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ORIGINAL RESEARCH

Child Care, Socio-economic Status and Problem Behavior: A Study of Gene–Environment Interaction in Young Dutch Twins

Christel M. Middeldorp · Diane J. Lamb · Jacqueline M. Vink · Meike Bartels · Catharina E. M. van Beijsterveldt · Dorret I. Boomsma

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Abstract The influences of formal child care before age 4 on behavioral problems at 3, 5, and 7 years of age were assessed in 18,932 Dutch twins (3,878 attended formal child care). The effect of formal child care was studied on the average level of problem behavior and as moderator of genetic and non-genetic influences, while taking into account effects of sex and parental socio-economic status (SES). There was a small association between attending formal child care and higher externalizing problems, especially when SES was low. Heritability was lower for formal child care and in lower SES conditions. These effects were largest at age 7 and for externalizing problems. In 7 year-old boys and girls, the difference in heritability between the formal child care group of low SES and the home care group of high SES was 30 % for externalizing and ∼20 % for internalizing problems. The decrease in heritability was explained by a larger influence of the environment, rather than by a decrease in genetic variance. These results support a bioecological model in which heritability is lower in circumstances associated with more problem behavior.

Keywords Child care · Internalizing problem behavior · Externalizing problem behavior · Gene–environment interaction · Twins · Genetics

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C. M. Middeldorp (✉) · D. J. Lamb · J. M. Vink · M. Bartels · C. E. M. van Beijsterveldt · D. I. Boomsma
Netherlands Twin Register, Department Biological Psychology, VU University, Van der Boechorststraat 1, 1081 BT Amsterdam, The Netherlands
e-mail: c.m.middeldorp@vu.nl

C. M. Middeldorp
Department of Child and Adolescent Psychiatry, GGZ inGeest/ VU Medical Center, Amsterdam, The Netherlands

C. M. Middeldorp · J. M. Vink · D. I. Boomsma
Neuroscience Campus Amsterdam (NCA), Amsterdam, The Netherlands

M. Bartels · D. I. Boomsma
EMGO+ Institute for Health and Care Research, VU University Medical Center, Amsterdam, The Netherlands

There is an ongoing debate about the effects of formal child care during the first years of life on the development of behavioral problems. Studies have yielded contradictory results reporting negative, positive as well as neutral effects of formal child care on problem behavior (for an overview of studies: see Zachrisson et al. (2013), Jaffee et al. (2011), Phillips and Lowenstein (2011). Several factors have been identified that may explain the discrepancies in results, including differences between countries, age of the child when effects are assessed, quality of care and parental socio-economic status. One review of short and long term effects of child care (Phillips and Lowenstein 2011) focused on studies performed in the USA, including the well-known NICHD study of early child care and youth development (NICHD SECCYD; (NICHD Early Child Care Res Network 1998, 2004; Vandell et al. 2010). This review reveals a fairly consistent picture of more hours spent in formal child care being associated with more problem behavior. However, this effect may be moderated by the quality of child care. For children from low income homes, spending more hours in high quality child care seems to be associated with less problem behavior (Phillips and Lowenstein 2011). Moreover, in a later US study, not included in the review, there was no effect of child care before age 3, after correcting for family background (Jaffee et al. 2011). European studies show more heterogeneous results (Jaffee et al. 2011;

Zachrisson et al. 2013). Two early studies performed in Sweden showed an association of child care and lower levels of problem behavior and this effect was larger when children entered formal child care before 1 year of age (Andersson 1989, 1992). Other European studies found no or a negative effect of hours spent in child care on problem behavior (Averdijk et al. 2011; Zachrisson et al. 2013). The relationship with socio-economic status (SES) also differs from studies in the USA. In Norway, attending formal child care is more frequent in families with higher maternal education and higher family income and is associated with slightly higher scores on problem behavior (Bekkhus et al. 2011). In the Netherlands, more problem behavior as a function of child care was reported for lower SES groups (van Beijsterveldt et al. 2005).

Phillips and Lowenstein (2011) pointed out that, in addition to the circumstances related to child care and family background, the effect of child care may depend on neurobiological based responses to stress and on the temperament of the child. Pluess and Belsky (2009, 2010), for example, found that children with a difficult temperament, in comparison to less difficult children, experienced *more* behavioral problems when the quality of the formal child care was low, but *fewer* behavioral problems when experiencing formal child care of high quality (Pluess and Belsky 2009, 2010). These effects were found at age 4.5 as well as at ages 10 and 11 years. Other studies have also indicated that a child's temperament, which is heritable (Saudino 2005, 2009; Groen-Blokhuis et al. 2011) can moderate the effect of type, quantity and quality of child care, with negative effects in difficult children, but not in easy children (Crockenberg and Leerkes 2005; Dettling et al. 2000).

When the expression of a child's genetic susceptibility to problem behavior depends on environmental conditions such as attending formal child care, gene–environment interaction is implied (Kendler 2001). This can be tested in a twin design in which environmental exposures are assessed and the influence of genetic and non-genetic factors on a trait are estimated conditional on the measured environmental exposure (Boomsma and Martin 2002; Eaves 1984; Purcell 2002). One twin study investigated gene–environment interaction for externalizing problems in preschool children, where preschool was defined as "formal, center-based day-care programs that include didactic learning objectives" (Tucker-Drob and Harden 2012). At age 5, though not at age 4, externalizing behavior was more heritable (67 %) in children who attended preschool than in children who did not (heritability of 19 %). There was no main effect of preschool attendance on externalizing problems. The same study also investigated the interaction of preschool exposure with common and unique environment and observed a significant interaction with the common environmental influences (Tucker-Drob and Harden 2012). At age 5, common environment explained 52 % of the variance in externalizing problems in children who did not attend preschool, but did not explain any variance in children who went to preschool.

Two theoretical models make different predictions regarding gene–environment interaction. The diathesis–stress model predicts that genetic vulnerability (diathesis) in the presence of environmental stress, will increase the likelihood of behavioral problems (e.g., Rende and Plomin (1992) and also predicts that the heritability of the trait will be higher for children in at risk environments. If formal child care is seen as a risk factor that increases the likelihood of behavioral problems, the diathesis–stress model predicts a higher heritability in groups that attend formal child care.

In contrast, the bioecological model predicts that risk environments will mask genetic differences between children, whereas enriched environments will enable underlying genetic differences to be amplified (Bronfenbrenner and Ceci 1994; Scarr and McCartney 1983). If formal child care is seen as a risk factor, this model predicts that the heritability of the trait will be lower in children who attend formal child care.

We contrast these two hypotheses in a large study on internalizing and externalizing problem behavior in twins of different ages, from a relatively homogeneous population. The general term 'problem behavior' is used when internalizing and externalizing problems are considered together. The goal was to investigate the effect of formal child care on mean problem behavior scores as well as the interaction between formal child care and genetic and non-genetic influences on problem behavior. Maternal ratings of problem behavior at ages 3, 5 and 7 years were analyzed in mono- and dizygotic twins, for whom information on formal care versus home care between ages 0 and 4 was available. Formal child care ends at age 4, because Dutch children go to school at this age. The sample consisted of twins born between 1986 and 2005 who received child care between 1986 and 2009. In addition to the effects of formal child care, several other factors were taken into account. The effects of sex and age were investigated since earlier analyses in this sample showed differences in mean scores as well as in the effects of genetic and environmental factors on problem behavior (Bartels et al. 2004; van Beijsterveldt et al. 2004). Following the results of the previous studies, which suggested that parental SES as well as the quality of formal child care can influence the effect of formal child care on problem behavior, these variables were also included. We used birth cohort as a proxy for quality of child care with the twins divided into two groups, born before or in 1999 and after 1999. In this period, there were several changes in the Netherlands that led to a lower quality of child care. In 1990, the national Child Care Stimulation Measure was established aiming to facilitate working mothers, which resulted in a large increase in the number of places for children in formal child care centers (from 17,000 to 59,000) (Deynoot-Schaub and Riksen-Walraven 2005). In 1995, child care policy was decentralized to the community. The number of child care centers kept growing, but new centers were mostly nonsubsidized as opposed to predominantly government-subsidized centers prior to 1995 (Deynoot-Schaub and Riksen-Walraven 2005; Vermeer et al. 2008). The percentage of children attending formal child care rose from ∼4 % of children below 4 years in 1991 to 20 % in 2002 (van IJzendoorn et al. 2004). The increase in available places came at the expense of quality. No centers of low quality were observed in 1995 and 37 % were of high quality, while in 2001, 6 % of the centers scored low (36 % in 2005) and only 18 % scored high (0 % in 2005) (Vermeer et al. 2008). The decrease in quality seems to continue. In 2008, quality was lower than in 2005 and from similar data from the UK, Canada, Midwestern US states, and Portugal, it appears that only Portugal scored lower than the Netherlands (de Kruif et al. 2009).

Method

Subjects

Parents of twins took part in large-scale survey studies of the Young Netherlands Twin Register (YNTR), established in 1987. Data collection is longitudinal, with 2–3 yearly assessments and recruitment of newborn twins is ongoing (Bartels et al. 2007; van Beijsterveldt et al. 2013). Data from the birth cohorts 1986–2005 were included in the current study. The surveys for the mothers included questions about formal child care when the twins were 3 and 5 years. From a total sample of 39,088 twins with data at either age, there were 25,416 twins with data both at ages 3 and 5. Seventy-seven percent of the mothers that participated at age 3 also completed the questionnaire at age 5. However, no surveys at age 5 were collected in 2008 and 2009 due to a transition to a new administration database and a shortage of staff. This explains the drop of 35 % between age 3 and age 5.

We analyzed data of children whose mothers reported consistently on formal child care at both ages. Consequently, 1,892 twins from the sample of 25,416 twins were excluded. Additional exclusion criteria were other child care arrangements than formal child care or home care, e.g., a child minder, nanny or medical day care facilities ($N = 3{,}602$ twins), discordance for child care arrangements within a pair ($N = 410$ twins), a severe handicap in at least one child from a pair ($N = 414$ twins), formal child care attendance shorter than 1 year ($N = 110$ twins), or missing data on socio-economic status ($N = 56$ twins). This left data for 18,932 twins, of which 3,878 were concordant for attending formal child care. The home care group also included children who went to a playgroup between ages 2.5 and 4, usually for 3 h once or twice a week.

In this group of 18,932 twins, maternal ratings on problem behavior were available for 9,276 complete and 134 incomplete (i.e., one twin of a pair) 3-year-old twin pairs, 9,416 complete and 13 incomplete 5-year-old twin pairs and 6,218 complete and 129 incomplete 7-year-old twin pairs. The discrepancies between the total number of twins with child care data and the number of twins with problem behavior scores at age 3 and age 5 is due to missingness of items at the other variables in the analyses, for example, too many items missing to calculate the problem behavior scores. The drop in the number of twins at age 7 partly reflects the ongoing data collection and the fact that no surveys at age 7 were collected in 2008 and 2009. Sixty-nine percent of the mothers who participated at age 3 also completed the questionnaire at age 7. The total group of complete twin pairs consisted of 1,474 monyzygotic male, 1671 dizygotic male, 1719 monozygotic female, 1543 dizygotic female and 3,059 dizygotic twin pairs of opposite sex. For same-sex twin pairs, zygosity was based on survey data for 5331 and on DNA markers for 1,076 pairs (van Beijsterveldt et al. 2013).

Measures

At age 3 years of the twins, the survey included questions about what type of child care the parents had arranged for their twins in the last 3 months. At age 5, the survey included the questions: “Did the twins go to child care outside home before age 4?” and “What kind of child care outside home did they attend?”. Answer categories were child care center, playground for toddler, medical day care center and an ‘other‘category of nonparental child care. If answers were inconsistent for age 3 and age 5, children were excluded from the analyses (see above).

Birth cohort was used as an indication of formal child care quality. The year 1999 was defined as cut-off for the switch in quality.

Family socio-economic status (SES) was based on the highest SES level of either parent. At 3 and 7 years of the offspring, a description of the occupation of the parents was available and SES was coded according to the standard classification of occupations (CBS 2001). All families were classified into three SES levels.

Problem behavior was assessed by the Achenbach System of Empirically Based Assessment (ASEBA) at 3 and 7 years of age. The Child Behavior Check List (CBCL) includes two broad categories of problem behavior: internalizing (INT) and externalizing (EXT). Two age-appropriate versions of the Child Behavior Check List (CBCL) were used. At age 3, parents reported on the behavior of their children by means of the CBCL 2/3 and, after 2004, the CBCL 1½–5 (Achenbach 1992). INT is assessed by the syndrome scales: "Anxious" and "Withdrawn/Depressed" and consists of 19 items, and EXT is assessed by: "Aggressive", "Oppositional" and "Overactive" and includes 31 items. At twins' ages 7, parents completed the CBCL 4–18 which assesses INT by the "Withdrawn", "Somatic Complaints" and "Anxious/Depression" scales (31 items), and EXT by the "Rule Breaking" and "Aggressive" syndrome scales (33 items) (Achenbach 1991). For INT at age 3 and 7, Cronbach's alpha's were respectively 0.79 and 0.81. For EXT Cronbach's alpha's were 0.92 and 0.89.

At age 5, problem behavior was assessed with a subset of 42 items of the Devereux Child Behavior (DCB) rating scale. The data for subscales "Aggressive Behavior" (AGG) (seven items) and "Anxiety Problems" (ANX) (five items) were included in the study (Spivack and Spotts 1966; van Beijsterveldt et al. 2004). Cronbach's alpha's were 0.75 and 0.62. The DCB AGG subscale overlaps with 4 items of the CBCL EXT scale, and two items of the ANX DCB subscale overlap with items from the CBCL INT scales.

Longitudinal correlations of the INT/ANX scales for age 3–5, 3–7 and 5–7 were 0.31, 0.34 and 0.39 respectively and for the EXT/AGG scales 0.42, 0.54 and 0.49.

Statistical analyses

A set of independent variables (formal child care, birth cohort, SES, sex and SES*child care) were analyzed as predictors of a child's problem behavior score. They were coded 0, 1 for child care (home care vs. formal child care); 0, 1 for birth cohort (born before or in 1999 or born after 1999); 0, 1, 2 for SES (low, middle, high) and 0 for boys and 1 for girls. The interaction of SES*child care was coded as 0 for the total group with SES 0, as 1 for formal child care with SES 1, and 2 for formal child care with SES 2.

Formal child care, birth cohort, SES and sex were also evaluated as moderators of the latent additive genetic (A), common environmental (C) and unique environmental (E) factors (see Fig. 1). Structural equation modeling (SEM) as implemented in the software package Mx was used to estimate the parameters and to test their significance (Neale et al. 2006). The fixed effects on problem behavior scores, the path coefficients from A, C and E to problem behavior scores, and the effects of the moderators on the path coefficients were estimated by maximum-likelihood. Significance of parameters was tested by likelihood-ratio tests, which indicate the decrease in likelihood for a more restricted model and which has a χ^2 distribution. The significance of the main and interaction effects was tested by constraining the effect at zero while all other effects were included in the model. Thus, the tests were performed one by one under the *full* model. Only when testing the main effect of child care and of SES on behavioral problems, the SES*child care interaction was omitted, since main and interaction effects are not independent. By including all moderating variables in the means model as fixed effects when testing for gene–environment interaction, we corrected for possible gene–environment correlation, taking into account the possibility that attending formal child care and levels of problem behavior might not be independent. Not considering gene–environment correlation may cause biased estimates of gene–environment interaction (Purcell 2002).

Van der Sluis et al. (2012) showed that the estimates of the effects of the moderators can be inflated when the moderator and the variable of interest are correlated, even if the effect of the moderator is included in the means model. However, in the current study, moderators are perfectly correlated within twins, in which case estimates are not inflated (van der Sluis et al. 2012).

Results

In line with the developments in the Netherlands, attendance of formal child care showed a steady increase between 1986 and 2005. In the birth cohorts 1986–1988, ~5 % of the children attended formal child care. After 1989, percentages steadily rose from ~10 % in the early nineties, to around 25 % in the late nineties and ~30 % in the beginning of the millennium. This was followed by a steep increase to ~46 % for the birth cohorts 2003–2005. There was little variation in quantity of formal child care attendance. Eighty-three percent of the children went 2 years or more to formal child care and 65 % went 3 years or more. Moreover, 76 % of the parents reported that their twins went 2 or 3 days to formal child care. So, the majority of the children went to formal child care for 2 years or more and attended 2 or 3 days per week.

The mean internalizing problem scores (INT/ANX) were fairly similar in boys and girls, although at all ages, due to the large sample size, the sex effect was significant (see Table 1). Mean INT/ANX in boys and girls respectively was 4.6 and 4.5 at age 3, 10.6 and 11.0 at age 5 and 4.4 and 4.7 at age 7. Mean externalizing problem behavior scores (EXT/AGG) were significantly higher in boys than in girls at all ages with far larger effect sizes than for

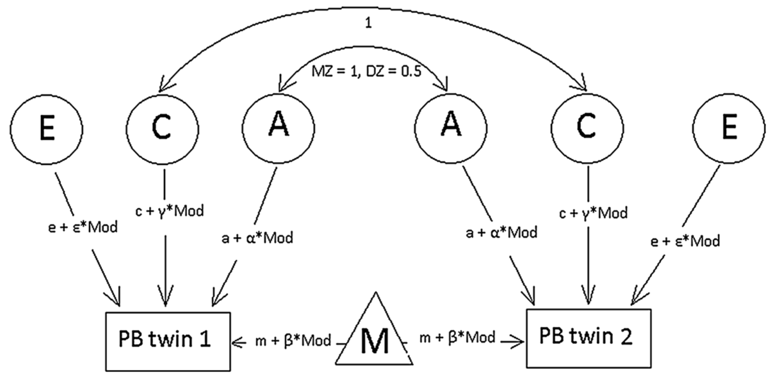

Fig. 1 Gene–environment interaction model. Measured problem behavior (PB) is represented in *rectangles*, and latent factors are symbolized by *circles* and represent additive genetic influences (A), common (C) and unique environment (E). Latent factors have zero means and unit variance. The influence of these factors on PB are given by path coefficients a, c and e. The path coefficients can be moderated by child care, birth cohort, SES and sex (Mod). The effect of the moderators on the path coefficients a, c and e are symbolized as α, γ and ε, respectively. $PB_{jp} = (\alpha_i{*}Mod_i){*}A_{jp} + (\gamma_i{*}\ Mod_i){*}C_{jp} + (\varepsilon_i{*}\ Mod_i){*}E_{jp}$, where i = moderator 1–4 for individual j (1, 2) within pair p. The variance of PB thus equals $V_{PB} = (a + \alpha_i{*}Mod_i)^2 + (c + \gamma_i{*}Mod_i)^2 + (e + \varepsilon_i{*}Mod_i)^2$. The twin pair covariance of PB depends on their genetic resemblance thus $Cov_{MZ} = (a + \alpha_i{*}Mod_i)^2 + (c + \gamma_i{*}Mod_i)^2$ and $Cov_{DZ} = ½\,(a + \alpha_i{*}Mod_i)^2 + (c + \gamma_i{*}Mod_i)^2$. Mean PB is symbolized by a triangle and is a function of sex, SES, child care, birth cohort and the interaction term SES*child care, the effect of these variables on PB is symbolized by β and equals: $m + \beta_k{*}Mod_k$, where k = 1, 5

Table 1 Means and maximum likelihood parameter estimates (standard error) for the effects of sex, SES, childcare, birth cohort, and SES*childcare on mean problem behavior at ages 3, 5 and 7 years

Mean	EXT 3 18.50	AGG 5 12.58	EXT 7 9.73
β sex	**−1.94 (0.14)*** **	**−0.52 (0.05)*** **	**−2.30 (0.11)*** **
β SES	**−1.45 (0.14)*** **	**−0.20 (0.05)*** **	**−1.07 (0.11)*** **
β childcare	**1.39 (0.57)* **	**0.30 (0.21)*** **	**1.53 (0.53)* **
β birth cohort	**−0.58 (0.22)** **	**−0.58 (0.08)*** **	**−0.78 (0.26)*** **
β SES*childcare	**−0.84 (0.35)* **	0.03 (0.13)	**−0.85 (0.31)** **
Mean	INT 3 5.19	ANX 5 1.75	INT 7 4.63
β sex	**−0.22 (0.06)*** **	**0.31 (0.05)*** **	**0.27 (0.08)*** **
β SES	**−0.43 (0.05)*** **	−0.06 (0.05)	**−0.21(0.08)*** **
β childcare	0.37 (0.23)	**0.33 (0.19)** **	0.76 (0.36)
β birth cohort	−0.01 (0.08)	**−0.33 (0.07)*** **	**−0.49 (0.18)** **
β SES*childcare	−0.27 (0.14)	−0.08 (0.12)	−0.37 (0.22)

Significant effects are given in bold

AGG aggression, *ANX* anxiety, *EXT* externalizing, *INT* internalizing

* $p < 0.05$; ** $p < 0.01$; *** $p < 0.005$

INT/ANX. Mean EXT/AGG in boys and girls was 16.7 and 14.8 at age 3, 12.4 and 11.7 at age 5, and 8.5 and 6.2 at age 7.

Figure 2 shows the observed averages of problem behavior as a function of birth cohort, age, SES and child care. Table 1 gives the parameters estimates for the predictors of problem behavior, obtained under the full model, thus including all main and moderator effects. The decrease in quality of day care in the Netherlands since 2000 was not associated with more problem behavior. Overall, children from later birth cohorts had significantly lower INT/ANX and EXT/AGG scores. More importantly, as Fig. 2 illustrates, the difference between the home care and formal child care groups was not larger in the subjects born after 1999. Children from higher SES groups show significantly less problem behavior. At each age, EXT/AGG was significantly higher in children who were in formal child care and the effects on EXT/AGG appeared to be largest in children from low SES families (significant interaction at age 3 and age 7). It should be noted that the effects of formal child care on EXT/AGG were only just significant ($p < 0.05$) at age 3 and age 7 and would not have been considered significant when correcting for multiple testing, even though sample size was large. For INT/ANX, the association with formal child care was only significant at age 5 without a significant SES*child care effect. Overall, the effects were small.

Turning to the results of the analyses of the moderation effects on the path coefficients, the first half of Table 2 shows results for EXT/AGG and the second half for INT/ANX. The SES*child care interaction term was generally

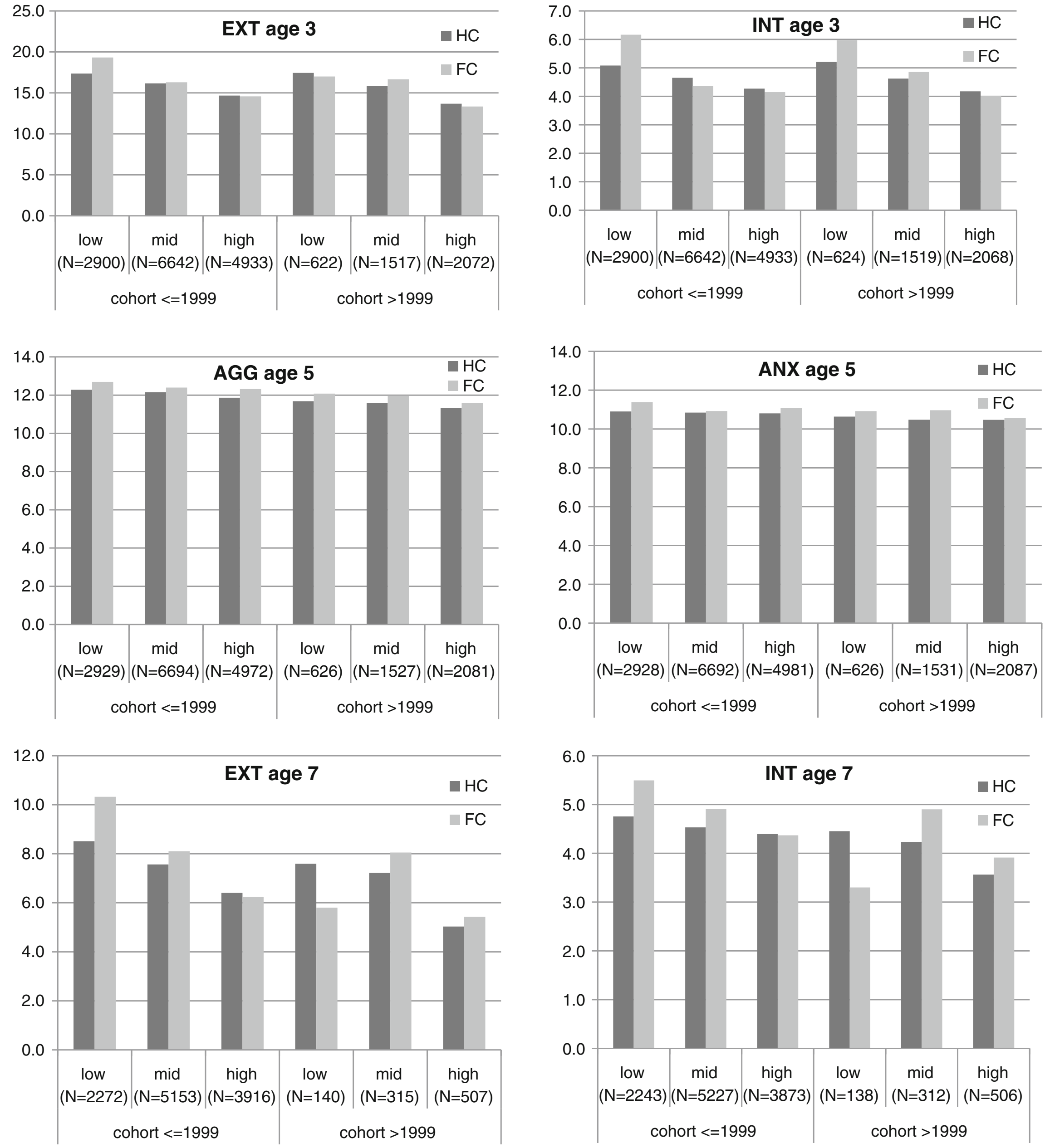

Fig. 2 Observed averages of internalizing and externalizing problem behavior scores for home care (HC) and formal child care (FC) children born before or in 1999 and after 1999 from low, middle or high SES groups

not significant as a moderator and was therefore excluded from these analyses. (The χ^2 (1df) of the moderation effect on A, C or E varied between 0.02 and 3.30, with the exception of the moderation of C for INT at age 3 and of E for AGG at age 5 for which χ^2 (1df) was 11.6 ($p < 0.001$) and 11.5 ($p < 0.001$) respectively.) Table 2 highlights all results with a p value $<$0.05 under the full model so that consistencies in results over age or phenotype are not overlooked due to correction for multiple testing. We will first discuss the results for formal child care on EXT/AGG. There is significant moderation of E at all ages ($p < 0.05$ at age 3 and age 5, and $p < 0.005$ at age 7) with an increase of E in children attending formal child care. At age 3, there is an additional negative effect of formal child care on A, and, at age 7, an additional positive effect on C (both p values $<$0.05). This signifies that at all ages the relative influence of A, i.e., the heritability, is lower in children attending formal child care.

The results for formal child care on INT/ANX were less consistent across the three ages, i.e., a negative effect on E at age 3 ($p < 0.05$), no significant effect at age 5, and, at age 7, a negative effect on A ($p < 0.05$) and a positive

Table 2 Maximum likelihood parameter estimates for path coefficients a, c and e, and for effects (standard errors) of the moderating variables sex, SES, childcare and birth cohort on the path coefficients for problem behavior at ages 3, 5 and 7 years

	EXT 3			AGG 5			EXT 7		
	a	c	e	a	c	e	a	c	e
Path coefficients	7.64 (0.30)	5.76 (0.39)	4.41 (0.12)	2.71 (0.13)	2.01 (0.18)	1.96 (0.05)	6.36 (0.21)	4.07 (0.40)	2.75 (0.09)
β sex	−0.31 (0.27)	**−1.00(0.35)****	0.01 (0.10)	−0.18 (0.11)	−0.29 (0.16)	**−0.17 (0.05)*****	**−1.30 (0.19)*****	−0.76 (0.41)	−0.03 (0.08)
β SES	−0.21 (0.17)	−0.30 (0.23)	**−0.33 (0.08)** ***	0.04 (0.08)	**−0.36 (0.12)*****	−0.03 (0.03)	**−0.26 (0.11)***	**−1.31 (0.26)*****	**−0.20 (0.05)*****
β childcare	**−0.66 (0.32)***	0.46 (0.39)	**0.34 (0.14)** *	0.12 (0.14)	−0.02 (0.22)	**0.13 (0.06)***	−0.42 (0.24)	**1.12 (0.45)***	**0.45 (0.11)*****
β birth cohort	**−0.73 (0.29)** *	**0.81 (0.35)***	**−0.26 (0.13)***	**−0.45 (0.13)*****	0.32 (0.17)	0.01 (0.06)	−0.23 (0.31)	0.20 (0.63)	−0.21 (0.14)
	INT 3			ANX 5			INT 7		
	a	c	e	a	c	e	a	c	e
Path coefficients	3.35 (0.12)	1.62 (0.25)	2.05 (0.05)	2.39 (0.13)	1.30 (0.19)	1.71 (0.05)	3.14 (0.20)	2.66 (0.20)	2.40 (0.08)
β sex	0.16 (0.09)	**−0.52 (0.18)***	**−0.14 (0.04)*****	0.01 (0.10)	0.10 (0.15)	0.13 (0.04)**	−0.04 (0.16)	0.01 (0.18)	**0.16 (0.07)****
β SES	**−0.22 (0.07)*****	**−0.40 (0.18)***	**0.07 (0.03)***	−0.00 (0.08)	0.03 (0.12)	0.04 (0.03)	0.04 (0.13)	**−0.49 (0.15)*****	−0.03 (0.05)
β childcare	−0.19 (0.16)	0.44 (0.33)	**−4.04 (0.06)***	0.23 (0.14)	−0.37 (0.24)	0.11 (0.06)	**−0.52 (0.26)***	0.47 (0.24)	**0.58 (0.10)*****
β birth cohort	−0.26 (0.13)	**0.67 (0.28)***	**−0.11 (0.05)***	**−0.32 (0.13)***	0.24 (0.16)	−0.10 (0.06)*	**−3.18 (1.23)*****	**0.98 (0.21)*****	**0.37 (0.11)*****

Significant effects are given in bold

AGG aggression, *ANX* anxiety, *EXT* externalizing, *INT* internalizing

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.005$

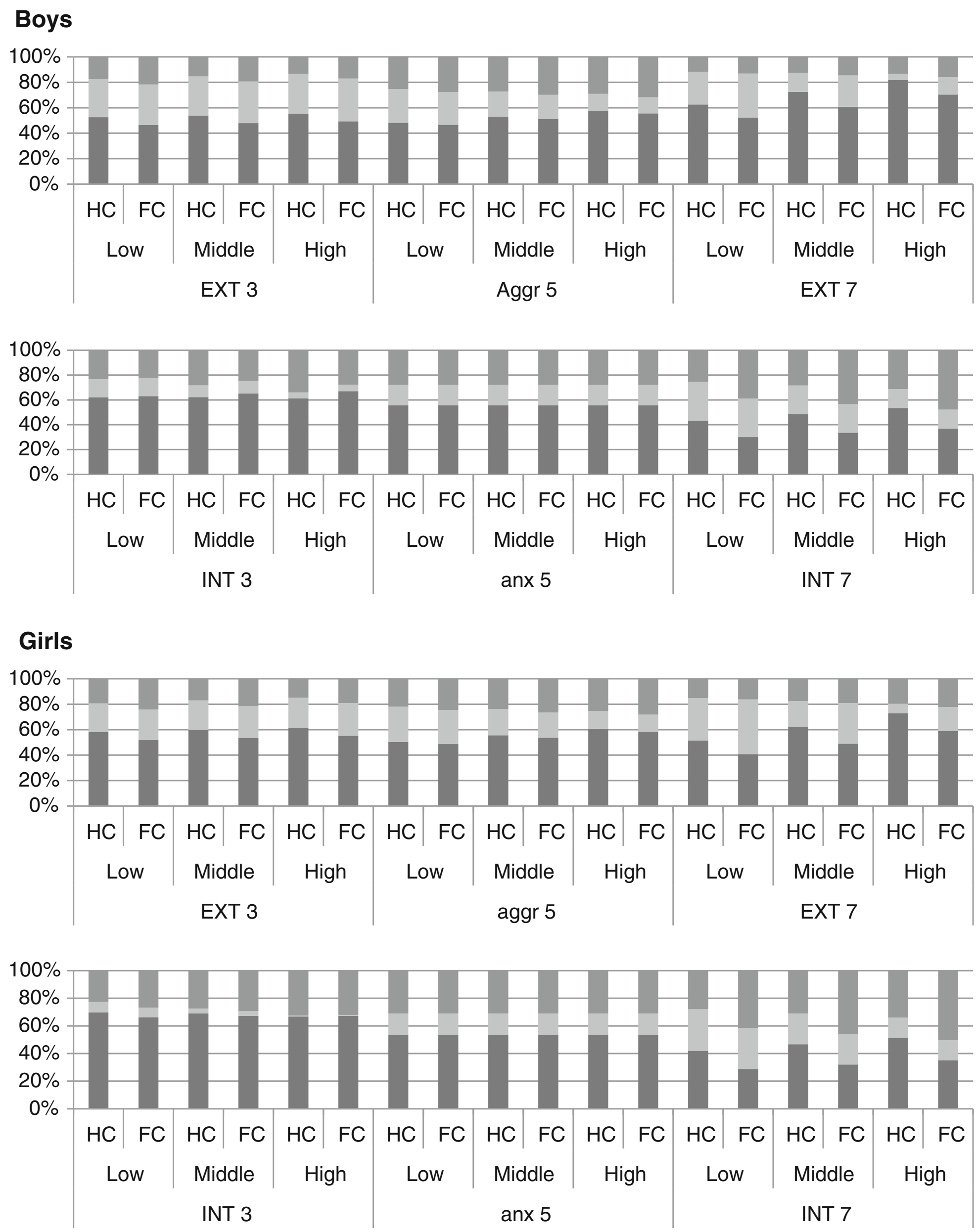

Fig. 3 Standardized estimates of A (*dark*), C (*light*) and E for problem behavior in boys and girls born before or at 1999 with low, middle or high SES in home care (HC) or formal child care (FC). These estimates were calculated using the significant moderation effects on the path coefficients as shown in Table 2

effect on E ($p < 0.005$). In sum, for INT/ANX, the largest effect was seen at age 7, in which the relative influence of A was lower in children attending formal child care, a similar effect as seen in EXT/AGG.

Birth cohort, defined as born before or in 1999 or born after 1999 and used as a proxy for child care quality, also showed significant moderation effects. Overall, the genetic variance was lower in children born after 1999, whereas the common environmental variance was higher. Consequently, heritability is lower in children born after 1999.

Significant moderation effects of SES were also found at all ages for EXT/AGG, and, at age 3 and 7, for INT/ANX, causing a lower heritability of problem behavior in children with lower SES. However, the moderation effects leading to the decrease in heritability differed over ages and phenotype. For EXT/AGG, there was significant moderation of E at age 3 and 7, of C at age 5 and 7, and of A at age 7. For INT/ANX, there was significant moderation of C at age 3 and 7, and of A at age 3. Overall, the lowering of the heritability is largely due to an increase in the effect of non-genetic influences, both C and E for EXT/AGG and only C for INT/ANX.

To illustrate the effects of formal child care and SES on the standardized variance components, Fig. 3 shows the standardized variance components for EXT/AGG and INT/ANX in boys and girls born before or in 1999, split by age, SES group, and the home care and child care groups. This Figure demonstrates that the heritability is lower in circumstances associated with more problem behavior, i.e., formal child care or lower SES and these effects are largest at age 7 and for EXT. In 7 year-old boys and girls, the difference in heritability between the formal child care group of low SES and the home care group of high SES is 30 % for EXT compared to a difference of ~20 % in INT.

Discussion

In a large sample of Dutch twins at age 3, 5 and 7 years, we tested two competing hypotheses regarding the question whether problem behavior is influenced by formal child care and whether the influence of genetic and environmental factors on problem behavior is moderated by the attendance of formal child care. The bioecological model proposes that genetic-make-up becomes less important in adverse environments (Bronfenbrenner and Ceci 1994) while the stress–diathesis model predicts the opposite, i.e., that heritability is higher in adverse environments. We saw that children who went to formal child care scored slightly higher on EXT/AGG, especially when these children came from a lower SES family. In addition, there was a main effect of lower SES on problem behavior. With respect to gene–environment interaction and heritability, the impact of environment was higher in the formal child care group, leading to a lower heritability. Moreover, children in the lower SES group were more influenced by environmental effects, thus heritability was lower in those groups. The effects of child care and SES on the influence of genetic and environmental factors were most pronounced at age 7 and for EXT/AGG. In sum, the results regarding SES and child care are in line with the bioecological model. In contrast, mean scores of children born after 1999 were lower than in children born before or in 1999, despite the decrease in quality of formal child care in the Netherlands. It follows from the similar mean differences between home care children and formal child care children born after 1999 that we did not detect an effect of lower formal child care quality on problem behavior. The positive effect of birth cohort on problem behavior could be due to other developments in the Netherlands between 1986 and 2007, such as the increase in income per household in the period which accompanied the increase in the number of working mothers (see http://www.cbs.nl/NR/rdonlyres/65CD877E–55FF-48C8-8629-A5D87B9E0B27/0/2012welvaartinnederland.pdf). Heritability was also lower in the later born children. This points to the stress–diathesis model.

Vendlinski et al. (2011) reviewed selected studies on gene–environment interaction in internalizing and externalizing problems, including antisocial behavior. Their overview shows that in five of the nine studies, results are in line with the stress diathesis model (Hicks et al. 2009b; Lau and Eley 2008; Lau et al. 2007; Rice et al. 2006; Silberg et al. 2001), in three with the bioecological model (Button et al. 2005; Hicks et al. 2009a; Tuvblad et al. 2006) and in one with both models depending on the environmental exposure (Button et al. 2008). In their own analyses of internalizing problems and several environmental risk factors, Vendlinski et al. (2011) also found support for both models. Just one of the reviewed studies investigated SES. In line with the current study, the results indicated a lower heritability when SES was low (Tuvblad et al. 2006). SES was also analyzed by Vendlinski et al. (2011), but as part of a composite measure of risk environment. None of the reviewed studies investigated birth cohort or formal child care. The more recent study of Tucker-Drob and Harden on child care (2012) reported higher heritabilities and less influence of the common environment on externalizing problem behavior in children who went to pre-school.

The results of previous studies and, even, within the current study, indicate that the outcomes of gene–environment interaction analyses on problem behavior in childhood do not show a uniform picture. An obvious explanation for the discrepant findings is that there are many differences across studies, including age of the subjects (mean age range from 8 years till 17 years), birth cohorts, environmental risk factors, raters (maternal or self report) and countries. The importance of the environmental risk factor under study is illustrated by our effects of birth cohort versus formal child care and SES, which have opposite effects on the heritability. And even the study of Tucker-Drob and Harden (2012), which is most similar to the current study, shows differences in the measured environmental risk factor. Preschool attendance rates were low before age 2 (only 15 %) and increased to 72 % before age 4 (Tucker-Drob and Harden 2012), whereas in our sample, 83 % of the children attending formal child care went there for 2 years or more. Moreover, formal child care and preschool seem to be different as preschool was defined as "formal, center-based day-care programs that include didactic learning objectives". Differences in findings across age and phenotype already become apparent from our analyses in which the effects are most significant for EXT and for age 7. The finding that the effect of formal child care on E and consequently on the heritability was most pronounced at age 7 might seem surprising, but is in line with Tucker-Drob and Harden (2012) who showed a significant interaction at age 5 (although in the opposite direction as in the current study), but not at age 4. A possible explanation is that there are other factors related to attending formal child care that have their effect at later ages. For EXT/AGG, it is apparent that the moderation effect of SES is also largest at age 7. Possibly, the expression of genetic factors for externalizing problem behavior depends more on the environment when children grow older. To summarize, conclusions regarding gene–environment interaction for problem behavior depend on the age of the subjects as well as the environmental risk factors that are investigated and both the stress–diathesis model and the bioecological model can apply.

Overall, heritability estimates for INT/ANX and EXT/AGG were around 50 and 60 % and the remaining part of the variance was explained by the common as well as the unique environment. Only at age 7, the heritability of INT was lower, around 30 and 40 %.

When investigating gene–environment interaction, it is important to consider the possibility of gene–environment correlation. Attending formal child care or parental SES are probably not randomly distributed over the population and might be associated with the genetic make-up of the child. We controlled for this potential gene–environment correlation by including the effects of formal child care and SES as fixed effects on the mean, in addition to modeling them as moderators.

We would like to emphasize that the main effects of formal child care on mean problem behavior were small. Comparing the magnitude of the significant effects of formal child care with the magnitude of the significant effects of SES on problem behavior, it is clear that the effect of SES is larger. The effect of formal child care was only marginally significant ($p < 0.05$) for EXT at two of the three ages despite the large sample size. It is of note that the association between formal child care and EXT was not influenced by formal child-care quality, as the mean EXT scores of children born after 1999, when quality of formal child care in the Netherlands was lower, were significantly lower. Therefore, our conclusion would be that negative effects of formal child care in the Netherlands are negligible, even though the quality of care has decreased. Our study underlines the effect of SES on problem behavior, both on internalizing and externalizing problems. Studies performed in the USA suggested that children with low SES benefit from formal child care, at least when the quality is high (Phillips and Lowenstein 2011). The current study shows the opposite effect with larger negative effects of formal child care in children with low SES on mean EXT/AGG. Given the importance of SES as a risk factor with potentially long lasting effects (Ramanathan et al. 2013), it is important to focus on this high risk group and investigate how formal child care might be beneficial for these children. Again, the results for the main effects underline that conclusions regarding child care cannot be easily generalized across countries (Averdijk et al. 2011; Zachrisson et al. 2013; Jaffee et al. 2011). Finally, attending formal child care might also be associated with other, non-genetic, factors not included in the model. This implies that the small association between formal child care and EXT does not need to be causal, but may be explained by these other factors (Crosby et al. 2010; Jaffee et al. 2011).

In summary, formal child care in the Netherlands is not strongly associated with problem behavior in children despite a decrease in quality after 1999. At age 7, attendance of formal child care, but especially lower SES are associated with larger effects of environment and thus lower heritability in line with the bioecological model. These results underline the importance of different studies across countries to investigate the effects of formal child care. For the Dutch situation, SES seems a more important risk factor than formal child care.

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References

Achenbach TM (1991) Manual of the child behavior checklist/4–18 and 1991 profile. University of Vermont, Department of Psychiatry, Burlington

Achenbach TM (1992) Manual of the child behavior checklist/2–3 and 1992 profile. University of Vermont, Department of Psychiatry, Burlington

Andersson BE (1989) Effects of public day-care: a longitudinal study. Child Dev 60:857–866

Andersson BE (1992) Effects of day-care on cognitive and socio-emotional competence of thirteen-year-old Swedish schoolchildren. Child Dev 63:20–36

Averdijk M, Besemer S, Eisner M, Bijleveld C, Ribeaud D (2011) The relationship between quantity, type, and timing of external childcare and child problem behaviour in Switzerland. Eur J Dev Psychol 8:637–660

Bartels M, van den Oord EJ, Hudziak JJ, Rietveld MJ, van Beijsterveldt CE, Boomsma DI (2004) Genetic and environmental mechanisms underlying stability and change in problem behaviors at ages 3, 7, 10, and 12. Dev Psychol 40:852–867

Bartels M, van Beijsterveldt CE, Derks EM, Stroet TM, Polderman TJ, Hudziak JJ et al (2007) Young Netherlands Twin Register (Y-NTR): a longitudinal multiple informant study of problem behavior. Twin Res Hum Genet 10:3–11

Bekkhus M, Rutter M, Maughan B, Borge AIH (2011) The effects of group daycare in the context of paid maternal leave and high-quality provision. Eur J Dev Psychol 8:681–696

Boomsma D, Martin NG (2002) Gene–environment interactions. In: D'haenen H, den Boer JA, Willner P (eds) Biological psychiatry. Wiley, New York, pp 181–187

Bronfenbrenner U, Ceci SJ (1994) Nature–nurture reconceptualized in developmental perspective—a bioecological model. Psychol Rev 101:568–586

Button TM, Scourfield J, Martin N, Purcell S, McGuffin P (2005) Family dysfunction interacts with genes in the causation of antisocial symptoms. Behav Genet 35:115–120

Button TM, Lau JY, Maughan B, Eley TC (2008) Parental punitive discipline, negative life events and gene–environment interplay in the development of externalizing behavior. Psychol Med 38:29–39

Crockenberg SC, Leerkes EM (2005) Infant temperament moderates associations between childcare type and quantity and externalizing and internalizing behaviors at years. Infant Behav Dev 28:20–35

Crosby DA, Dowsett CJ, Gennetian LA, Huston AC (2010) A tale of two methods: comparing regression and instrumental variables estimates of the effects of preschool child care type on the subsequent externalizing behavior of children in low-income families. Dev Psychol 46:1030–1048

de Kruif REL, Riksen-Walraven JM, Deynoot-Schaub MJJM, Helmerhorst KOW, Tavecchio LWC, Fukkink RG (2009) Pedagogische kwaliteit van de opvang voor 0- tot 4-jarigen in Nederlandse kinderdagverblijven in 2008 [Educational quality of day care for 0 till 4 year olds in Dutch child care centers] Nederlands Consortium Kinderopvang Onderzoek

Dettling AC, Parker SW, Lane S, Sebanc A, Gunnar MR (2000) Quality of care and temperament determine changes in cortisol concentrations over the day for young children in childcare. Psychoneuroendocrinology 25:819–836

Deynoot-Schaub MJJM, Riksen-Walraven JM (2005) Child care under pressure: the quality of Dutch Centers in 1995 and in 2001. J Genet Psychol 166:280–296

Eaves LJ (1984) The resolution of genotype × environment interaction in segregation analysis of nuclear families. Genet Epidemiol 1:215–228

Groen-Blokhuis MM, Middeldorp CM, van Beijsterveldt CEM, Boomsma DI (2011) Crying without a cause and being easily upset in two-year-olds: heritability and predictive power of behavioral problems. Twin Res Hum Genet 14:393–400

Hicks BM, DiRago AC, Iacono WG, McGue M (2009a) Gene–environment interplay in internalizing disorders: consistent findings across six environmental risk factors. J Child Psychol Psychiatry 50:1309–1317

Hicks BM, South SC, DiRago AC, Iacono WG, McGue M (2009b) Environmental adversity and increasing genetic risk for externalizing disorders. Arch Gen Psychiatry 66:640–648

Jaffee SR, Van Hulle C, Rodgers JL (2011) Effects of nonmaternal care in the first 3 years on Children's Academic Skills and behavioral functioning in childhood and early adolescence: a sibling comparison study. Child Dev 82:1076–1091

Kendler KS (2001) Twin studies of psychiatric illness: an update. Arch Gen Psychiatry 58:1005–1014

Lau JY, Eley TC (2008) Disentangling gene–environment correlations and interactions on adolescent depressive symptoms. J Child Psychol Psychiatry 49:142–150

Lau JYF, Gregory AM, Goldwin MA, Pine DS, Eley TC (2007) Assessing gene–environment interactions on anxiety symptom subtypes across childhood and adolescence. Dev Psychopathol 19:1129–1146

Neale MC, Boker SM, Xie G, Maes HH (2006) Mx: statistical modeling, 6th edn. Department of Psychiatry, Medical College of Virginia, Richmond

NICHD Early Child Care Res Network (1998) Early child care and self-control, compliance and problem behavior at 24 and 36 months. Child Dev 69:1145–1170

NICHD Early Child Care Res Network (2004) Type of child care and children's development at 54 months. Early Child Res Q 19:203–230

Phillips DA, Lowenstein AE (2011) Early care, education, and child development. Annu Rev Psychol 62:483–500

Pluess M, Belsky J (2009) Differential susceptibility to rearing experience: the case of. J Child Psychol Psychiatry 50:396–404

Pluess M, Belsky J (2010) Differential susceptibility to parenting and quality child care. Dev Psychol 46:379–390

Purcell S (2002) Variance components models for gene–environment interaction in twin analysis. Twin Res 5:554–571

Ramanathan S, Balasubramanian N, Krishnadas R (2013) Macroeconomic environment during infancy as a possible risk factor for adolescent behavioral problems. JAMA Psychiatry 70:218–225

Rende R, Plomin R (1992) Diathesis–stress models of psychopathology: a quantitative genetic perspective. Appl Prev Psychol 1:177–182

Rice F, Harold GT, Shelton KH, Thapar A (2006) Family conflict interacts with genetic liability in predicting childhood and adolescent depression. J Am Acad Child Adolesc Psychiatry 45:841–848

Saudino KJ (2005) Behavioral genetics and child temperament. J Dev Behav Pediatr 26:214–223

Saudino KJ (2009) The development of temperament from a behavioral genetics perspective. Adv Child Dev Behav 37:201–231

Scarr S, McCartney K (1983) How people make their own environments—a theory of genotype–environment effects. Child Dev 54:424–435

Silberg J, Rutter M, Neale M, Eaves L (2001) Genetic moderation of environmental risk for depression and anxiety in adolescent girls. Br J Psychiatry 179:116–121

Spivack G, Spotts J (1966) The Devereux Child Behavior (DCB) Rating Scale. Devon, A: The Devereux Foundation

Tucker-Drob EM, Harden KP (2012) Gene–preschool interaction on the development of early externalizing problems. J Child Psychol Psychiatry 54:77–85

Tuvblad C, Grann M, Lichtenstein P (2006) Heritability for adolescent antisocial behavior differs with socioeconomic status: gene–environment interaction. J Child Psychol Psychiatry 47:734–743

van Beijsterveldt CEM, Verhulst FC, Molenaar PCM, Boomsma DI (2004) The genetic basis of problem behavior in 5-year-old Dutch twin pairs. Behav Genet 34:229–242

van Beijsterveldt TCEM, Hudziak JJ, Boomsma DI (2005) Short-and long-term effects of child care on problem behaviors in a Dutch sample of twins. Twin Res Hum Genet 8:250–258

van Beijsterveldt CE, Groen-Blokhuis M, Hottenga JJ, Franic S, Hudziak JJ, Lamb D et al (2013) The Young Netherlands Twin Register (YNTR): longitudinal twin and family studies in over 70,000 children. Twin Res Hum Genet 16:252–267

van der Sluis S, Posthuma D, Dolan CV (2012) A note on false positives and power in G × E modelling of twin data. Behav Genet 42:170–186

van IJzendoorn MH, Tavecchio LWC, Riksen-Walraven JM (2004) De kwaliteit van de Nederlandse kinderopvang [Quality of Dutch child care]. Boom, Amsterdam

Vandell DL, Belsky J, Burchinal M, Steinberg L, Vandergrift N (2010) Do effects of early child care extend to age 15 years? Results from the NICHD study of early child care and youth development. Child Dev 81:737–756

Vendlinski MK, Lemery-Chalfant K, Essex MJ, Goldsmith HH (2011) Genetic risk by experience interaction for childhood internalizing problems: converging evidence across multiple methods. J Child Psychol Psychiatry 52:607–618

Vermeer HJ, van IJzendoorn MH, de Kruif REL, Fukkink RG, Tavecchio LWC, Riksen-Walraven JM et al (2008) Child care in the Netherlands: trends in quality over the years 1995–2005. J Gen Psychol 169:360–385

Zachrisson HD, Dearing E, Lekhal R, Toppelberg CO (2013) Little evidence that time in child care causes externalizing problems during early childhood in Norway. Child Dev 84:1152–1170