result of high or low cortisol response for many years, the relation between the functioning of the HPA axis and behavior may change with age as well (Lopez, Vasquez, & Olson, 2004).

Gender

Most studies have investigated the relation between cortisol levels and aggression in samples that consist mainly of boys (e.g., Gerra et al., 1997, 1998; McBurnett et al., 1996; Van Bokhoven et al., 2005). In the other studies the sample consisted of both boys and girls (e.g., Granger et al., 1998; Tennes & Kreye, 1984), or girls only (e.g., Azar et al., 2004; Pajer et al., 2001). Many researchers have concluded that from toddlerhood or preschool-age onward, boys are more aggressive than girls (e.g., Alink et al., 2006b [chapter 2]; Tremblay et al., 1999). At the same time, some gender differences in level of cortisol have been found, although results of these studies are mixed. Increased activity of the HPA axis in response to stressors or physical exercise for adult men compared to women has been reported (Kudielka et al., 2004; Putnam, Chrousos, Nieman, & Rubinow, 2005). In their review, Kudielka and Kirschbaum (2005) reported that studies investigating gender differences in cortisol responses in children reveal either no differences or heightened cortisol responses in boys. Results of studies addressing gender differences in basal cortisol are also mixed. Kudielka et al. (2004) reported no gender differences in basal cortisol in a sample consisting of older adults, younger adults, and children. However, Pajer et al. (2001) showed that boys had lower basal cortisol levels than girls. Differences in the relation between cortisol (reactivity) and aggression for boys and girls have never been investigated. Since gender differences have been found for both level of aggression and level of cortisol, it is possible that differences also exist for the relation between these constructs. For example, Wright (2000) reported that cortisol reactivity was significantly related to aggression in girls but not in boys. Gender may thus moderate the association between cortisol and aggression.

Cortisol assessment and type of stressor

Several differences regarding study design were apparent. One of those is the setting in which cortisol is assessed. In a number of studies baseline cortisol was obtained directly upon arrival at the center, while in other studies participants

performed a nonstressful task before collecting samples for baseline cortisol determination. Since activity of the HPA axis may vary across situations (Gunnar et al., 1997), differences in results may be due to the context in which cortisol assessments took place.

In addition, in some studies assessments took place in a social setting, such as peer-group settings (e.g., Gunnar et al., 2003), whereas others used cortisol data obtained at a research center or laboratory. Lopez et al. (2004) noted that, when placed in a social setting, aggressive children may be more engaged in stressful peer interactions than shy children. This may result in higher levels of cortisol in aggressive children, whereas in a nonsocial environment their cortisol levels are lower than those of more inhibited children. Similarly, the specific stressor that was used to evoke reactivity of the HPA axis may also account for differences in relations between cortisol and aggression. Stressors that are likely to provoke aggression (e.g., a competitive setting, used by Van de Wiel et al., 2004; or playgroup sessions with unfamiliar peers, Granger, Stansbury, & Henker, 1994) will be more stressful for aggressive than for nonaggressive participants. Aggressive children may act more aggressively than nonaggressive children when confronted with these types of stressors, possibly implying a more stressful situation for aggressive children.

Other characteristics of the stressor may moderate the relation between cortisol reactivity and aggression as well. On the basis of their meta-analysis, Dickerson and Kemeny (2004) concluded that two elements are necessary for a stressor to elicit a substantial response of the HPA axis in adults: outcome uncontrollability and social-evaluative threat. These factors may also be essential for cortisol reactions in children. When a stressor does not elicit substantial physiological stress responses in most children, any relation between behavior and cortisol reactivity will remain unnoticed. Consequently, it is possible that this relation is only identified when a relatively strong stressor has been used.

Timing of cortisol assessment

The activity of the HPA axis normally follows a diurnal rhythm, which is established in humans in the first year of life (Gunnar & Donzella, 2002; Watamura, Donzella, Kertes, & Gunnar, 2004). This diurnal curve shows the highest levels approximately 30 minutes after wake-up, followed by a steep decline during the next two hours and a more gradual decline in the afternoon and evening (Kirschbaum & Hellhammer, 1989). Due to this diurnal rhythm, level of cortisol is highly dependent on time of day of assessment and the relation of cortisol values to behavior may vary across times of day. Tout et al. (1998) for example, found that morning and afternoon values were differently associated to child behavior.

A factor that is related to both time of day of sampling and situation of baseline sampling is the *law of initial value* (Lacey, 1956; Lewis & Ramsay, 1995a, 1995b; Ramsay & Lewis, 2003). This law denotes that reactivity of the HPA axis is related to the baseline value. When this baseline value is high (e.g., due to sampling in the morning or due to a stressful situation before or anticipation to the procedure) the cortisol reactivity to a stressor can be blunted. Consequently, results of studies addressing cortisol reactivity and aggression may depend on factors that influence the height of the baseline cortisol level (e.g., time of day of sampling and possible stressful situation before sampling).

Cortisol measures

Across all studies assessing cortisol, three different measures have been used: Cortisol has been measured in saliva, plasma, and urine (after filtering and metabolizing by the kidney and the liver, cortisol has been changed to so-called 17-hydroxycorticoids, this is considered a reliable index of cortisol secretion; Genuth, 1993). Several studies have reported high correlations between salivary and plasma cortisol levels (Kirschbaum & Hellhammer, 1989, 1994; Schwartz, Granger, Susman, Gunnar, & Laird, 1998), although absolute levels of cortisol found in saliva are very much lower than cortisol levels in blood plasma. In contrast to salivary and plasma cortisol which reflect HPA activity at a certain time point, urinary cortisol levels reflect the integrated function of the HPA axis over a period of time. This difference probably accounts for the fact that Putignano and colleagues (2001) did not find a significant relation between salivary and urinary cortisol levels. Whereas cortisol assessment in saliva is a nonstressful, noninvasive technique, obtaining blood samples to assess plasma cortisol levels can be very stressful and may therefore confound basal cortisol levels. However, as far as saliva samples are concerned, another factor appears to compromise measurement of cortisol. In some studies, oral stimulants (e.g., powdered drink mixes such as Kool-Aid) have been used. Schwartz et al. (1998) investigated the impact of oral stimulants on levels of salivary cortisol and on associations between cortisol and behavior. They found that the use of oral stimulants sometimes increased levels of cortisol and attenuated the relation between cortisol and behavior.

Assessment of aggression: observation or questionnaires?

Different methods have been used to assess level of aggression. A clear distinction can be made between questionnaires and observations. These methods may lead to differences in level of aggression (Karp, Serbin, Stack, & Schwarzman, 2004; McEvoy, Estrem, Rodriguez, & Olson, 2003). McEvoy et al. (2003) found that teachers perceived a larger number of children to be aggressive than impartial observers. This may be due to the fact that teachers see children in more different situations than observers do. Teachers may also be predisposed to view a child as aggressive, because of a certain reputation the child has. This bias is less present in independent observers of child behavior. Independent observers are usually trained to have the same view on the behavior of the children. However, when parents are asked to complete a questionnaire regarding their child's aggressive behavior, different parents may have different interpretations of the items. These differences between levels of aggression assessed with independent observations or with questionnaires may also result in differences in the relation between cortisol and aggression.

Research designs

Behavior and cortisol levels have not always been assessed at the same time point. Whereas most studies had cross-sectional research designs, in some studies aggression was assessed several months after the cortisol levels were obtained (e.g., Gunnar et al., 2003), while in others cortisol levels were measured some time after child behavior was assessed (e.g., Azar et al., 1998). Because both behavior

and the HPA axis are susceptible to change, these differences in design might also account for differences in outcomes.

Statistical analyses

Studies also differed in the statistical processing of the data. Some studies noted that the distribution of cortisol values was positively skewed and therefore the raw data were transformed (e.g., natural logarithm transformation; Azar et al., 2004; Oosterlaan et al., 2005), whereas other studies used the raw cortisol values in their analyses. Studies also differed in the use of covariates in the analyses. In several studies, time of day of cortisol sampling was related to levels of cortisol and was therefore used as a covariate (e.g., Granger et al., 1998). Some studies also statistically corrected for other variables that were related to cortisol levels, such as demographic factors, use of oral contraceptives, or body mass (e.g., Pajer et al., 2001; Schulz et al., 1997). These different ways of treating cortisol data may account for differences in the relation between cortisol (reactivity) and behavior.

In sum, substantial differences exist regarding the outcomes, research methods, and samples of studies investigating the association of basal cortisol and cortisol reactivity with aggression in children and adolescents. In this second part of the paper we tested the relation of aggression with both baseline cortisol levels and cortisol reactivity in two meta-analyses. We also investigated whether differences in effect sizes were related to the use of clinical versus nonclinical groups, age and gender of the participants, setting and time of sampling, type of stressor in the case of cortisol reactivity, cortisol measure (saliva, plasma, or urine), use of oral stimulants when salivary cortisol was used, measurement of aggressive behavior, research design (concurrent or nonconcurrent assessments), data transformation, or the use of covariates in the analyses.

Method

Inclusion of studies in the meta-analyses

An overview of the studies that were included in the meta-analyses is presented in Table 5.1. Seven of the studies that assessed cortisol reactivity after a stressor also reported the relation between baseline cortisol and aggression (Alink et al., 2006c; Blair, Granger, & Razza, 2005; Gerra et al., 1997, 1998; Granger, Stansbury, & Henker, 1994; Granger et al., 1998; Van de Wiel et al., 2004). These studies were included in both meta-analyses.

McBurnett and colleagues published several papers concerning basal salivary cortisol and aggression in (partly) the same group of 7- to 12-year-old children diagnosed with Conduct Disorder (McBurnett et al., 1996; McBurnett, Lahey, Rathouz, & Loeber, 2000; McBurnett, Pfiffner, Capasso, Lahey, & Loeber, 1997; N = 67, 38, and 42 respectively). Because in a meta-analysis it is necessary that studies are independent, studies using the same sample of participants

cannot be included in a meta-analysis more than once. Since the 1996 paper reported on the largest group of participants, this study was included in our meta-analysis.

Coding system

The coding system for characteristics of sample and study design is presented in Table 5.2. The variables "Stressor provoking aggression?" and "Type of stressor" were only coded for studies addressing cortisol reactivity. Because all studies reporting on cortisol reactivity had a concurrent research design and in only one of these studies basal cortisol samples were assessed in a situation with peers, we did not use "Research design" and "Baseline cortisol assessment in setting with peers" as moderators in the meta-analysis on cortisol reactivity and aggression. To assess intercoder reliability, ten randomly selected studies were coded by two coders. The agreement between the coders across the moderator variables was 100%.

Table 5.2

Coding system for studies on cortisol and aggression

Variable	Coding system
Sample	
Age of children at cortisol sampling	1 = 0-5 years 2 = 5-12 years 3 = 12-19 years
Children clinically referred or meeting DSM criteria?	0 = no 1 = yes
Gender of children in sample	1 = mainly boys (> 80%) 2 = mixed 3 = mainly girls (> 80%)
Design	
Research design	1 = concurrent assessment cortisol and aggression 2 = nonconcurrent assessment cortisol and aggression
Aggression observed?	0 = no, only questionnaires and/or interviews 1 = yes, at least one of the measures was observation
Baseline cortisol assessment in setting with peers?	0 = no 1 = yes
Time of cortisol sampling	1 = morning 2 = (after)noon 3 = varied
Stressor provoking aggression?	0 = no 1 = yes
Type of stressor	1 = weak 2 = strong (uncontrollable outcome and social-evaluative threat)
Cortisol measure	1 = saliva 2 = plasma 3 = urine
Oral stimulants used (in case of saliva)?	0 = no 1 = yes
Cortisol data transformed?	0 = no 1 = yes
Covariates used in analyses?	0 = no 1 = yes

Meta-analytic procedures

Five studies reported results separately for boys and girls (Alink et al., 2006c; Gunnar et al., 2003; Granda, 1982; Tout et al., 1998; Wright, 2000). We calculated effect sizes for both subsamples. The two effects computed for these subsamples were considered as independent outcomes in the analyses. With multiple measures of cortisol and/or aggression within one study (Alink et al., 2006c; McBurnett et al., 1996; Oosterlaan et al., 2005; Scerbo & Kolko, 1994; Schulz et al., 1997; Shoal et al., 2003; Van Goozen et al., 1998), we first conducted a meta-analysis within the study, and included the combined effect size in the final meta-analytic dataset. Within the domains of basal cortisol level and cortisol reactivity, every child was thus included only once in the meta-analysis.

Instead of comparing cortisol reactivity of aggressive and nonaggressive groups, in three studies cortisol increasers versus nonreactors (or decreasers) were compared regarding their aggression scores (Scarpa & Kolko, 1996; Van de Wiel et al., 2004; Wright, 2000). For these studies *p* values and sample sizes were used to compute effect sizes. Because this comparison may have resulted in different outcomes compared with the other studies, we used the information concerning whether or not cortisol reactivity groups were compared as a moderator in the meta-analysis concerning reactivity.

Statistical analyses

Two meta-analyses were conducted, one for the relation between basal levels of cortisol and aggression and one for the relation between change in levels of cortisol in response to a stressor and levels of aggression. The meta-analyses were performed using the Comprehensive Meta-Analysis (CMA) program (Borenstein, Rothstein, & Cohen, 2005, Version 2). For each study, an effect size (correlation) was calculated. Effect sizes indicating a positive relation between basal cortisol or cortisol reactivity and aggression were given a positive sign (higher basal cortisol levels, higher poststressor than prestressor levels associated with higher aggression rates). When effect sizes indicated a negative relation between basal cortisol or cortisol reactivity and aggression, they were given a negative sign (lower basal cortisol levels, lower poststressor than prestressor levels associated with higher aggression rates).

Using CMA, combined effect sizes were computed. Significance tests and moderator analyses were performed through fixed or random effects models, depending on the homogeneity of the study outcomes. Fixed effects models are based on the assumption that results cannot be generalized and may be regarded as applying only to the specific set of studies at hand (Rosenthal, 1995). Significance tests and moderator analyses in random models (Hedges & Olkin, 1985) can be generalized to the population of studies from which the current set of studies was drawn (Rosenthal, 1995). Whether fixed or random models can be used depends on the homogeneity of the set of effect sizes. To test the homogeneity of the overall and specific sets of effect sizes, we computed *Q* statistics (Borenstein et al., 2005). In addition, we computed 95% confidence intervals (*CI*s) around the point estimate of each set of effect sizes. When the set was homogeneous, *CI*s were based on fixed estimates. In case of heterogeneity of the set, we based

*CI*s on random estimates. *Q* statistics and *p* values were also computed to assess differences between combined effect sizes for specific subsets of study effect sizes grouped by moderators. Fixed effects model tests were used in the case of homogeneous sets of outcomes, and more conservative random effects model tests were used in the case of heterogeneous outcomes. Contrasts were only tested when at least two of the subsets consisted of more than three studies.

Funnel plots for both sets of studies were examined in order to detect possible publication bias. A funnel plot is a plot of each study's effect size against its standard error (usually plotted as 1/SE). It is expected that this plot has the size of a funnel, because studies with smaller sample sizes (larger standard errors) have increasingly large variation in estimates of their effect size as random variation becomes increasingly influential, whereas studies with larger sample sizes have smaller variation in effect sizes (Duval & Tweedie, 2000b; Sutton, Duval, Tweedie, Abrams, & Jones, 2000). However, smaller studies with nonsignificant results or with effect sizes in the non-hypothesized direction are less likely to be published. Therefore, a funnel plot may be asymmetrical around its base. The degree of asymmetry in the funnel plot was examined by estimating the number of studies which have no symmetric counterpart on the other side of the funnel. The *trim and fill* method was used to evaluate and to test the influence of possible adjustments of the sets of studies for publication bias (Duval & Tweedie, 2000a, 2000b).

For each study, Fisher's *Z* scores were computed as equivalents for correlations. Fisher's *Z* scores have better distribution characteristics than correlations (Mullen, 1989), and thus are recommended to be used in multivariate analyses. No outliers (standardized *z*-values smaller than -3.27 or larger than 3.27; Tabachnick & Fidell, 2001) were found for study effect size. In a multivariate approach we investigated whether the effects of the significant sample-related moderators were still significant after controlling for the study design characteristics and the other sample-related moderators. To reduce the relatively large number of covariates in proportion to the relatively small number of studies, we computed an index for the overall quality of study design. The number of favorable design characteristics of each study was counted. Favorable design characteristics were: assessment of salivary cortisol instead of urine or plasma cortisol, no use of oral stimulants, saliva collection at same time of day (morning or afternoon) for all participants, concurrent assessment of cortisol and aggression, cortisol assessment in situations without peers, aggression rated by observers (among other measures), and transformation of skewed cortisol data. The index for quality of design was used as a covariate in the multivariate analyses reported below.

Results

Basal cortisol levels

The meta-analysis concerning the relation between basal levels of cortisol and aggression included 24 studies with 28 study outcomes. Data were presented for

1,658 children. The combined effect size for the relation between basal cortisol and aggression was not significant (r = -.05, p = .23, 95% *CI* = -.13, .03) in a heterogeneous set of studies (Q = 65.14, p < .01). No significant relation between basal levels of cortisol and aggressive behavior existed in the total set of studies. Using the trim and fill method (Duvall & Tweedie, 2000a, 2000b), seven studies with a negative effect size (the hypothesized direction) appeared to be symmetrically unmatched. After trimming these studies and filling the missing counterparts of the trimmed studies, the effect size (r) was .04 (95% *CI* = -.05, .12).

We tested whether moderators regarding sample characteristics (whether or not the sample consisted of clinical participants, age group, and gender) were associated with effect size (Table 5.3). Contrasting effect sizes of studies involving children with clinical levels of problem behavior (k = 7, n = 289) with studies assessing normally developing children (k = 21, n = 1,369), revealed that the combined effect size of clinical samples was significantly larger (r = -.24, p < .01) than that of nonclinical samples (r = .01, p = .78), Q = 8.35, p < .01. In clinical samples a significant negative relation between basal cortisol levels and aggression was found, meaning that lower basal levels of cortisol were associated with higher levels of aggression.

The contrast for age group was also significant (Q = 11.39, p < .01). The 12 studies focusing on school-aged children (n = 770) showed the largest effect size in the hypothesized direction (r = -.18, p < .01). The effect sizes for the sets of studies with samples consisting of children younger than 5 years of age (k = 11, n = 550) and for studies with adolescent samples (k = 5, n = 338) were not significant (r = .09, p = .12; and r = .01, p = .93, respectively). The effect size for studies focusing on children between 5 and 12 years of age was significantly different from the effect size for the set of studies investigating the youngest group (Q = 11.11, p < .01). Thus, lower cortisol levels (hypoactivity) were associated with higher levels of aggression in studies investigating school-aged children whereas no significant associations were found in studies on either preschoolers or adolescents (using random effects models).

In our meta-analysis we were able to compare studies with samples that consisted mainly of boys (k = 17, n = 970), only of girls (k = 6, n = 365), or with mixed gender (k = 5, n = 323). In the different subsets, there were no significant associations between aggression and cortisol levels.

Because use of clinical groups and age groups were related (χ^2 [2, N = 28] = 7.73, p < .05; clinical samples consisted more often of children in the middle age group than of older or younger children), large effect sizes may be due to the use of clinical groups, or to the focus on a certain age group, or to both. To unravel the influence of these two study characteristics, we combined them into a variable with six categories (1 = age < 5, nonclinical sample; 2 = age < 5, clinical sample; 3 = age between 5 and 12, nonclinical sample; 4 = age between 5 and 12, clinical sample; 5 = age > 12, nonclinical sample; 6 = age > 12, clinical sample). Studies focusing on children younger than 5 years of age with clinical levels of problem behavior were absent and only one study investigated adolescents with clinical levels of problem behavior (Pajer et al., 2001). These categories (2 and 6) were excluded from the analysis. The contrast for the remaining categories was significant (Q = 26.90, p < .01). Effect sizes for all subgroups except for the nonclinical adolescents (k = 4, n = 291)

Table 5.3

Meta-analytic results of studies relating basal cortisol and aggression (k = 28 study outcomes)

Characteristics	*k*	*n*	*r*	95% *CI*	*Q* [a]	*p*
Total set	28	1,658	-.05	-.13, .03	65.14**	
Sample						
Clinical					8.35**	.00
no	21	1,369	.01	-.07, .10	41.74**	
yes	7	289	-.24**	-.38, -.09	9.77	
Age					11.39**	.00
0-5 years	11	550	.09	-.02, .19	14.05	
5-12 years	12	770	-.18**	-.29, -.07	20.64*	
12-19 years	5	338	.01	-.16, .17	7.76	
Gender					1.64	.44
mainly boys	17	970	-.09	-.20, .01	35.05**	
mixed	5	323	.09	-.17, .33	17.36**	
only girls	6	365	-.06	-.16, .05	1.60	
Study design						
Research design					0.00	.97
concurrent	21	954	-.05	-.16, .05	47.97**	
nonconcurrent	7	704	-.05	-.19, .09	15.94*	
Aggression observed?					3.73	.05
no	19	1,162	-.10*	-.19, -.01	36.38**	
yes	9	496	.06	-.07, .20	15.61*	
Setting cortisol assessment					2.07	.15
without peers	18	1,208	-.09*	-.18, -.00	34.99**	
with peers	10	450	.04	-.11, .19	18.80*	
Time of cortisol sampling					0.41	.82
morning	8	764	-.06	-.17, .05	12.91	
(after)noon	5	169	-.13	-.39, .16	12.71*	
varied	15	725	-.03	-.15, .10	34.87**	
Cortisol measure					0.48	.79
saliva	20	1,400	-.06	-.16, .04	54.04**	
urine	4	101	.04	-.30, .37	8.38*	
plasma	4	157	-.09	-.24, .07	0.37	
Oral stimulants used? [b]					0.21	.65
no	11	1,066	-.05	-.18, .09	43.32**	
yes	8	294	-.09	-.23, .05	9.84	
Cortisol data transformed?					0.61	.44
no	20	1,178	-.03	-.13, .07	48.87**	
yes	8	480	-.10	-.24, .04	14.47*	
Covariates used in analyses?					0.03	.86
no	21	1,226	-.05	-.14, .05	43.64**	
yes	7	432	-.07	-.25, .12	20.13**	

Note. *k* = number of studies; *n* = total number of participants; *CI* = confidence interval. When study outcomes for one of the subgroups were heterogeneous, results from random effects model tests were reported.

[a] *Q* statistic for moderator stands for effect of contrasts (*df* = number of subgroups – 1), *Q* statistic for subgroup stands for homogeneity (*df* = *k* -1).

[b] The subsets consisted only of studies in which salivary cortisol was assessed.

* $p < .05$. ** $p < .01$.

were significant (Table 5.4). Because of a lack of studies in categories 2 and 6 (see above), we could only test the difference between subsets of studies using clinical and nonclinical samples focusing on children between 5 and 12 years of age. In studies within this age group, effect sizes for both clinical and nonclinical sets of studies were significant in the hypothesized direction, but the combined effect size for the clinical studies was larger (r = -.26, $p < .01$, k = 6, n = 242) than

the combined effect size for the nonclinical studies (r = -.11, p < .05, k = 6, n = 528), Q = 3.81, p = .05. We also tested differences in effect size between subsets of studies focusing on different age groups of normally developing (nonclinical) children. The contrast for age group within the nonclinical subset was significant (Q = 12.85, p < .01). The combined effect size of the 11 (nonclinical) studies investigating children younger than 5 years of age (r = .11, p < .05, n = 550) differed significantly from the combined effect size of the 6 studies focusing on (nonclinical) school aged children (r = -.11, p < .05, n = 528), Q = 12.82, p < .01. The effect size of the subset with adolescents did not differ from the other two subsets. Taken together, within the studies focusing on children between 5 and 12 years of age, there was a significant negative effect size, but this was larger for the clinical than for the nonclinical subset. Within the set of studies on nonclinical samples, studies that focused on the youngest age group showed a significant *positive* relation between basal cortisol and aggression, which differed significantly from the *negative* relation that was found in studies investigating children between 5 and 12 years of age. In the youngest age group higher levels of cortisol (hyperactivity) were associated with higher levels of aggression, and in the group of children aged 5 to 12 years lower levels of cortisol (hypoactivity) were associated with higher levels of aggression. The latter association was stronger in clinical school-aged groups. Note that the effect for the subset of the 11 studies investigating preschoolers is slightly different from that presented in Table 5.3 because contrasts based on the combination of age group and clinical status reflect the fixed effects model tests since the subsets of outcomes were homogeneous. However, one of the subsets based on age group was heterogeneous and therefore we based effect sizes and Q statistics on random effects models.

Table 5.4

Meta-analytic results of studies relating basal cortisol and aggression, age groups and clinical status combined

Characteristics	*k*	*n*	*r*	95% *CI*	*Q* [a]	*p*
Age and clinical status [b]	27	1,611			26.90**	.00
0-5 years, nonclinical	11	550	.11*	.03, .20	14.05	
5-12 years, nonclinical	6	528	-.11*	-.20, -.02	7.85	
5-12 years, clinical	6	242	-.26**	-.38, -.14	8.98	
12-19 years, nonclinical	4	291	.01	-.10, .13	6.99	

Note. k = number of studies; n = total number of participants; *CI* = confidence interval.
[a] Q statistic for moderator stands for effect of contrasts (df = number of subgroups – 1), Q statistic for subgroup stands for homogeneity (df = k -1).
[b] The only study investigating a clinical sample of adolescents (Pajer et al., 2001) was not included.
* p < .05. ** p < .01.

We also tested whether characteristics of study design (concurrent vs. non-concurrent research design, aggression observed or not, setting of cortisol assessment, time of cortisol sampling, cortisol measure, use of oral stimulants or not, transformation of cortisol data vs. use of raw data, and use of covariates in analysis or not) were associated with effect size. The combined effect size for the subset of studies that did not use observational measures of aggressive behavior was significant (r = -.10, p < .05, k = 19, n = 1,162). This effect size was slightly larger than the nonsignificant effect size for the subset in which observations of aggression were used (r = .06, p = .37, k = 9, n = 496), Q = 3.73, p = .05. In addition,

the combined effect size for the subset of studies that assessed basal cortisol in a setting without peers was significant (r = -.09, p < .05, k = 18, n = 1,208). However, this did not differ significantly from the effect size for the subset in which basal cortisol was assessed with peers present (r = .04, p = .62, k = 10, n = 450), Q = 2.07, p = .15. None of the other study design characteristics were significantly related to effect size (Table 5.3).

Multivariate approach

To test whether the sample characteristics age group and clinical status (whether or not the sample consisted of clinical participants) were associated with effect size after controlling for quality of study design (see Method of Meta-Analyses, page 91), gender, and either clinical or age group, two MANOVAs were conducted. In the first MANOVA, the factor was clinical status, the dependent variable was Fisher's Z for study outcomes, and quality of study design, age, and gender were entered as covariates. After controlling for quality of study design, age, and gender, the effect of clinical status remained significant, $F(1, 23) = 6.68$, $p < .05$, partial $\eta^2 = .23$. The combined effect size of the clinical samples was significantly larger than the combined effect size of the nonclinical samples. In the second MANOVA, the factor was age group, and quality of study design, clinical status, and gender were entered as covariates. When the effects of quality of study design, clinical status, and gender were taken into account, the effect of age group was not significant, $F(2, 22) = 1.16$, $p = .33$, partial $\eta^2 = .10$. We also performed these analyses using Fisher's Z weighted for standard error in order to give studies with larger sample sizes more weight in the analyses. Results were highly comparable for both analyses, clinical status: $F(1, 23) = 6.34$, $p < .05$, partial $\eta^2 = .22$; age group: $F(2, 22) = 0.51$, $p = .61$, partial $\eta^2 = .04$.

Cortisol reactivity

We found 10 studies with 12 study outcomes reporting a relation between cortisol reactivity to a stressor and level of aggressive behavior. Data were reported for 671 children. Overall, the combined effect size was not significant (r = -.02, 95% CI = -.17, .13, p = .75; Table 5.5). The set of studies was heterogeneous (Q = 36.01, p < .01). Cortisol reactivity was not significantly related to aggressive behavior in the total set of samples. Using the trim and fill method (Duvall & Tweedie, 2000a, 2000b), no asymmetry was found in the funnel plot, therefore evidence for publication bias was absent.

We also computed combined effect sizes for each subgroup of studies based on clinical status, age group, and gender, and we tested whether these moderators were associated with effect size. Because for the contrasts on clinical status one of the two subsets was smaller than four studies, the significance of this contrast was not tested. For age group and gender we excluded subgroups with fewer than four studies when contrasts were tested. None of the combined effect sizes of the subsets regarding age group, clinical status, and gender were significant (Table 5.5). For age group and gender, the combined effect sizes of the subgroups did not differ significantly (Q = 0.72, p = .40; and Q = 0.95, p = .33, respectively).

Table 5.5

Meta-analytic results of studies relating cortisol reactivity and aggression (k = 12 study outcomes)

Characteristics	*k*	*n*	*r*	95% *CI*	*Q*[a]	*p*
Total set	12	671	-.02	-.17, .13	36.01**	
Sample						
Clinical						
no	9	530	-.09	-.23, .07	21.12**	
yes	3	141	.20	-.10, .47	3.99	
Age[b]					0.72	.40
0-5 years	4	353	-.12	-.28, .04	6.00	
5-12 years	3	101	.06	-.23, .34	3.36	
12-19 years	5	217	.03	-.28, .34	19.46**	
Gender[b]					0.95	.33
mainly boys	6	204	.10	-.06, .26	6.19	
mixed	4	362	-.06	-.33, .21	17.92**	
only girls	2	105	-.31	-.70, .22	5.82*	
Study design						
Aggression observed?					0.15	.70
no	7	288	.00	-.23, .24	20.61**	
yes	5	383	-.06	-.25, .14	12.64*	
Time of cortisol sampling					1.14	.29
morning	0					
(after)noon	7	300	-.12	-.36, .14	25.75**	
varied	5	371	.05	-.13, .23	10.26*	
Stressor provoking aggression?					0.06	.80
no	8	573	-.04	-.19, .12	21.06**	
yes	4	98	.03	-.41, .46	14.85**	
Type of stressor					1.54	.22
weak	8	564	.04	-.14, .21	25.55**	
strong	4	107	-.18	-.46, .12	7.10	
Cortisol measure[c]						
saliva	10	611	-.06	-.22, .10	31.09**	
urine	0					
plasma	2	60	.18	-.17, .50	2.07	
Oral stimulants used?						
no	7	458	-.06	-.22, .09	13.57*	
yes	3	153	-.11	-.57, .40	14.84**	
Cortisol data transformed?						
no	10	516	-.03	-.22, .16	35.69**	
yes	2	155	-.02	-.18, .14	0.32	
Covariates used in analyses?						
no	9	338	-.06	-.26, .14	24.35**	
yes	3	333	.05	-.21, .31	10.79**	
Cort. reactivity groups compared?					0.17	.69
no	8	577	.01	-.15, .16	22.69**	
yes	4	94	-.09	-.48, .33	11.78**	

Note. *k* = number of studies; *n* = total number of participants; *CI* = confidence interval. Contrasts were not computed when in one of the subgroups $k < 4$. When study outcomes for one of the subgroups were heterogeneous, results from random effects model tests were reported.

[a] *Q* statistic for moderator stands for effect of contrasts (*df* = number of subgroups – 1), *Q* statistic for subgroup stands for homogeneity (*df* = *k* -1)

[b] Contrast was tested without subgroup of $k < 4$ studies.

[c] The subsets consisted only of studies in which salivary cortisol was assessed.

* $p < .05$. ** $p < .01$.

In addition, we investigated whether study design characteristics were related to differences among effect sizes. Only the contrasts for measure of aggression (whether or not observations were used), time of cortisol sampling, stressor provoking aggression or not, type of stressor, and comparison of cortisol reactivity groups could be tested, since for these moderators at least two subsamples consisted of more than three studies. Again, none of the effect sizes for the different subgroups based on these design characteristics were significant. Additionally, the contrasts that could be tested were not significant. Moreover, the combined effect size of the subset of 8 studies in which either a correlation between cortisol reactivity and level of aggression, or a comparison between high and low aggression groups was reported (r = .01, 95% *CI* = -.15, .16) was highly comparable to that of the total set of studies that also included the four study outcomes for comparison of reactivity groups (r = -.02, 95% *CI* = -.17, .13). Including the four study outcomes for comparison of reactivity groups did not change any of the results.

Discussion

Overall, our meta-analyses showed that basal cortisol and cortisol reactivity are not consistently associated with aggression. The relation between basal cortisol and aggressive behavior was only significant in three subgroups of children: preschoolers, school-aged children, and children with clinical levels of problem behavior. Higher levels of aggression were associated with higher basal levels of cortisol (hyperactivity) in preschoolers, and with lower basal levels of cortisol (hypoactivity) in school-aged children and children with clinical levels of problem behavior. Study design characteristics did not affect the relation between cortisol (reactivity) and aggressive behavior.

A developmental perspective on basal cortisol in relation to aggression

The paradoxical findings that suggest an association of higher levels of aggression with higher basal cortisol levels in preschoolers, but with lower cortisol levels in school-aged children and children with clinical levels of problem behavior may be explained along different lines of reasoning. The association between high basal levels of cortisol and high levels of aggression at an early age may be due to a common antecedent factor. Substantial levels of stress early in life or even before birth are associated with the development of aggressive behavior (for a review, see McBurnett et al., 2003) and may result in higher basal levels of cortisol, in particular higher evening levels (Gunnar & Cheatham, 2003). Huizink, Mulder, and Buitelaar (2004) concluded in their review that prenatal stress may result in general susceptibility to psychopathology in rodents and nonhuman primates by early programming of, for instance, functioning of the HPA axis. It is likely that this animal model is, at least partially, applicable to humans; in fact, there is some evidence that supports the applicability of this model in humans (Huizink

et al., 2004). Furthermore, Essex, Klein, Cho, and Kalin (2002) investigated salivary cortisol levels of preschoolers in relation to maternal levels of stress in a longitudinal study. They found that exposure to maternal stress beginning in infancy in combination with high levels of concurrent maternal stress predisposed 4-year-old children to increased HPA functioning. Moreover, problem behavior of children may be a source of parental stress, potentially leading parents to use harsh and inconsistent discipline (Prior, Smart, Sanson, Pedlow, & Oberklaid, 1992). Children with conduct problems have indeed been found to be subjected to more harsh punishment and inconsistent discipline than other children (Patterson, Reid, & Dishion, 1992). This, in turn, may result in higher levels of stress for the child and consequently affect HPA axis functioning.

The relation between high basal cortisol levels and high levels of aggression may also be mediated by memory and learning processes. In their review, Heffelfinger and Newcomer (2001) concluded that increased activity of the HPA axis is related to impaired memory and learning function. The hippocampus plays an important role in the underlying mechanisms of the impaired learning processes as a result of early stress. The secretion of high levels of cortisol early in life is associated with hippocampal damage (e.g., cell loss, reduced levels of hippocampal steroid receptors, involution of the dendritic processes of hippocampal neurons, inhibition of synaptic plasticity; Heffelfinger & Newcomer, 2001; Kaufman, Plotsky, Nemeroff, & Charney, 2000; Wellberg & Seckl, 2001). Since the hippocampus is involved in memory and learning processes (Heffelfinger & Newcomer, 2001), damage to the hippocampus may cause impaired memory and learning function (Lemaire, Koehl, Le Moal, & Abrous, 2000; Welberg & Seckl, 2001). Therefore, children with high levels of cortisol may be less likely to learn from (negative) consequences of their (aggressive) behavior. Stress in early childhood may thus increase cortisol levels, leading to impaired learning which in turn predicts insensitivity to discipline and negative feedback from peers, and subsequently maintenance and further development of their aggressive behavior.

If high levels of stress continue to exist for an extensive period of time, this may cause a downregulation of the HPA axis, resulting in lower levels of basal cortisol or hypoactivity (Fries, Hesse, Hellhammer, & Hellhammer, 2005; Gunnar & Vasquez, 2001). In line with this hypothesis, our results indicate that between the ages of 5 and 12 years lower levels of cortisol (hypoactivity) were associated with higher levels of aggression. Thus, children who experienced high levels of stress during early development are likely to show high levels of aggression, and may have an elevated level of cortisol in early childhood, resulting in a downregulated HPA axis producing lower levels of cortisol at school age.

The association of lower levels of cortisol with higher levels of aggression in school-aged children may also be partly explained by mechanisms described in the sensation seeking and fearlessness hypotheses posed by Raine (1996). Children with low cortisol levels may be underaroused and as a result act aggressively in order to compensate for low levels of arousal. Additionally, children with low basal levels of cortisol may have a lack of fear. Because they do not (or to a lesser extent) experience the emotion of fear, they may not experience the consequences of their aggressive behavior (e.g., getting punished for acting aggressively, or seeing someone get hurt as a result of the child's aggressive behavior) as negative

or aversive. Therefore, they may not connect negative consequences to their aggressive actions and do not unlearn this behavior.

The relation between low basal cortisol and aggression appears to be stronger in clinical groups than in groups of normally developing school-aged children. Some of the children with clinical levels of problem behavior are likely to have experienced severe and chronic stressors early in life (Loeber, Green, Lahey, Frick, & McBurnett, 2000). Chronic stress (as opposed to mild stress) in particular seems to produce change in the functioning of the HPA axis (Essex et al., 2002). Thus, this biological system may be severely dysregulated in some children with clinical levels of problem behavior. As a result, the relation between cortisol levels and aggression may be strongest in these children. In the same vein, Adam, Klimes-Dougan, and Gunnar (in press) suggested that only children with the most severe level of Disruptive Behavior Disorder exhibit abnormally low basal levels of cortisol. Since in the studies of our meta-analyses most children in the clinical groups had one or more externalizing disorders (e.g., CD, ODD, or ADHD), it is likely that extreme levels of aggression were also present, resulting in a larger range of aggressive behaviors in clinical groups. Consequently, an association between basal cortisol and aggression may be more easily detected in clinical groups than in normal groups, where the range of level of aggression is more restricted. Because six of seven studies concerning clinical groups investigated children between 5 and 12 years of age, we do not know whether the strong effect of clinical status is restricted to this age group. Our multivariate analyses did reveal that clinical status is most strongly associated with effect size, even after controlling for the effects of age group and quality of study design.

Genetic influences may also explain the relation between basal levels of cortisol and aggressive behavior. The activity of the HPA axis is partly genetically determined. Bartels, De Geus, Kirschbaum, Sluyter, and Boomsma (2003) showed that in a group of 12-year-old twin pairs there was a significant genetic contribution to basal cortisol levels, with the highest heritability (60%) for morning levels obtained 45 minutes after awakening. Similar findings were reported by Wüst, Federenko, Hellhammer, and Kirschbaum (2000). Likewise, a moderate to high genetic influence has been reported for aggressive behavior (Hudziak et al., 2003; Van Beijsterveld, Bartels, Hudziak, & Boomsma, 2003). Knowing that both HPA axis functioning and aggression are influenced by genetic effects, various hypotheses concerning the relation between cortisol levels and aggression can be formulated. The genetic contribution to aggression may be partly mediated through genetic effects on the functioning of the HPA axis. On the opposite, the genetic influence on the HPA axis may be mediated by the genetic effects on aggression. An alternative hypothesis is the presence of an underlying genetic defect that accounts for both aggressive behavior and altered HPA axis functioning (Bartels et al., 2003). Children who are genetically predisposed to be intrinsically reactive to environmental input (early stressors in particular) may be at risk for altered HPA axis functioning as well as for the development of high levels of aggressive behavior. Future research is needed to resolve this issue of causality.

No relation between basal cortisol and aggression was found in studies investigating adolescents. The set of adolescent studies consisted of only five studies (n = 338), which precluded the possibility to test contrasts within the

set. Therefore, we cannot draw firm conclusions or construct clear hypotheses concerning the nonsignificant relation between basal cortisol and aggression in adolescence. In addition, cortisol level and aggression are not differently related in boys and girls, suggesting that comparable mechanisms are at work in both genders despite the much higher levels of aggression in boys.

Effects of study design

The relation between basal cortisol levels and aggression appears to be robust against the influence of most study design characteristics investigated in our meta-analyses. This relation is not associated with the use of a concurrent or nonconcurrent design, time of cortisol sampling, cortisol measure, use of oral stimulants, transformation of cortisol data, and use of covariates in the analyses. However, there is some evidence that the measure of aggressive behavior and the setting of cortisol assessment may be important. A significant negative relation between basal cortisol and aggression was found in studies that used questionnaires, interviews, and/or self reports to assess aggressive behavior, whereas this relation was nonsignificant in studies that (additionally) made use of observation of aggression. A negative relation between basal cortisol and aggression was also found in studies that assessed basal cortisol levels in a situation with no peers present, but not in studies that obtained cortisol just after a peer group setting, although the contrast between sets of studies using cortisol assessments with and without peers was not significant. Nevertheless, this may suggest that cortisol levels assessed in a nonsocial situation provide the best indication of normal HPA axis functioning.

None of the sample or study design characteristics investigated in our meta-analyses were associated with the relation between cortisol reactivity and aggression. This may be partly due to the relatively small number of study outcomes regarding the association between cortisol reactivity and aggression (k = 12, N = 671) and to the fact that the designs of the studies assessing cortisol reactivity were heterogeneous. The influence of several study characteristics could not be tested because of the small number of studies to which the particular characteristic applied.

Limitations and recommendations for further research

One of the limitations of the current meta-analyses is the heterogeneity of the studies. For example, different measures were used to assess level of aggression, cortisol was assessed at different times of the day, and the types of stressors that were used varied considerably. Although the influence of the study design characteristics that we tested was limited, the heterogeneity complicated the comparison of the study outcomes and often forced us to use significance tests and moderator analyses in the more conservative random effects models.

The effect size for the subgroup of studies reporting data on preschoolers was significant using the fixed effects models, but not when the random effect models were used. The subset itself was homogeneous and therefore, interpreting fixed effects models is justified. However, more studies on the relation between cortisol and aggression in preschoolers are needed in order to draw clear

conclusions regarding the strength and direction of the relation. In addition, when using the multivariate approach, controlling for the effects of study design, clinical status, and gender, the effect of age group was not significant. Quality of study design may be confounded with age group in the sense that studies on school-aged children had also the most preferable design characteristics, generating the largest effect sizes. The nonsignificant effect of age in the multivariate analysis may also be due to the fact that clinical samples (with larger effect sizes) were not equally distributed among the different age groups: Six clinical samples consisted of school-aged children, one of adolescents, and there was no study on preschoolers with clinical levels of problem behavior. However, our finding that differences between age groups were also significant when only subsets of studies on nonclinical groups were compared is a strong indication for the effect of age group independent of the clinical status of the sample. Nevertheless, more studies on clinical samples with different ages are needed to fully clarify this issue.

Investigating the relation between cortisol and aggression in clinical samples consisting of preschoolers and adolescents is also relevant in order to confirm our tentative conclusion that the association between basal levels of cortisol and aggression is stronger in clinical groups. In the current meta-analysis we were not able to test for the effect of clinical status in these age groups, due to the lack of studies on clinically referred groups of preschoolers and adolescents.

A limitation that specifically applied to the meta-analysis concerning cortisol reactivity and aggression is the relatively small number of studies reporting on this topic. This often precluded examination of potentially meaningful moderating study characteristics. Relatively large sets of studies are needed in order to be able to examine the influence of various moderators. In addition, as a result of both small sample size and heterogeneity, we could only use broad categories for the moderators. More specific categories for some moderators (e.g., type of stressor, assessment of aggression) might reveal the influence of these moderators more clearly.

Another drawback is the fact that most of the studies made use of cortisol assessment at only one point in time. Level of cortisol is susceptible to influences of environment, time of day, time since awakening, mood, food intake, and so forth (Gunnar & White, 2001). In addition, in several studies basal cortisol was assessed directly upon arrival at the laboratory. It is possible that these assessments actually reflected the anticipatory stress and the stress of coming to the laboratory instead of basal cortisol levels. Assessment of basal cortisol levels at home or after a nonstressful situation, during several days at the same time of day is preferable in order to obtain a reliable level of basal cortisol. Based on their meta-analysis, Dickerson and Kemeny (2004) listed some useful suggestions for optimal assessment of cortisol reactivity: cortisol assessments 21-40 minutes after stressor, assessment of several poststressor samples in order to measure trajectories for recovery, assessments of cortisol in the afternoon, and use of a stressor in which the elements of uncontrollability and social-evaluative threat are present.

In the current meta-analyses, we used a specific and narrow definition of aggression that only included aversive behavior that may cause or threaten harm to people, objects, or animals. Only studies that used measures that were consistent with this definition were selected. As a result, the behaviors that were

measured in the different studies were comparable and they were not confounded with other, nonaggressive, externalizing behaviors. However, Lopez et al. (2004) hypothesized that different types of aggression might be differentially related to basal levels of cortisol. They suggest that higher levels of offensive aggression, with its roots in difficulties with impulse control and underarousal, may be related to lower levels of cortisol, whereas higher levels of defensive aggression, motivated by excessive fear, may be related to higher levels of cortisol. Whether offensive or defensive aggression was assessed in the studies in our meta-analyses was not clear. Therefore, we were not able to test this hypothesis. Future research is needed to investigate the association between levels of cortisol and these particular types of aggression in different age groups.

Conclusion

The results of our meta-analyses show that thus far, the hypothesized association between cortisol reactivity and aggression has not been empirically confirmed. There is some evidence that basal cortisol levels are related to aggression, but only in specific subgroups of children. Higher levels of aggression are associated with higher basal levels of cortisol (hyperactivity) in preschoolers, and with lower basal levels of cortisol (hypoactivity) in school-aged children and children with clinical levels of problem behavior. The proposed effects of stress, parenting, and learning processes on this relation throughout development, and especially in clinical samples, deserve further research attention. Specifically, longitudinal studies are needed in order to test our hypotheses concerning these factors as explanatory mechanisms for the association of higher levels of aggression with higher basal cortisol in preschoolers and with lower basal levels of cortisol in school-aged children, the latter association being stronger in children with clinical levels of problem behavior. Finally, future research in this area with more frequent cortisol assessments, and more differentiated assessments of aggression may add to our insight in the relation between cortisol and aggressive behavior in children and adolescents.