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Chapter 3

The predictive value of stress-related neurobiological parameters for disruptive behaviors after 5-year follow-up in delinquent male adolescents

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ABSTRACT

Background: A small number of longitudinal studies on the predictive value of stress-related neurobiological parameters for several measures of future disruptive behavior, have revealed promising results. We assessed the predictive value of heart rate, heart rate variability (HRV) and cortisol for future rule-breaking behavior and reactive and proactive aggression, taking into account disruptive behavior at baseline.

Methods: Participants were 78 delinquent males, mean age 13.7 years. At baseline assessment, cortisol, heart rate and HRV were measured at rest and in response to a standardized public speaking task. At baseline assessment and at 5-year follow-up, disruptive behavior disorders (DBD) were assessed using a structured psychiatric interview. The subscales rule-breaking behavior and aggressive behavior of the Youth Self Report were administered, as well as the Reactive-Proactive Aggression Questionnaire.

Results: Low resting HRV significantly predicted reactive aggression at follow-up, over and above baseline reactive aggression (Beta = -.435; R^2 = 15.4%). Furthermore, there were significant interactions between neurobiological parameters and baseline disruptive behavior in relation to disruptive behavior at follow-up. These interactions showed that high resting heart rate and low resting HRV predicted aggressive behavior at follow-up, when baseline aggression was low. Attenuated heart rate responsivity predicted proactive aggression at follow-up, when baseline proactive aggression was high.

Conclusions: Our findings provide evidence that neurobiological parameters have predictive value for juvenile disruptive behavior after 5-year follow-up, over and above baseline disruptive behavior. Furthermore, results indicate that distinctive neurobiological profiles may underlie reactive and proactive aggression.

INTRODUCTION

Since juveniles who display disruptive behavior are at risk for a series of negative outcomes later in life (Kimonis & Frick, 2010; Loeber et al., 2009b; Maughan & Rutter, 2001), an extensive body of research has focused on factors predicting future deviancy. Over the last decades, interest in neurobiological markers has increased substantially. In this respect, juvenile disruptive behavior has fairly consistently been associated with decreased activity of stress-related neurobiological systems, such as the autonomic nervous system (ANS, represented by heart rate, heart rate variability (HRV)) and the hypothalamic-pituitary-adrenal-axis (HPA-axis, represented by it's final product cortisol) (Beauchaine, 2001; Raine, 2002a; van Goozen et al., 2007). These associations have often been explained by theories on low (autonomic) arousal and emotional dysregulation. Low arousal, as reflected by decreased ANS / HPA-axis (re)activity, is regarded as a marker of fearlessness and sensation seeking, which in turn may predispose to disruptive behavior (Raine, 1993; Raine, 2002a; van Goozen et al., 2007; Zuckerman, 1979). Emotional dysregulation, as reflected by decreased parasympathetic activity, is regarded as a hallmark for psychopathology, including disruptive behavior (Beauchaine, 2001; Porges, 1995; Porges, 2007).

The small number of longitudinal studies on the predictive value of neurobiological parameters for future disruptive behavior, have revealed promising results. The predictive value of low resting heart rate and cortisol for future antisocial, delinquent or aggressive behavior was reported throughout different age ranges (Baker et al., 2009; Raine et al., 1990; Raine et al., 1997; Shoal et al., 2003). Furthermore, attenuated heart rate reactivity as well as stronger HRV reactivity predicted registered reoffending in our current sample (De Vries-Bouw et al., 2011). However, studies that controlled for levels of disruptive behavior at baseline, revealed more diverging results (Baker et al., 2009; Raine et al., 1995; Sondeijker et al., 2008; van Bokhoven et al., 2005a). It is expected that baseline disruptive behavior influences the relation between neurobiological parameters and disruptive behavior at follow-up, because disruptive behavior has convincingly shown to predict future similar behavior (Burke et al., 2002; Loeber et al., 2009b), and (baseline) disruptive behaviors show cross-sectional associations with neurobiological parameters (Beauchaine, 2001; Fairchild et al., 2008; Ortiz & Raine, 2004; Popma et al., 2006). Nevertheless, previous studies showed first evidence for low resting heart rate and cortisol to predict behavioral outcome, in juveniles displaying disruptive behavior at baseline (Raine et al., 1995; Sondeijker et al., 2008). These results could, however, not be confirmed in other studies (Baker et al., 2009; van Bokhoven et al., 2005a). Therefore, it is of particular importance to

incorporate the (interacting) effect of baseline disruptive behavior, when studying the predictive value of neurobiological parameters for future disruptive behavior.

Another explanation for the diverging results as mentioned above, may be the variety of measures for disruptive behavior that were employed. With respect to delinquency, associations between officially registered and self-reported (re)offending were shown to be low (Maxfield et al., 2000; Wittebrood, 2000). Regarding categorical compared to dimensional measures, studying disruptive behavior categorized in disorders is useful for clinical purposes. However, DBD diagnoses are heterogeneous, with different types of aggression combined in one category. Dimensional measures of, for example, aggression can distinguish between levels of severity of disruptive behavior. Furthermore, cross-sectional studies have shown interesting differences in neurobiological correlates of various types of aggression like reactive and proactive aggression (Lopez-Duran et al., 2009; Scarpa et al., 2009; van Bokhoven et al., 2005b). Reactive aggression is a rather immediate and impulsive response to a source of provocation or threat, and is usually accompanied by the expression of anger (i.e., hot-blooded, or emotional; Dodge et al., 1997; Vitaro et al., 2006). Reactive aggression has been associated with decreased HRV and skin conductance, and increased cortisol (Lopez-Duran et al., 2009; Scarpa et al., 2009; van Bokhoven et al., 2005b). In contrast, proactive aggression is often goal-oriented, planned and unprovoked. Proactive responses are instrumental, in that they are fueled by reward contingencies that aim to achieve a goal such as possessions or the domination of others (Dodge et al., 1997; i.e., cold-blooded, or instrumental; Vitaro et al., 2006). In cross-sectional studies, proactive aggression has been related to increased HRV and skin conductance, but not cortisol (Lopez-Duran et al., 2009; Scarpa et al., 2009; van Bokhoven et al., 2005b). Notably, both types of aggression did not relate to resting heart rate (Scarpa et al., 2009). The predictive value of ANS and HPA-axis functioning for future proactive and reactive aggression has not been studied yet. It is thus important to extend the cross-sectional findings in longitudinal designs.

In the present study we examined the predictive value of cortisol, heart rate and heart rate variability, measured at rest and during psychosocial stress, for disruptive behavior after 5-year follow-up in delinquent male adolescents. We studied DBD diagnoses as well as dimensional measures of rule-breaking and proactive and reactive aggression. Furthermore, to study the exclusive value of neurobiological parameters over and above disruptive behavior, we incorporated levels of disruptive behavior measured at baseline.

METHODS

Sample and procedures

Our study was designed as a prospective longitudinal study on male adolescents who were followed across a period of five years during adolescence. The baseline assessment was conducted in 2002 – 2004, the follow-up assessment in 2006 – 2009. At baseline, 112 participants were included (mean age 13.7 years, SD 0.7) in the area of Amsterdam, The Netherlands. Participants were included after attending a delinquency diversion program after having committed a minor offense. Participants and their parents underwent behavioral assessment, which included a structured psychiatric interview and questionnaires. Participants underwent neurobiological assessment at home (cortisol) and during a visit at the laboratory (cortisol and autonomic measures).

Follow-up assessment was conducted after a mean of 4.7 years, SD 0.5. Of the total original sample, 75.9% participants and / or their parents (n = 85) were assessed. Re-assessment was refused by 20.5% of the participants (n = 23), 1.8% did not live in the Netherlands at the time of approach (n = 2) and 1.8% was untraceable (n = 2). There were no significant differences between participants and non-participants in age, neurobiological and behavioral parameters at baseline. Participants and parent underwent similar behavioral assessment as in the baseline study. Of the group of 85 participants at follow-up, 69.4% completed the entire follow-up assessment (n = 59). The mean IQ in the sample was 95.0, SD 11.6. Fourty-five percent had a low SES, 30.9% a middle SES and 24.4% a high SES. Fourty-four percent was of Caucasian ethnicity, 25.6% of Surinam / Antillean, 23.1% of Mediterranean and 7.7% of other ethnicity. The study was approved by the Medical Ethics Committee of the VU University medical center Amsterdam, and participants and their parents gave written informed consent for both baseline and follow-up assessment.

Behavioral assessment at baseline and follow-up

To assess the presence of psychiatric diagnoses of disruptive behavior disorders at both baseline and follow-up assessment, the National Institute of Mental Health (NIMH) Diagnostic Interview Schedule for Children (DISC), version IV (Shaffer et al., 2000) was used, which is an extensive structured psychiatric interview. The sections on oppositional defiant disorder (ODD) and conduct disorder (CD) were obtained by trained interviewers from both participants and parents separately. Participants were scored as having a disruptive behavior disorder (DBD), when ODD and/or CD was scored in either of the separate interviews (Pajer et al., 2001).

To obtain dimensional data on disruptive behavior problems, participants

filled out the Youth Self Report (YSR), which is a widely used questionnaire to assess behavioral problems in children and adolescents (Achenbach, 2001; Verhulst et al., 1997). Within the externalizing dimension, we used raw scores of the subscales 'rule-breaking behavior' and 'aggressive behavior'. Because we used a revised version of the YSR at follow-up assessment compared to baseline assessment, we only used the corresponding items that were on both pre-revised and revised versions. We therefore excluded 7 items from the baseline YSR and 3 items from the follow-up YSR.

To obtain more detailed information on different forms of aggression, participants filled out the Reactive-Proactive Aggression Questionnaire (RPQ, Raine et al., 2006). At baseline, the RPQ was obtained from a subsample of 60 participants. This 23-item self-report questionnaire contains 11 items on reactive aggression and 12 items on proactive aggression to be scored on a three-point scale. The RPQ has shown good reliability and validity (Raine et al., 2006). Descriptive statistics for all behavioral outcome measures are presented in Table 1.

Psychosocial stress task procedure at baseline

The participants performed a psychosocial stress test procedure in the laboratory, consisting of a public speaking task (PST) in front of a one-way screen with video recording (Jansen et al., 2000), which is an effective stressor in both children and adults (Dickerson & Kemeny, 2004). The procedure is described in detail elsewhere (Popma et al., 2006). Briefly, there was a 50 minute resting period prior to the PST and a 60 minute resting period afterwards. After the resting period, an unfamiliar test assistant explained the PST itself, which consisted of a 5 minute speech on a topic of choice preceded by 10 minutes of preparation. It was suggested that a 'jury' of three psychologists was behind a one-way screen, judging the participants' performance. This judgment was always positive, thereby ending the stressful situation.

Procedure for recording of autonomic measures and saliva collection at baseline

Heart rate and heart rate variability (HRV) were measured continuously during the stress task procedure as an index of autonomic / parasympathetic activity, using the VU-Ambulatory Monitoring System (AMS, (Klaver et al., 1994). For the analysis of HRV, we performed spectral analyses using Kubios HRV software, developed by the Biosignal Analysis and Medical Imaging Group, University of Kuopio, Finland. For the purpose of this study, we used high-frequency heart rate variability (0.15 – 0.40 Hz, (Berntson et al., 1997). More details on the recording procedure are provided in chapter 2 of this thesis. The mean heart rate / HRV during the second half of the initial resting period (after participants had adjusted to the setting) was used as basal value.

The mean heart rate / HRV during the first minute of the speech was used as value during stress. The difference between these two measures was computed as measure of responsivity to stress.

During the stress test procedure, saliva was sampled using the Salivette sampling device (Sarstedt, Nümbrecht, Germany) for cortisol analyses. Participants were instructed not to eat and drink (besides water) during the entire test session. Samples were taken 25 minutes before the start of the PST (basal measure) and 20 minutes after finishing the talk (measure during stress). The difference between these two measures was computed as measure of responsivity to stress.

Participants also sampled saliva at home in the morning to obtain a cortisol awakening response (CAR). The procedure is described in detail elsewhere (Popma et al., 2007a). Briefly, saliva was sampled immediately after awakening and 30 and 60 minutes after awakening. To minimize artifacts due to differences in awakening time, subjects waking up more than 2 SD earlier or later than the mean awakening time (7:21 h) were excluded. For the other 2 morning samples, a time window of ± 15 minutes was allowed.

Uncentrifuged saliva samples were stored at -20°C until analysis. Salivary cortisol levels were determined in duplicate by direct radioimmunoassay, using 125I-cortisol and antiserum made against the 3-CMO-BSA conjugate (Sulon, 1978). The lower detection limit of the assay was 7 ng/dl, with mean intra- and inter-assay coefficients of variation of respectively 4.3% and 9.4%.

Statistical analyses

Analyses were performed using SPSS version 19.0. We considered p-values < .05 statistically significant, unless otherwise noted. Cortisol and heart rate variability values were positively skewed, therefore square-root transformations were applied. Square-root transformations were also applied on the subscale 'aggressive behavior' of the YSR and both subscales of the CBCL, as well as the RPQ subscale 'proactive aggression'. All values were normally distributed after transformation.

As measures of the cortisol awakening response (CAR), the area under the curve with reference to the ground (AUCg) and with reference to the increase (AUCi) were computed. The AUCg reflects the mean cortisol secreted within one hour after awakening, whereas the AUCi reflects the total increase in cortisol secretion from baseline during the first hour after awakening (Edwards et al., 2001).

Correlations between dimensional measures of disruptive behavior at baseline and neurobiological parameters at baseline as well as the corresponding measures of disruptive behavior at baseline were assessed by computing Pearson's correlations.

To determine the predictive value of neurobiological parameters for disruptive behavior at follow-up, we used linear regression analyses. First, we conducted single linear regression analyses with each separate neurobiological parameter as independent variable and each single type of disruptive behavior at follow-up as dependent variable (basic models). Second, we used multiple linear regression analyses to assess to what extend neurobiological parameters predict disruptive behavior at follow-up, over and above disruptive behavior at baseline (controlling for the effect of baseline disruptive behavior). For this purpose, in each basic model we entered the corresponding type of disruptive behavior at baseline as independent variable. We reported the R^2 for the exclusive predictive value of the neurobiological parameters for disruptive behavior, over and above baseline disruptive behavior. Third, we assessed whether the predictive value of neurobiological parameters for disruptive behavior at follow-up is different for various levels of disruptive behavior at baseline (moderating effect of baseline disruptive behavior). For this purpose, in each basic model we entered the corresponding type of disruptive behavior at baseline as well as the interaction between the neurobiological parameter and disruptive behavior at baseline as independent variables. In the case of a significant interaction ($p < .10$) we conducted simple slope analyses according to the procedures described by Aiken and West (1991). For DBD as outcome measure, the same procedures were followed using logistic regression analyses. In all regression analyses, we used standardized variables. The interaction variables in the third step were computed as the product of the standardized variables and were not standardized themselves.

RESULTS

At follow-up, 19 participants (24.7%) were diagnosed with a disruptive behavior disorder. Descriptive statistics of behavioral parameters at follow-up as well as neurobiological predictors at baseline are presented in Table 1.

Table 1. Descriptive statistics of neurobiological predictors and behavioral outcome measures

	N	Mean	Median	SD	Min	Max
Neurobiological parameters at baseline						
HR resting	51	78.2	77.5	9.6	60.6	107.0
HR response	51	9.5	10.8	11.1	-11.2	37.5
HRV resting	50	1532	1237	1222	165	4636
HRV response	50	-391	-176	1132	-3197	1638
Cortisol CAR AUCg	67	164.3	167.7	35.7	82.2	248.0
Cortisol CAR AUCi	67	18.9	15.1	31.2	-40.6	96.1
Cortisol response	49	0.3	0.6	1.8	-3.3	7.6
Behavioral parameters at follow-up						
Rule-breaking	64	5.3	5.0	3.5	0	13
Aggression	64	5.6	5.0	4.7	0	21
Proactive aggression	62	4.3	4.0	3.5	0	14
Reactive aggression	62	9.2	9.5	4.2	0	18
DBD Present	19 (24.7%)					

Heart rate is expressed in bpm, HRV in ms^2, cortisol in nmol/l. We presented raw values in the table. Analyses were performed with transformed variables (see Statistical analyses).
HR: heart rate; HRV: heart rate variability; CAR: Cortisol Awakening Response; AUCg/i: Area Under the Curve with respect to ground/increase; DBD: Disruptive Behavior Disorder.

Predictive value of separate neurobiological parameters for disruptive behavior at follow-up

The predictive value of each neurobiological parameter for disruptive behavior at follow-up is presented in Table 2, step 'Bivariate'. Low resting HRV significantly predicted rule-breaking and aggressive behavior, as well as proactive and reactive aggression at follow-up. High resting heart rate as well as reduced HRV responsivity (i.e. a smaller decrease of HRV in response to stress) significantly predicted proactive aggression at follow-up. Cortisol values, either at baseline or in response to stress, did not significantly predict disruptive behavior at follow-up. None of the neurobiological parameters significantly predicted a diagnoses of disruptive behavior disorder (DBD) at follow-up.

Predictive value of neurobiological parameters for disruptive behavior at follow-up, controlled for baseline disruptive behavior

We assessed to what extend the neurobiological parameters predict disruptive behavior at follow-up, over and above disruptive behavior at baseline. Results are presented in Table 2, step 'Controlled'. After controlling for baseline reactive aggression, the predictive value of low resting HRV for reactive aggression remained

significant. The part of the variance of reactive aggression that was explained by resting HRV exclusively, was 15.4%. The remaining associations turned into trends toward significance or became non-significant, or showed interactions with baseline disruptive behavior (see next paragraph).

Interactions between neurobiological parameters and disruptive behavior at baseline in relation to disruptive behavior at follow-up

We assessed whether the predictive value of neurobiological parameters for disruptive behavior at follow-up was different for various levels of disruptive behavior at baseline. We found interactions between resting heart rate and baseline general aggression in relation to general aggression at follow-up (B = -.268; p = .087), between resting heart rate variability and baseline general aggression in relation to general aggression at follow-up (B = .258; p = .076) and between heart rate response and baseline proactive aggression in relation to proactive aggression at follow-up (B = -.532; p = .039). Single slope analyses for high and low levels of the disruptive behavior T0 are presented in Figure 1 A-C. There was a significant predictive value of high resting heart rate for general aggression when baseline aggression scores were low, not when baseline aggression scores were high (figure 1A). Low resting heart rate variability had a predictive value for general aggression when baseline aggression was low (figure 1B). An attenuated heart rate response had a predictive value for proactive aggression when proactive aggression scores at baseline were high (figure 1C).

Furthermore, we found an interaction between HRV response and baseline DBD in relation to DBD at follow-up (B = 1.380; p = .061). When the relationship between HRV response and DBD at follow-up was stratified for high and low levels of disruptive behavior at baseline (resp. present or absent baseline DBD), both appeared not significant (baseline DBD present: Exp(B) = 1.893; p = .123; baseline DBD absent: Exp(B) = 0.476; p = .223).

Table 2. The predictive value of separate neurobiological parameters for disruptive behavior at follow-up

Predictor	Step	Rule-breaking				Aggression				Proactive aggression				Reactive aggression				Disruptive behavior disorder		
		N	Beta	p	R²	N	Beta	p	R²	N	Beta	p	R²	N	Beta	p	R²	N	Exp(B)	p
HR resting	Bivariate	40	.165	.280		40	.263	.082		39	.319	.033*		39	.217	.155		51	1.155	.636
	Controlled	40	.107	.449	.012	40	---	---	---	30	.149	.341	.027	29	.135	.473	.017	51	1.061	.866
HR response	Bivariate	40	-.147	.403		40	-.250	.152		39	-.088	.638		39	.039	.833		51	0.677	.213
	Controlled	40	-.116	.468	.011	40	-.105	.521	.008	39	---	---	---	29	-.001	.998	.000	51	0.858	.664
HRV resting	Bivariate	40	-.369	.018*		40	-.442	.004**		39	-.438	.004**		39	-.401	.010*		50	0.579	.104
	Controlled	40	-.267	.073	.066	40	---	---	---	30	-.311	.071	.071	29	-.435	.026*	.154	50	0.561	.111
HRV response	Bivariate	40	.185	.241		40	.218	.163		39	.315	.043*		39	.105	.510		50	1.289	.401
	Controlled	40	.153	.285	.024	40	.086	.560	.007	30	.268	.107	.076	29	.107	.574	.011	50	---	---
Cortisol CAR AUCg	Bivariate	54	-.004	.977		54	.068	.647		52	.031	.833		52	.047	.753		67	1.097	.751
	Controlled	54	.000	.998	.000	54	.072	.587	.005	28	.143	.523	.011	27	.026	.916	.000	67	1.285	.465
Cortisol CAR AUCi	Bivariate	54	-.021	.874		54	.016	.902		52	-.025	.853		52	-.050	.706		67	0.987	.965
	Controlled	54	-.039	.738	.002	54	.010	.933	.000	28	.019	.899	.000	27	.033	.854	.001	67	0.876	.700
Cortisol response	Bivariate	39	-.202	.160		39	-.215	.135		38	-.121	.408		38	-.181	.213		49	0.713	.371
	Controlled	39	-.150	.272	.027	39	.191	.141	.045	29	-.097	.457	.016	28	-.237	.115	.084	49	1.011	.979

Step 'Bivariate' refers to bivariate associations between neurobiological predictors and disruptive behavior at follow-up. Step 'Controlled' refers to associations between neurobiological predictors and behavioral outcomes, when controlled for baseline disruptive behavior. R^2 in step 'Controlled' represents the part of the explained variance of disruptive behavior by a neurobiological parameter, when controlled for baseline disruptive behavior. In case of a significant interaction between neurobiological predictor and baseline disruptive behavior in relation to disruptive behavior at follow-up, step 'Controlled' was not presented in the table.

HR: heart rate; HRV: heart rate variability; CAR AUCg/i: cortisol awakening response area under the curve with respect to the ground / increase
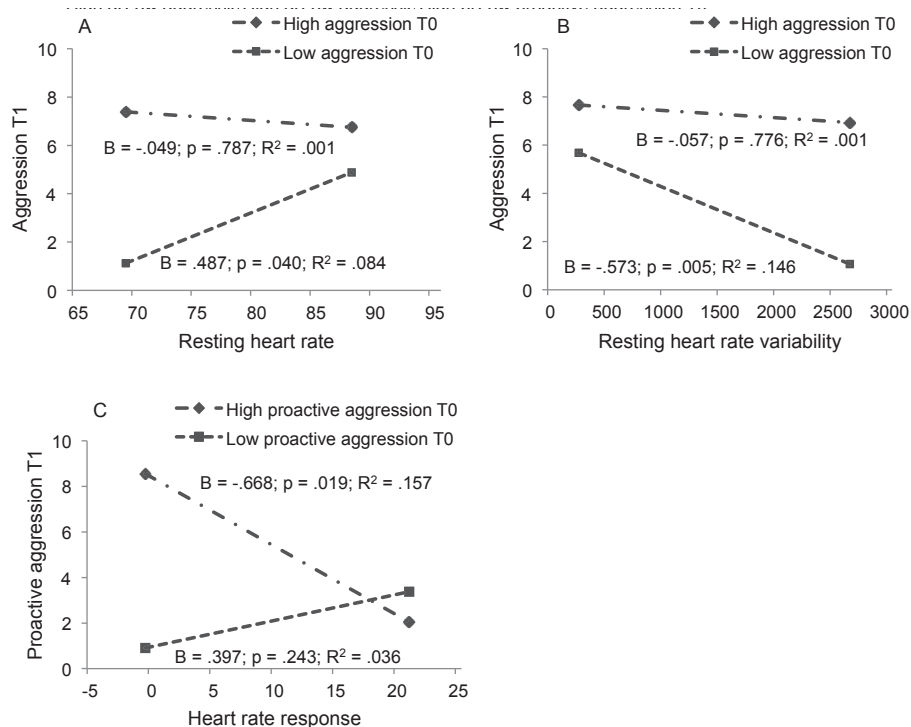
* p <.05 ** p <.01

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Figure 1. Interactions between A. resting heart rate and baseline aggression in relation to aggression at follow-up, B. resting heart rate variability and baseline aggression in relation to aggression at follow-up, C. heart rate response and baseline proactive aggression in relation to proactive aggression at follow-up. Single slopes are presented for high and low values of the aggression measure at baseline (respectively 1 SD above and below the mean).

DISCUSSION

In the present study we examined the predictive value of heart rate, HRV and cortisol for disruptive behavior after 5-year follow-up in delinquent male adolescents. Furthermore, we studied the exclusive predictive value of neurobiological parameters over and above baseline disruptive behavior.

The results of our study reveal a number of bivariate associations between neurobiological parameters and dimensional measures of disruptive behavior at follow-up. Moreover, our results provide further evidence that stress-related neurobiological parameters have predictive value for juvenile disruptive behavior after 5-year follow-up, even when baseline disruptive behavior was taken into account. We need to emphasize that the bivariate associations have to be interpreted with caution, because the effect of disruptive behavior at baseline is not taken into account. Our

results were as expected, since literature has shown that that disruptive behavior at baseline predicts disruptive behavior at follow-up (Burke et al., 2002; Loeber et al., 2009b), while neurobiological parameters show cross-sectional associations with (baseline) disruptive behavior (Beauchaine, 2001; Fairchild et al., 2008; Ortiz & Raine, 2004; Popma et al., 2006). Because we were interested in the exclusive predictive value of the neurobiological parameters over and above baseline disruptive behavior, we will further interpret our results with baseline disruptive behavior taken into account.

We found predictive values of heart rate and HRV for specific measures of aggression. With respect to general aggression, high resting heart rate and low resting HRV predicted self-reported general aggressive behavior, when baseline levels of aggression were low. Our result on resting HRV is the first to reveal a predictive value of low resting HRV for future aggressive behavior. This results extends previous cross-sectional findings in which associations between low resting HRV and disruptive behavior have been reported (Beauchaine, 2001; Beauchaine et al., 2008; Gordis et al., 2010; Pine et al., 1998). Our result on resting heart rate may seem surprising, since not high but low resting heart rate is considered a robust correlate of juvenile disruptive behavior (Ortiz & Raine, 2004). However, our study is not the first to show opposite results. Two previous cross-sectional studies found higher resting heart rate, which is thought to be characteristic of temperamentally more fearful children, in DBD boys compared to normal controls (de Wied et al., 2009; Zahn & Kruesi, 1993). Similar to our results, De Wied and coworkers (2009) found a specific pattern of high resting heart rate and low HRV, which may indicate a specific subgroup of disruptive juveniles, characterized by higher anxiety levels and poor emotional control. Results implicate that resting heart rate as neurobiological correlate of disruptive behavior still needs further study.

In addition to a general measure of aggressive behavior, we studied reactive and proactive aggression. Our results revealed that low resting HRV predicted reactive aggression at follow-up, over and above baseline reactive aggression. The predictive value of resting HRV for proactive aggression was in the same direction, although it did not reach statistical significance. This indicates that low resting HRV is a correlate of reactive aggression in specific, which is in line with cross-sectional results from Scarpa (2009). The low resting HRV may reflect emotional dysregulation, which in turn may thus predispose to reactive 'emotional' aggression (Beauchaine, 2001).

Furthermore, attenuated heart rate responsivity predicted proactive aggression at follow-up, when baseline proactive aggression was high, but did not predict reactive aggression at follow-up. This finding extends the literature in two ways. First, attenuated heart rate responsivity has previously been found in relation to registered

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reoffending (De Vries-Bouw et al., 2011). To our knowledge, our current study is the first that examined the association between heart rate reactivity and specific types of aggression. Our result indicates that attenuated heart rate responsivity is a correlate of proactive 'cold-blooded' aggression in specific, which fits in with the low arousal / fearlessness theory (Raine, 1993; Raine, 2002a). Low arousal, as reflected by attenuated heart rate reactivity, is regarded as a marker of fearlessness, which thus appears to predispose to proactive aggression in particular. Second, we found that attenuated heart rate reactivity can predict proactive aggression, once this type of aggression is present, indicating that attenuated heart rate responsivity is related to persistent proactive aggression. This extends findings from Raine (1995), who found a predictive value of low resting heart rate for adult delinquency, when levels of antisocial behavior in adolescence were high. A predictive value of neurobiological parameters for persistent disruptive behavior may have potential clinical relevance for screening and intervention purposes, although findings need replication in larger and different samples, with other neurobiological parameters and measures of disruptive behavior as well. Our results on reactive and proactive aggression provide further evidence for differences in neurobiological correlates of specific types of aggression.

We did not find a predictive value of neurobiological parameters for a DBD diagnosis at follow-up. A single previous study also found no predictive value of heart rate and cortisol in children with DBD for the presence of DBD in adolescence (van Bokhoven et al., 2005a). This indicates that the studied neurobiological parameters are less suitable to distinguish between the presence or absence of a clinical disorder at follow-up. This may be explained by the heterogeneous aspect of DBD diagnoses. Different types of aggression, like reactive and proactive aggression as discussed above, are combined in one category. Furthermore, a dichotomous classification lacks variation and power. We neither found a predictive value of neurobiological parameters for self-reported rule-breaking behavior. Previous studies focused on officially registered (re)offending, and did find associations with heart rate and HRV (De Vries-Bouw et al., 2011; Raine et al., 1990; Raine et al., 1995). Inconsistency between previous results and our current results on self-reported rule-breaking behavior may be explained by the small correlation between registered and self-reported offending (Maxfield et al., 2000). Official records reflect only part of all offenses committed by an individual, whereas serious / violent offenses tend to be underrepresented in self-reports (Maxfield et al., 2000). When studying associations between neurobiological parameters and delinquent behavior, it is important to realize that using self-reports may reveal different results compared to using officially registered reports.

We did not find a predictive value of cortisol, either in basal conditions or in

response to stress, for disruptive behavior at follow-up. Previous results were not consistent. Shoal (2003) and Sondeijer (2008) reported a predictive value of basal cortisol for future disruptive behavior, whereas Van Bokhoven and coworkers, who studied basal and reactive cortisol, could not confirm this (van Bokhoven et al., 2005a). Although we could not replicate the findings of Shoal and Sondeijker, our effect size of 8.4% (the proportion of the variance of reactive aggression explained by cortisol responsivity exclusively), exceeded Sondeijkers effect size of 0.5%. Future studies are warranted to further explore the predictive value of cortisol measures for future disruptive behavior.

Some limitations of the present study should be noted. First, we studied a small, specific population of delinquent male adolescents. Although studying such a specific group has evident relevance, results cannot be generalized to other samples like clinic-referred disruptive behavior disordered juveniles, very young offenders or girls. Furthermore, the small sample size limited power to incorporate additional parameters to control for confounding effects, like smoking or SES. Second, our measures in resting conditions were assessed prior to the public speaking task. Although participants were instructed to spend this time as relaxed as possible and they did not know the content of the task beforehand, neurobiological levels may have been influenced by anticipatory stress.

Despite the limitations, our results provide further evidence that stress-related neurobiological parameters can predict future juvenile disruptive behavior, also when baseline disruptive behavior is taken into account. Furthermore, results indicate that specific parameters predict either reactive or proactive aggression. It should be noted that our results are not consistent throughout all associations studied, and need replication and extension in larger and other samples. Future studies are highly recommended to incorporate baseline levels of disruptive behavior, because baseline disruptive behavior influences the associations between neurobiological parameters and future disruptive behavior. Moreover, other factors that are known to relate to disruptive behavior should be taken into account as well, preferably from comprehensive biopsychosocial models. This may ultimately lead to improved identification and more effective interventions for juveniles at risk for a deviant development.

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