Genes, Brain and Behavior
Official publication of the International Behavioural and Neural Genetics Society

Physiological reactivity to infant crying: a behavioral genetic study

D. Out, S. Pieper, M. J. Bakermans-Kranenburg* and M. H. van IJzendoorn

Institute of Education and Child Studies, Centre for Child and Family Studies, Leiden University, Leiden, The Netherlands
**Corresponding author: M. J. Bakermans-Kranenburg, Centre for Child and Family Studies, Leiden University, PO Box 9555, 2300 RB Leiden, The Netherlands. E-mail: bakermans@fsw.leidenuniv.nl*

In this study, we examined adults' cardiac reactivity to repeated infant cry sounds in a genetically informative design. Three episodes of cry stimuli were presented to a sample of 184 adult twin pairs. Cardiac reactivity increased with each cry episode, indicating that subjects were increasingly sensitized to repeated infant distress signals. Non-parents showed more cardiac reactivity than parents, and males displayed a larger increase in heart rate (HR) in response to repeated cry sounds than females. Multivariate genetic modeling showed that the genetic component of adults' HR while listening to infant crying was substantial. Genetic factors explained 37–51% of the variance in HR and similar genes influenced HR at baseline and HR reactivity to infant crying. The remaining variance in HR across the cry paradigm was accounted for by unique environmental influences (including measurement error). These results point to genetic and experiential effects on HR reactivity to infant crying that may contribute to the explanation of variance in sensitive and harsh parenting.

Keywords: Behavior genetics, crying, heart rate, heritability, infant, parenting, twins

Received 17 December 2009, revised 09 March 2010; 13 May 2010; 24 June 2010, accepted for publication 25 June 2010

Infant crying alerts the environment, conveys a sense of urgency and can motivate parents to alleviate the infant's distress (Bowlby 1969; Murray 1979; Zeifman 2001), but it can also evoke intense negative emotions in parents and may trigger abuse, neglect and infanticide (Soltis 2004). Physiological response to infant crying is considered an important mechanism explaining these divergent caregiving behaviors (McCanne & Hagstrom 1996; Murray 1985). In this first behavior genetic study of cardiac reactivity to infant crying, we examined whether genetic factors contribute to individual differences in physiological responsivity to cry sounds.

Both males and females, parents and non-parents respond with physiological arousal to infant cry sounds, as manifested by cardiac acceleration and increases in skin conductance (Frodi *et al*. 1978a; Groh & Roisman 2009). Infant cries elicit greater autonomic arousal in adults than other sounds with comparable annoying features (Murray 1985), which may indicate empathic distress that facilitates sensitive caregiving. Indeed, parents who display a strong physiological response to cry sounds perceive these stimuli as more aversive and distressing (Frodi *et al*. 1978a,b) are more alerted (Fleming *et al*. 2002) and are more likely to respond quickly (Del Vecchio *et al*. 2009). However, crying can also be a major trigger of child abuse, neglect and infanticide (Barr *et al*. 2006; Soltis 2004). Abusive parents are more negatively affected by the aversive features of crying and overreact to stressful child-related stimuli, showing more hostile attributions (Bauer & Twentyman 1985) and heightened physiological reactivity (McCanne & Hagstrom 1996). It has been shown that abusive parents display increased autonomic nervous system activity during a wide range of conditions, including cry sounds, pleasant child-related stimuli, aversive non-child related stimuli such as a cold pressor task and also during baseline conditions (e.g. Casanova *et al*. 1992 1994; Frodi & Lamb 1980; for a review, see McCanne & Hagstrom 1996). Because physiological hyperreactivity to infant crying has also been found in adults at risk for child abuse who had no children of their own (e.g. Crowe & Zeskind 1992), more basal biological and genetic factors may affect reactivity to stressful child stimuli. Indeed, previous behavior genetic studies showed that cardiac reactivity to other psychological stressors is heritable (e.g. De Geus *et al*. 2007; for a review, see Hewitt & Turner 1995).

In a genetically informative study, we examined adults' cardiac reactivity to repeated cry sounds. Because infant cry sounds consist of many vocalizations and of an acoustic structure that changes over time (Green *et al*. 1998), we presented cry sounds varying in pitch while measuring adults' heart rate (HR). Second, we investigated the extent to which genetic and environmental influences contribute to the explanation of variance in cardiac reactivity to cry sounds, using a multivariate behavioral genetic approach that takes into account both baseline HR and HR during exposure to the cry sounds. We hypothesized that genetic factors influence individual differences in cardiac reactivity, that there would be a substantial overlap in genes affecting HR at baseline and during the presentations of the cry stimuli and that new genetic effects might emerge during the cry episodes.

doi: 10.1111/j.1601-183X.2010.00624.x

Materials and methods

Subjects

Participants were recruited using the municipal registers of five cities in the western region of the Netherlands, through advertisements and a website asking for participants and by word of mouth. The sample consisted of 50 male and 134 female twin pairs; mean age was 33.0 years (SD = 10.8, range 18–69). The twins were from a predominantly middle-class population; their mean educational level was 3.46 (SD = 0.93) on a scale ranging from 1 (elementary school) to 5 (Bachelor's or Master's degree). Twenty-nine percent of the participants were parents; the mean age of their children was 12.02 years (SD = 7.27). Ninety-three twin pairs (51%) were monozygotic (MZ) and 91 (49%) were dizygotic (DZ). Zygosity was determined on the basis of a zygosity questionnaire with items on similarities between twin members in childhood, experiences of mistaking one twin for another in childhood and the twins' own opinion with regard to their zygosity (Magnus *et al*. 1983). The validity of this questionnaire was established in previous studies comparing the zygosity classification with the results of DNA analyses (Eisen *et al*. 1989; Magnus *et al*. 1983). In this study, genetic analyses of six polymorphisms were conducted; results indicated that 12 twin pairs (6.5% of the sample) classified as MZ on the basis of the questionnaire were in fact DZ. Twin pairs were invited to the lab and were tested individually in two quiet rooms. The lab visit started with several cognitive assessments after which an electrocardiographic device was fitted. Following an hour long interview, the cry paradigm was administered, which lasted about 30 min. Permission for this study was obtained from the ethics committee of the Faculty of Social and Behavioral Sciences, and informed consent was obtained for all participants.

Instruments

Cry stimuli

Cry sounds were derived from the spontaneous crying of a healthy 2-day old, full birth-weight, full-term female infant, midway between scheduled feedings. A 10-s portion of the sustained period of crying, containing seven expiratory sounds, was selected for presentation. The peak fundamental frequencies (Peak F_0) of the entire cry were 515 ± 15 Hz. Two new 10-s cry stimuli were created by digitally increasing the original cry by approximately 200 and 400 Hz, respectively, resulting in two new 10-s cry sounds with an overall Peak F_0 of 714.5 Hz (700 Hz cry) and 895.8 Hz (900 Hz cry). Changes in the Peak F_0 of these two cries were made with comparable changes in the harmonic structures of the seven cry expirations across the entire 10-s cry sound segments while holding the temporal components constant. Digitally manipulated cry sounds have been successfully used in previous studies, showing their validity in terms of perception and (anticipated) caregiving responses (Dessureau *et al*. 1998; Schuetze & Zeskind 2001; Schuetze *et al*. 2003). The 500 Hz cry is characteristic of the cries of normal, healthy infants (LaGasse *et al*. 2005); fundamental frequencies of 700 and 900 Hz (and even higher) are observed in transient pain cries of healthy infants (Porter *et al*. 1988; Zeskind & Collins 1987) and also in the cries of infants with medical and neurological conditions (Soltis 2004).

Cry paradigm

The cry paradigm was administered using a laptop with E-prime software (Version 1.1; Psychology Software Tools, Inc., PA, USA). The stimuli were presented at the same volume through Sennheiser HD202 headphones. During the baseline condition, participants were instructed to relax and look at three landscape photographs that were presented for 6 min in total. After a practice trial during which the 500 Hz cry was presented, the cry stimuli were presented in three cycles or *episodes*. Each episode consisted of three cry sounds (500, 700 and 900 Hz sounds), which were presented in a random order. Each cry sound was followed by the collection of a saliva sample, which took about a minute. Because of the saliva samples, the cry sounds were presented with an intertrial interval of 1 min. Thus, participants listened to nine cry sounds in total that were grouped in three episodes of 2 min and 30 s each.

Cardiac activity

Heart rate was recorded with the Ambulatory Monitoring System (VU-AMS5fs; TD-FPP, Vrije Universiteit, Amsterdam, the Netherlands; http://www.psy.vu.nl/vu-ams/; De Geus *et al*. 1995; Willemsen *et al*. 1996). The electrocardiogram (ECG) signal was recorded continuously using three disposable pregelled Ag-AGCL electrodes (ConMed, New York, USA) that were placed below the right collar bone 4 cm to the right of the sternum, 4 cm under the left nipple and at the lateral right side. The full ECG signal was stored at a 16-bit sampling rate. Heart rate responses were synchronized to the cry sounds using an Event Marker button on the AMS device. The experimenter pushed the button 2 s before each cry sound was presented, leaving markers that allowed for accurate labeling of each cry sound.

Statistical analyses

Data processing

Physiological measures were available for 331 individuals (90%); attrition was mostly because of equipment failure and incorrect markers. Mean HR was calculated by peak detection of the R-wave via a Matlab script (Version 7.6.0; MathWorks, MA, USA). The resulting interbeat intervals were visually inspected; in the case of irregularities, peak detection of the raw signal was repeated after using a 5–50 Hz zero-phase shifting bandpass filter. On the basis of standardized scores, six participants with outlying HR values for baseline and for the cry stimuli were identified. For each of them, we winsorized the HR values, that is replaced them with the next highest value of the remaining distribution (Tabachnik & Fidell 2001), while ensuring that the differences between HR values of one individual (pattern of reactivity) remained intact. Baseline levels of HR were averaged across the resting conditions and HR levels during the presentation of the cry stimuli were aggregated across each cry pitch as well as across each cry episode.

Descriptive analyses

We employed multilevel regression models to estimate the effects of cry pitch and episode on adults' HR. Multilevel analyses match the hierarchical structure of the data: the separate measurements of HR were nested within individuals, while individuals were nested within twin pairs. Thus, three levels were specified: stimulus, person and twin level. Gender was entered into the model at the twin level, parental status was entered at the person level and episode and cry pitch were entered into the model at the stimulus level. All independent variables were centered around their mean. Multilevel regression models were fitted using MLWIN, Version 2.02 (Rasbash *et al*. 2005). Fixed regression coefficients were estimated by maximum likelihood and tested using two-tailed *z*-tests. Likelihood ratio tests were used to evaluate the variance of the random intercepts and of the random slopes as well as overall model improvement.

We started with an intercept-only model, which decomposed the variance in HR into three independent components (pertaining to the twin, person and stimulus level). Gender and parental status were added to the intercept-only model to examine their effects on HR. Episode (baseline, cry episode 1, cry episode 2 and cry episode 3) and cry pitch (0 for baseline, 500, 700 and 900 Hz) were subsequently added to the model as continuous variables. In the next step, the regression coefficient for episode was allowed to be random at the person level in order to examine whether the increase or the decrease in HR during the cry paradigm varied significantly between persons. In addition, we examined whether there was a random effect of cry pitch. Lastly, we tested for interaction effects between gender or parental status on the one hand and episode or cry pitch on the other hand.

Behavior genetic analyses

Behavior genetic analyses using structural equation modeling were conducted to examine the relative contribution of genetic and environmental factors to HR at baseline and during the cry episodes. Monozygotic and DZ twins differ in their genetic relatedness: MZ twins share 100% of their genes, whereas DZ twins share on average 50% of their genes. By comparing the resemblance of MZ twins for a trait with the resemblance of DZ twins, it is possible to estimate to what extent genetic factors explain phenotypic variation for that trait (Plomin *et al*. 2005). Environmental influences are *shared* by both members of a twin pair when these influences make them more similar in their behavior, whereas *unique* environmental factors make twins more different.

A multivariate genetic analysis was conducted including HR at baseline and during each of the three cry episodes (Neale & Cardon 1992; Plomin *et al*. 2005). The basic path model of genetic and environmental influences on HR was specified using a triangular or Cholesky decomposition (Figure 1). To quantify and test the significance of genetic factors (*A*), shared environmental (*C*) and unique environmental factors (*E*, including measurement error), each of these influences were modeled as latent (unmeasured) factors affecting individual differences in HR. The contribution of genetic factor *A* to baseline levels of HR refers to the heritability of HR at baseline. Genetic influences on HR during the first cry episode are represented by genetic factor *A* (i.e. the genes that affect baseline levels of HR may also influence HR during cry episode 1) and by genetic factor A_{cry1} (i.e. genes that affect HR only while listening to cry episode 1). Therefore, the heritability of HR during cry episode 1 is the summed effect of factors *A* and A_{cry1}. Similarly, HR during the second cry episode is influenced by the genetic factors that also affect HR at baseline (*A*) and during the first cry episode (A_{cry1}), whereas new genetic effects may also emerge (A_{cry2}). Finally, HR during the third cry episode is a function of the genetic factors influencing HR during previous episodes (*A*, A_{cry1}, A_{cry2}) and new genetic effects (A_{cry3}).

Thus, the extent to which HR during the various parts of the cry paradigm loads on the same genetic and environmental factors indicates continuity. For example, genetic factor *A* may be considered a common genetic factor when the factor influences baseline levels of HR as well as HR during (one of) the cry episodes. However, the effect of a common factor may increase or decrease when going from one episode to the next. The extent to which HR during various parts of the cry paradigm is not influenced by the same genetic or environmental factors indicates change, for example when novel genetic effects emerge during one of the cry episodes (A_{cry1}, A_{cry2}, A_{cry3}).

Model fitting procedure

All genetic analyses were carried out using the software package MX Version 1.7.03 (Neale *et al*. 2003). Gender, age and parental status were included as covariates. The full model including all genetic, shared environmental and unique environmental factors was fitted to the data, and the significance of *A* and *C* was tested by comparing the fit of a *CE*, *AE* and *E* model to that of the full, saturated *ACE* model. When the fit of one of these nested models is not significantly worse compared with that of the *ACE* model, the simpler and more parsimonious model is preferred. After selection of the best-fitting model, we tested whether the cry episodes resulted in the emergence of new genetic or shared environmental factors by constraining the corresponding path coefficients to zero. Similarly, we tested for common genetic or shared environmental factors by constraining the parameters for the respective factor to the subsequent episode(s) of the cry paradigm to zero. Finally, to examine whether the effect of a common factor was amplified or deamplified by the following episode, we specified a model that constrained the respective genetic or environmental path coefficients to be equal. Likelihood ratio tests were used to compare the fit of each nested model to the full model. The difference in fit is distributed as χ^2 with the difference in number of fixed parameters of the two models as the degrees of freedom.

Results

Cardiac reactivity during the cry paradigm

The effects of episode and cry pitch on HR were examined using multilevel analyses. Descriptive statistics for HR during the cry paradigm are listed in Table 1, and results of the intercept-only model are presented in Table 2 (Model 1). The estimated value of the intraclass correlation was 31.82/(31.82 + 50.98 + 14.47) = 0.33 for the twin level, and 50.98/(31.82 + 50.98 + 14.47) = 0.52 for the person level, providing evidence for a three-level hierarchical structure. Across all episodes of the cry paradigm, the mean HR for this sample was 71.86 beats per minute. Gender and parental status were then added as predictors to the intercept-only model (Model 2), but this did not result in an improved fit (χ^2 [2] = 4.98, $P = 0.08$). Heart rate was not significantly associated with parental status ($z = -0.76$, $P = 0.45$), but males had lower mean HR than females ($z = -2.09$, $P = 0.04$). Episode and cry pitch were subsequently added (Model 3). The fit of this model was good in comparison with the previous model (χ^2 [2] = 452.21, $P < 0.01$). There was no effect of cry pitch on HR ($z = 0.32$, $P = 0.75$), but each subsequent episode of the cry paradigm elicited a significant increase in HR of 1.39 beats per minute compared to the previous episode ($z = 20.43$, $P < 0.01$).

In addition, there was a random effect of episode at the person level (χ^2 [2] = 29.63, $P < 0.01$), which indicated that the effect of episode on HR varied significantly across persons (Model 4). In other words, some participants showed a larger increase in HR over the course of the cry paradigm than other participants. The covariance between the random intercepts and random slopes was also significant (χ^2 [1] = 11.08, $P < 0.01$): adults with a higher mean HR displayed larger increases in HR during the cry paradigm than adults with a lower mean HR ($r = 0.41$). The addition of a random effect of cry pitch at the person level did not result in an improved model fit (χ^2 [3] = 5.50, $P = 0.14$; not reported in Table 2).

Lastly, adding the interactions between gender and parental status, on the one hand, and episode and pitch, on the other hand, resulted in a significant improvement in model fit (χ^2 [4] = 11.13, $P = 0.03$; Model 5). There was a significant interaction between episode and gender ($z = 2.38$, $P = 0.02$) and between episode and parental status ($z = 2.45$, $P = 0.01$): the increase in HR during the cry paradigm was larger for males than for females, and larger for non-parents than for parents.

Behavior genetic analyses of cardiac reactivity

Because the descriptive analyses indicated that there was an accumulation of reactivity over the course of the cry paradigm, the behavior genetic analyses focused on baseline levels of HR and mean HR during each of the three cry episodes. The analysis included 71 MZ twin pairs and 67 DZ twin pairs with complete data for each episode of the cry paradigm. Gender, age and parental status were included as covariates. The variance component estimates of the final model are shown in Figure 1 and in Table 3, including the 95% confidence intervals for the estimates.

Table 1: Means and standard deviations of mean HR at baseline and during each cry episode

	Males				Females					
	Children[†]		No children[‡]		Children[§]		No children[¶]		Total*	
	M	SD	*M*	SD	*M*	SD	*M*	SD	*M*	SD
Baseline	66.91	10.31	65.87	8.68	69.11	8.04	70.16	9.52	68.89	9.27
Cry episode 1	69.00	10.25	68.55	9.24	71.20	7.94	71.98	9.23	70.97	9.13
Cry episode 2	70.26	9.87	70.48	9.13	72.54	8.44	73.46	9.81	72.49	9.47
Cry episode 3	71.15	10.24	72.07	9.10	72.72	8.24	74.67	10.01	73.50	9.57

*$n = 319–329$.
†$n = 27–28$.
‡$n = 56–58$.
§$n = 65–69$.
¶$n = 169–175$.

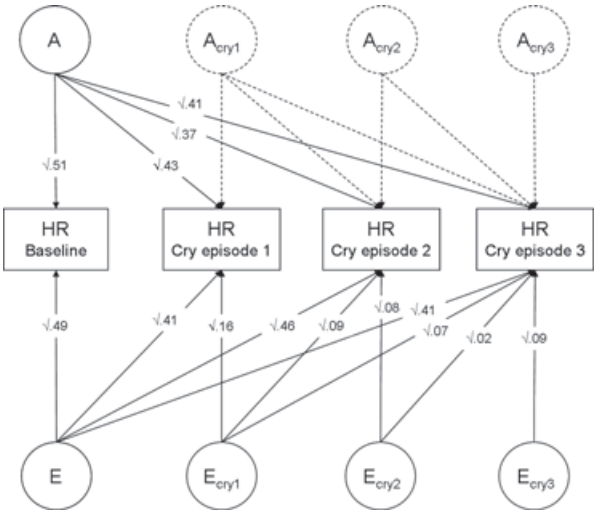

Figure 1: Variance component estimates for genetic and unique environmental influences on HR during the cry paradigm. Variance component estimates are based on the final model. Non-significant path loadings are indicated by dotted lines.

For all episodes of the cry paradigm, the MZ twin correlations were higher than the DZ twin correlations, which suggests heritability of individual differences in HR (baseline $r_{MZ} = 0.51$, $P < 0.01$, $r_{DZ} = 0.26$, $P = 0.03$; cry episode 1 $r_{MZ} = 0.49$, $P < 0.01$, $r_{DZ} = 0.19$, $P = 0.12$; cry episode 2 $r_{MZ} = 0.41$, $P < 0.01$, $r_{DZ} = 0.13$, $P = 0.27$ and cry episode 3 $r_{MZ} = 0.44$, $P < 0.01$, $r_{DZ} = 0.24$, $P = 0.04$). The AE model including genetic and unique environmental factors was the best-fitting model for HR during the cry paradigm (χ^2 [10, $N = 138$] = 0.43, $P > 0.99$) as the fit of this model was not significantly worse compared to the full *ACE* model.

The following sequence of models was tested to examine whether genetic influences on HR were similar for all episodes or specific to (one of) the cry episodes. Constraining the coefficients for the third and fourth genetic factor (A_{cry2} and A_{cry3}) to zero did not result in a significantly worse model fit (χ^2 [3, $N = 138$] = 0.32, $P = 0.96$). Similarly, constraining factor A_{cry1} (as a new genetic effect emerging during the cry episodes) to zero did not result in a significantly worse model fit (χ^2 [3, $N = 138$] = 6.63, $P = 0.09$). Thus, the results of the multivariate genetic analysis provide evidence for continuity of genetic effects on HR during the cry paradigm. One common genetic factor accounted for 51% of the variance in HR at baseline and between 37% and 43% of the variance during the cry episodes. The magnitude of these genetic influences on HR did not differ between the episodes of the cry paradigm (χ^2 [3, $N = 138$] = 4.59, $P = 0.21$).

The remaining variance in HR across the cry paradigm was accounted for by unique environmental influences (including measurement error). The first factor (*E*) explained between 41% and 49% of the variance in HR during baseline and cry episodes, indicating that there was a substantial overlap in unique environmental factors that affected adults' HR during the various parts of the task. Two other factors (E_{cry1} and E_{cry2}) represented unique environmental influences that were similar for two or more cry episodes. Lastly, episode-specific unique environmental influences accounted for a small part of the variance in HR in each of the cry episodes.

Discussion

In this study, we examined adults' cardiac reactivity to repeated presentations of infant cry sounds in a genetically informative design. Although no differences were found in cardiac reactivity for cry stimuli varying in pitch, there was an increase in reactivity, with each cry episode eliciting a higher HR compared to the previous one. Non-parents and males showed a larger increase in cardiac reactivity over the course of the cry episodes than parents and females. Multivariate genetic modeling showed that genetic influences contributed significantly to individual differences in cardiac reactivity to infant cry sounds. The heritability of HR at baseline and during each cry episode was substantial (37–51%), and similar genes influenced both HR at baseline and HR reactivity to infant crying. There was no evidence for genetic influences that were specific to the cry episodes.

Table 2: Effects of episode and cry pitch on HR

	Model 1	Model 2	Model 3	Model 4	Model 5
Fixed effects					
Intercept	71.86 ± 0.58 (<0.01)	72.84 ± 0.75 (<0.01)	72.84 ± 0.74 (<0.01)	72.84 ± 0.74 (<0.01)	72.86 ± 0.74 (<0.01)
Gender		−2.72 ± 1.31 (.04)	−2.69 ± 1.30 (.04)	−3.12 ± 1.29 (0.02)	−2.69 ± 1.30 (.04)
Parental status		−0.88 ± 1.15 (.45)	−0.88 ± 1.15 (.44)	−0.53 ± 1.13 (.64)	−0.97 ± 1.15 (.40)
Episode			1.39 ± 0.07 (<0.01)	1.39 ± 0.08 (<0.01)	1.40 ± 0.10 (<0.01)
Cry pitch			0.02 ± 0.07 (.75)	0.02 ± 0.07 (.74)	0.03 ± 0.09 (.77)
Episode × parental status					−0.41 ± 0.17 (.01)
Episode × gender					0.42 ± 0.18 (.02)
Pitch × parental status					0.11 ± 0.15 (.47)
Pitch × gender					−0.14 ± 0.15 (.37)
Variance components					
Twin level					
Intercept (σ^2_{v0})	31.82 ± 7.17	30.28 ± 7.02	29.93 ± 6.98	29.79 ± 6.79	29.70 ± 6.78
Person level					
Intercept (σ^2_{u0})	50.98 ± 5.99	50.90 ± 5.98	51.11 ± 5.98	51.35 ± 5.90	51.29 ± 5.90
Slope episode (σ^2_{u3})				0.52 ± 0.14	0.47 ± 0.14
Covariance intercept/slope episode (σ^2_{u03})				2.11 ± 0.63	2.06 ± 0.63
Episode level					
Intercept ($\sigma^2{}_e$)	14.47 ± 0.38	14.47 ± 0.38	12.41 ± 0.32	11.87 ± 0.33	11.86 ± 0.33
Deviance	19333.01	19328.03	18875.82	18846.19	18835.06

Values refer to the estimates ± SE (two-sided *P* value *Z*-test).

Table 3: Genetic and unique environmental influences on adults' HR responses during the cry paradigm

	Genetic influences (*A*)	Unique environmental influences (*E*)			
	A (%)	*E* (%)	E_{cry1} (%)	E_{cry2} (%)	E_{cry3} (%)
Baseline	51 (36–64)	49 (36–64)			
Cry episode 1	43 (25–58)	41 (27–59)	16 (13–20)		
Cry episode 2	37 (20–52)	46 (31–64)	9 (6–12)	8 (6–10)	
Cry episode 3	41 (23–56)	41 (27–59)	7 (5–9)	2 (1–4)	9 (7–11)

$n = 71$ MZ twin pairs, $n = 67$ DZ twin pairs. 95% confidence intervals for each estimate are provided between parentheses. A, genetic factor for HR during all episodes of the cry paradigm; E, unique environmental factor for HR during all episodes; E_{cry1}, unique environmental factor for all cry episodes; E_{cry2}, unique environmental influences for cry episodes 2 and 3 and E_{cry3}, unique environmental factor for the cry episode 3.

Most of the previous research on physiological reactivity to cry sounds did not investigate how reactivity develops during the task but instead averaged reactivity across cry sounds (e.g. Boukydis & Burgess 1982; Zeskind 1987) or focused on second-to-second changes in HR (e.g. Wiesenfeld *et al*. 1981; Zeskind 1987). This study is the first to show the cumulative effects of cry stimuli presented in relatively quick succession. The results indicate that adults become increasingly sensitized to repeated infant distress signals, which may form the basis for attributions of increased urgency and aversiveness, and reflect a preparation for more active responses. Del Vecchio *et al*. (2009) have shown that mothers who displayed strong HR responses to infant cries presented as long as 10 min responded more quickly and were more likely to check on their infant. To our knowledge, only Crowe and Zeskind (1992) used a similar approach and found a marginally higher HR after the presentation of phonated and hyperphonated cry sounds for adults at risk for child abuse, but not for the control group. It should be noted that the intertrial intervals were much larger in their study than in our study. A shorter time interval between the stimuli as used in our study makes sensitization more likely to occur, especially because the cries within each episode varied in acoustic properties (Vila *et al*. 2007).

Even in the presence of genetic influences on physiological responses to crying, this study suggests that caregiving experience plays a role: adults with no children of their own showed more cardiac reactivity than parents. In addition, males displayed a larger increase in HR in response to repeated cry sounds than females. Gender differences in physiological responses to infant crying are generally not found (Frodi & Lamb 1978; Frodi *et al*. 1978a,b; Groh & Roisman 2009; cf. Brewster *et al*. 1998), though Wiesenfeld *et al*. (1981) found gender differences in cardiac reactivity when parents listened to the cries from their own infant. In addition, males and females differ in their hormonal responses to (unfamiliar) infant cries (Fleming *et al*. 2002; Stallings *et al*. 2001) and following interaction with their own infants (Feldman *et al*. in press). This study extends these findings by showing that gender differences in physiology may emerge in response to *repeated* presentations of infant cry sounds.

With regard to differences in cardiac reactivity between parents and non-parents, Pedersen *et al*. (1996) suggested that parents may show less reactivity than non-parents because they perceive infant cries more accurately, are more adept in selecting an appropriate response and understand the basic resilience of infants. Indeed, previous studies have shown that caregiving experience fine-tunes cry perception (Green *et al*. 1987; Gustafson & Harris 1990) and that parents experienced less negative emotions when listening to cries than non-parents (Zeskind & Lester 1978). The few studies that compared the effects of infant crying on physiological responses and brain activation in parents and non-parents yielded diverging results (Boukydis & Burgess 1982; Murray 1985; Purhonen *et al*. 2001; Seifritz *et al*. 2003). Our findings of larger increases in HR for males and non-parents may partly explain the elevated risk of child maltreatment in families with stepparents (van IJzendoorn *et al*. 2009) when male partners without children of their own become a member of a family that includes their partner's children. In future studies, this issue could be investigated further by including a group of non-biological (step and adoptive) parents.

Several studies have suggested that specific basal neurobiological factors may affect parents' physiological and caregiving responses to crying (e.g. Crowe & Zeskind 1992; Newman 2007; Stallings *et al*. 2001; Swain *et al*. 2007). This study is the first to show that genetic influences account for a substantial part of the variance in adults' HR while listening to infant crying. The heritability of HR at baseline and during the cry episodes varied between 37% and 51%, which is comparable to the heritability estimates reported in the study by De Geus *et al*. (2007) who studied cardiac reactivity to a mental stress task in a sample of middle-aged adults. In addition, multivariate analyses showed mainly continuity of genetic effects on adults' HR during the cry paradigm. There was a single genetic factor that influenced both HR at baseline and HR reactivity to infant crying, and the magnitude of this genetic effect was similar for the baseline and cry conditions. Finally, unique environmental influences (which include measurement error) also contributed significantly to the variance in adults' HR: some of them affected HR during more than one episode, whereas others were specific for one episode.

There was no evidence that exposure to the cry stimuli triggered new genetic effects on adults' HR: similar genetic mechanisms contributed to HR during baseline condition and when exposed to infant cry sounds. This genetic effect on overall HR levels may subsequently influence parental sensitivity to infant signals: preliminary support for this

hypothesis comes from studies showing that adults at risk for abusing their children display physiological hyperreactivity not only to stressful infant stimuli but also in response to pleasant child stimuli, non-child related aversive stimuli and even during baseline conditions (e.g. Casanova *et al*. 1992 1994; Frodi & Lamb 1980). Recent studies have identified genetic polymorphisms involved in the adrenergic (McCaffery *et al*. 2002) and serotonergic system (McCaffery *et al*. 2003; Williams *et al*. 2008) that influence HR and blood pressure at rest and in response to stress.

Nevertheless, the absence of a stress-specific genetic effect is in contrast to previous studies on cardiovascular reactivity, showing amplification of existing genetic effects as well as new genetic effects emerging during stress (De Geus *et al*. 2007; Wang *et al*. 2009). Lack of power for this nearly significant effect because of the modest sample size in this study may account for the different results. Furthermore, the activation of stress-specific genes may also depend on the nature of the stressor. De Geus *et al*. (2007) used mental stress tasks lasting 8.5 min each, and Wang *et al*. (2009) included a social competence interview of 10 min. Listening to continuous infant crying for such a period of time may elicit higher levels of arousal and uncover new genetic effects. Thus, future studies may examine physiological reactivity to an extended period of infant crying (e.g. McCanne & Hagstrom 1996).

This study shows that adults' cardiac reactivity to cry sounds is not only a function of the distress signals emitted by the infant but is also dependent on genetic factors affecting adults' HR, thereby making some adults physiologically more reactive to stressful child stimuli than others (e.g. Riem *et al*. in press). Whether and how this genetic effect is translated in terms of caregiving behavior may also depend on additional environmental risk factors. For example, Caspi *et al*. (2002) reported increased levels of antisocial behavior in adults with low MAOA (monoamine oxidase A) activity dependent on whether they had experienced childhood maltreatment. Interestingly, Casanova *et al*. (1994) have shown that abused mothers display a different physiological response pattern while viewing smiling and crying infants compared to non-abused mothers. In addition, genetic vulnerability may only be translated into less sensitive parenting in the presence of high levels of daily stressors (van IJzendoorn *et al*. 2008). These findings are noteworthy because excessive crying and cry sounds with abnormal acoustic features are known to cause severe stress for parents (Barr *et al*. 2006; Soltis 2004).

This study has some limitations. First, we found no differences in adult cardiac responses to the 500, 700 and 900 Hz cry sounds. Cry sounds with a high fundamental frequency are indicative of severe infant distress (Porter *et al*. 1988) and may elicit higher levels of physiological and perceived arousal in adults than cries with a lower fundamental frequency (Zeskind *et al*. 1985). However, although several studies showed that high-pitched cry sounds were *perceived* as more urgent and arousing (for a review, see LaGasse *et al*. 2005), results with regard to increased *physiological* arousal in adults appear to be equivocal (Boukydis & Burgess 1982; Crowe & Zeskind 1992; Frodi *et al*. 1978b, 1981; Zeskind 1987). In addition, the short intertrial intervals in our study may have diminished differences in physiological reactivity. Second, no control stimuli were included in order to investigate whether adults' cardiac responses were specific for *cry sounds* or simply represented responses to aversive auditory stimuli. It should, however, be noted that Murray (1985) has convincingly shown that cries elicit greater physiological arousal than other aversive sounds. Investigating the cumulative effect of repeated infant distress signals on adults' HR would not have been possible when control stimuli had been included as well (see, for example Crowe & Zeskind 1992 and Zeskind 1987 for studies with similar designs).

Third, only nine cry sounds of short duration were used and presented in a laboratory context. Although the use of standardized stimuli presented in a standardized context is a necessary condition when examining genetic influences on adults' responses to crying, future research may combine these experimental measures with more dynamic measures of perception and observed caregiving (Del Vecchio *et al* 2009; Hubbard & van IJzendoorn 1991). Ambulant measures of HR (e.g. Pieper *et al*. 2007) in the home environment may be combined with assessments of parents' perception of their infants' crying, and with observation of their caregiving behavior. Finally, a limitation may be that our sample size is relatively small compared to previous studies that used a similar genetic approach to cardiac reactivity (De Geus *et al*. 2007; Wang *et al*. 2009). Because of insufficient power, it was not possible to test whether males and females differed in the heritability of HR.

This is the first behavior genetic study on physiological responses to infant crying. We found that adults displayed an increase in cardiac reactivity to repeated presentations of cry stimuli and that similar genes contributed to HR at baseline and HR reactivity to infant crying. This genetic effect on adults' HR while listening to cry sounds may prove to be especially important in explaining why parenting stress because of excessive and aversive crying may lead to less optimal and even abusive parenting.

References

Barr, R.G., Trent, R.B. & Cross, J. (2006) Age-related incidence curve of hospitalized Shaken Baby Syndrome cases: convergent evidence for crying as a trigger to shaking. *Child Abuse Negl* **30**, 7–16.

Bauer, W.D. & Twentyman, C.T. (1985) Abusing, neglectful, and comparison mothers' responses to child-related and non-child-related stressors. *J Consult Clin Psychol* **53**, 335–343.

Boukydis, C.F.Z. & Burgess, R.L. (1982) Adult physiological response to infant cries: effects of temperament of infant, parental status, and gender. *Child Dev* **53**, 1291–1298.

Bowlby, J. (1969) *Attachment and Loss: Vol. 1. Attachment*. Random House, London.

Brewster, A.L., Nelson, J.P., McCanne, T.R. & Milner, J.S. (1998) Gender differences in physiological reactivity to infant cries and smiles in military families. *Child Abuse Negl* **22**, 775–788.

Casanova, G.M., Domanic, J., McCanne, T.R. & Milner, J.S. (1992) Physiological responses to non-child-related stressors in mothers at risk for child abuse. *Child Abuse Negl* **16**, 31–44.

Casanova, G.M., Domanic, J., McCanne, T.R. & Milner, J.S. (1994) Physiological responses to child stimuli in mothers with and

without a childhood history of physical abuse. *Child Abuse Negl* **18**, 995–1004.
Caspi, A., McClay, J., Moffitt, T.E., Mill, J., Martin, J., Craig, I.W., Taylor, A., & Poulton, R. (2002) Role of genotype in the cycle of violence in maltreated children. *Science* **297**, 851–854.
Crowe, H.P. & Zeskind, P.S. (1992) Psychophysiological and perceptual responses to infant cries varying in pitch: comparison of adults with low and high scores on the Child Abuse Potential Inventory. *Child Abuse Negl* **16**, 19–29.
De Geus, E.J.C., Willemsen, G.H.M., Klaver, C.H.A.M. & van Doornen, L.J.P. (1995) Ambulatory measurement of respiratory sinus arrhythmia and respiration rate. *Biol Psychol* **41**, 205–227.
De Geus, E.J.C., Kupper, N., Boomsma, D.I. & Snieder, H. (2007) Bivariate genetic modeling of cardiovascular stress reactivity: Does stress uncover genetic variance? *Psychosom Med* **69**, 356–364.
Del Vecchio, T., Walter, A. & O'Leary, S.G. (2009) Affective and physiological factors predicting maternal response to infant crying. *Infant Behav Dev* **32**, 117–122.
Dessureau, B.K., Kurowski, C.O. & Thompson, N.S. (1998) A reassessment of the role of pitch and duration in adults' responses to infant crying. *Infant Behav Dev* **21**, 367–371.
Eisen, S., Neuman, R., Goldberg, J. & True, W. (1989) Determining zygosity in the Vietnam Era – Twin Registry: an approach using questionnaires. *Clin Genet* **35**, 423–432.
Feldman, R., Gordon, I., Schneiderman, I., Weissman, O. & Zagoory-Sharon, O. (in press) Natural variations in maternal and paternal care are associated with systematic changes in oxytocin following parent-infant contact. *Psychoneuroendocrinology* (in press).
Fleming, A.S., Corter, C., Stallings, J. & Steiner, M. (2002) Testosterone and prolactin are associated with emotional responses to infant cries in new fathers. *Horm Behav* **42**, 399–413.
Frodi, A.M. & Lamb, M.E. (1978) Sex differences in responsiveness to infants: a developmental study of psychophysiological and behavioral responses. *Child Dev* **49**, 1182–1188.
Frodi, A.M. & Lamb, M.E. (1980) Child abusers' responses to infant smiles and cries. *Child Dev* **51**, 238–241.
Frodi, A.M., Lamb, M.E., Leavitt, L.A. & Donovan, W.L. (1978a) Fathers' and mothers' responses to infant smiles and cries. *Infant Behav Dev* **1**, 187–198.
Frodi, A.M., Lamb, M.E., Neff, C., Sherry, D., Leavitt, L.A. & Donovan, W.L. (1978b) Fathers' and mothers' responses to the faces and cries of normal and premature infants. *Dev Psychol* **14**, 490–498.
Frodi, A.M., Lamb, M.E. & Wille, D. (1981) Mothers' responses to the cries of normal and premature infants as a function of the birth status of their own child. *J Res Pers* **15**, 122–133.
Green, J.A., Jones, L.E. & Gustafson, G.E. (1987) Perception of cries by parents and nonparents: relation to cry acoustics. *Dev Psychol* **23**, 370–382.
Green, J.A., Gustafson, G.E. & McGhie, A.C. (1998) Changes in infants' cries as a function of time in a cry bout. *Child Dev* **69**, 271–279.
Groh, A.M. & Roisman, G.I. (2009) Adults' autonomic and subjective emotional responses to infant vocalizations: the role of secure base script knowledge. *Dev Psychol* **45**, 889–893.
Gustafson, G.E. & Harris, K.L. (1990) Women's responses to young infants' cries. *Dev Psychol* **26**, 144–152.
Hewitt, J.K. & Turner, J.R. (1995) Behavior genetic studies of cardiovascular responses to stress. In Turner, J.R., Cardon, L.R. & Hewitt, J.K. (eds), *Behavior Genetic Approaches in Behavioral Medicine*. Plenum Press, New York, pp. 87–103.
Hubbard, F.O.A. & van IJzendoorn, M.H. (1991) Maternal unresponsiveness and infant crying across the first 9 months: a naturalistic longitudinal study. *Infant Beh Dev* **14**, 299–312.
LaGasse, L.L., Neal, A.R. & Lester, B.M. (2005) Assessment of infant cry: acoustic cry analysis and parental perception. *Ment Retard Dev Disab Res Rev* **11**, 83–93.
Magnus, P., Berg, K. & Nance, W.E. (1983) Predicting zygosity in Norwegian twin pairs born 1915–1960. *Clin Genet* **24**, 103–112.
McCaffery, J.M., Pogue-Geile, M.F., Ferrell, R.E., Petro, N. & Manuck, S.B. (2002) Variability within α- and β-adrenoreceptor genes as a predictor of cardiovascular function at rest and in response to mental challenge. *J Hypertens* **20**, 1105–1114.
McCaffery, J.M., Bleil, M., Pogue-Geile, M.F., Ferrell, R.E. & Manuck, S.B. (2003) Allelic variation in the serotonin transporter gene-linked polymorphic region (5-HTTLPR) and cardiovascular reactivity in young adult male and female twins of European-American descent. *Psychosom Med* **65**, 721–728.
McCanne, T.R. & Hagstrom, A.H. (1996) Physiological hyperreactivity to stressors in physical child abusers and individuals at risk for being physically abusive. *Aggress Violent Behav* **1**, 345–358.
Murray, A.D. (1979) Infant crying as an elicitor of parental behavior: An examination of two models. *Psychol Bull* **86**, 191–215.
Murray, A.D. (1985) Aversiveness is in the mind of the beholder: perception of infant crying by adults. In Lester, B.M. & Boukydis, C.F.Z. (eds), *Infant Crying: Theoretical and Research Perspectives*. Plenum Press, New York, pp. 217–240.
Neale, M. & Cardon, L. (1992) *Methodology for Genetic Studies of Twins and Families*. Kluwer Academic, Dordrecht.
Neale, M.C., Boker, S.M., Xie, G. & Maes, H.H. (2003) *Mx: Statistical Modeling*, 6th edn. Department of Psychiatry, Richmond, VA.
Newman, J.D. (2007) Neural circuits underlying crying and cry responding in mammals. *Behav Brain Res* **182**, 155–165.
Pedersen, F.A., Huffman, L.C., del Carmen, R. & Bryan, Y.E. (1996) Prenatal maternal reactivity to infant cries predicts postnatal perceptions of infant temperament and marriage appraisal. *Child Dev* **67**, 2541–2552.
Pieper, S., Brosschot, J.F., van der Leeden, R. & Thayer, J.F. (2007) Cardiac effects of momentary assessed worry episodes and stressful events. *Psychosom Med* **69**, 901–909.
Plomin, R., DeFries, J.C., McClearn, G.E. & McGuffin, P. (2005) *Behavioral Genetics*, 4th edn. Worth Publishers, New York.
Porter, F.L., Porges. S.W. & Marshall, R.E. (1988) Newborn pain cries and vagal tone: parallel changes in response to circumcision. *Child Dev* **59**, 495–505.
Purhonen, M., Kilpeläinen-Lees, Pääkkönen, A., Yppärilä, H., Lehtonen, J. & Karhu, J. (2001) Effects of maternity on auditory event-related potentials to human sound. *Neuroreport* **12**, 2975–2979.
Rasbash, J., Charlton, C., Browne, W.J., Healy, M. & Cameron, B. (2005) MLwiN Version 2.02. Centre for Multilevel Modelling, University of Bristol.
Riem, M.E., Pieper, S., Out, D., Bakermans-Kranenburg, M.J. & van IJzendoorn, M.H. (in press) Oxytocin receptor gene and depressive symptoms associated with physiological reactivity to infant crying. *Soc Cogn Affect Neurosci* (in press).
Schuetze, P. & Zeskind, P.S. (2001) Relations between women's depressive symptoms and perceptions of infant distress signals varying in pitch. *Infancy* **2**, 483–499.
Schuetze, P., Zeskind, P.S. & Eiden, R.D. (2003) The perceptions of infant distress signals varying in pitch by cocaine-using mothers. *Infancy* **4**, 65–83.
Seifritz, S., Esposito, F., Neuhoff, J.G., Lüthi, A., Mustovic, H., Dammann, G., Von Bardeleben, U., Radue, E.W., Cirillo, S., Tedeschi, G. & Di Salli, F. (2003) Differential sex-independent amygdala response to infant crying and laughing in parents versus nonparents. *Biol Psychiatry* **54**, 1367–1375.
Soltis, J. (2004) The signal functions of early infant crying. *Behav Brain Sci* **27**, 443–490.
Stallings, J., Fleming, A.S., Corter, C., Worthman, C. & Steiner, M. (2001) The effects of infant cries and odors on sympathy, cortisol, and autonomic responses in new mothers and nonpostpartum women. *Parent Sci Pract* **1**, 71–100.
Swain, J.E., Lorberbaum, J.P., Kose, S. & Strathearn, L. (2007) Brain basis of early parent-infant interactions: psychology, physiology, and *in vivo* functional neuroimaging studies. *J Child Psychol Psychiatry* **48**, 262–287.
Tabachnik, B.G. & Fidell, L.S. (2001) *Using Multivariate Statistics*, 4th edn. Allyn and Bacon, Boston.

van IJzendoorn, M.H., Bakermans-Kranenburg, M.J. & Mesman, J. (2008) Dopamine system genes associated with parenting in the context of daily hassles. *Genes Brain Behav* **7**, 403–410.

van IJzendoorn, M.H., Euser, E.M., Prinzie, P., Juffer, F. & Bakermans-Kranenburg, M.J. (2009) Elevated risk of child maltreatment in families with stepparents but not with adoptive parents. *Child Maltreat* **14**, 369–375.

Vila, J., Guerra, P., Munoz, M.A., Vico, C., Viedma-del Jesús, M.I., Delgado, L.C., Perakakis, P., Kley, E., Mata, J.L. & Rodriguez, S. (2007) Cardiac defense: from attention to action. *Int J Psychophysiol* **66**, 169–182.

Wang, X.L., Ding, X.H., Su, S.Y., Li, Z.B., Riese, H., Thayer, J.F., Treiber, F. & Snieder, H. (2009) Genetic influences on heart rate variability at rest and during stress. *Psychophysiology* **46**, 458–465.

Wiesenfeld, A.R., Malatesta, C.Z. & Deloach, L.L. (1981) Differential parental response to familiar and unfamiliar infant distress signals. *Infant Beh Dev* **4**, 281–295.

Willemsen, G.H.M., De Geus, E.J.C., Klaver, C.H.A.M., van Doornen, L.J.P. & Carroll, D. (1996) Ambulatory monitoring of the impedance cardiogram. *Psychophysiology* **33**, 184–193.

Williams, R.B., Marchuk, D.A., Siegler, I.C., Barefoot, J.C., Helms, M.J., Brummett, B.H., Surwit, R.S., Lane, J.D., Kuhn, C.M., Gadde, K.M., Ashley-Koch, A., Svenson, I.K. & Schanberg, S.M. (2008) Childhood socio-economic status and serotonin transporter gene polymorphism enhance cardiovascular reactivity to mental stress. *Psychosom Med* **70**, 32–39.

Zeifman, D.M. (2001) An ethological analysis of human infant crying: answering Tinbergen's four questions. *Dev Psychobiol* **39**, 265–285.

Zeskind, P.S. (1987) Adult heart-rate responses to infant cry sounds. *Br J Dev Psychol* **5**, 73–79.

Zeskind, P.S. & Collins, V. (1987) Pitch of infant crying and caregiving responses in a natural setting. *Infant Bev Dev* **10**, 501–504.

Zeskind, P.S. & Lester, B.M. (1978) Acoustic features and auditory perceptions of the cries of newborns with prenatal and perinatal complications. *Child Dev* **49**, 580–589.

Zeskind, P.S., Sale, J., Maio, M.L., Huntington, L. & Weiseman, J.R. (1985) Adult perceptions of pain and hunger cries: a synchrony of arousal. *Child Dev* **56**, 549–554.

Acknowledgments

We thank Philip Sanford Zeskind for providing the cry stimuli and advice on their use. We are grateful to Fieke Pannebakker, Jolanda den Heijer, Femke Pijlman and several students for their contribution to various parts of the study. Last but not the least, we thank the twins who participated in the study. M.J.B.K. and M.H.vIJ. were supported by awards from the Netherlands Organization for Scientific Research (M.J.B.K.: VIDI grant no. 452-04-306; M.H.vIJ.: SPINOZA prize).