

# The role of the Children of Twins design in elucidating causal relations between parent characteristics and child outcomes

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**Background:** Determination of causal connections between parental measures and child outcomes using typical samples is limited by the inability to account for all confounds, both environmental and genetic. This paper discusses the strength of the Children of Twins (COT) design to highlight the role of specific environments. **Methods:** A new analytical model is presented which helps differentiate and quantify the environmental and genetic processes underlying associations between family-level risk factors and child adjustment. In order to illustrate the COT design, the relation between smoking during pregnancy and child birth weight (BW) is examined in a sample of female twins and their children from Norway and the United States. **Results:** The results illustrate that smoking during pregnancy is influenced by genetic factors. However, the Children of Twins model supports the claim that smoking during pregnancy has a direct environmental influence on BW and that genetic and shared environmental confounds cannot account for the association. **Conclusions:** An assessment of the strengths and limitations of the Children of Twins design and a comparison with other research strategies suggest that the design plays a unique role in the study of developmental psychology and psychopathology. Finally, the authors describe how methodological advances and future applications of the design will provide additional insight into the causal processes underlying children's adjustment to environmental stimuli. **Keywords:** Children of twins, gene-environment correlation, parenting, smoking, birth weight. **Abbreviations:** COT: Children of Twins; SDP: smoking during pregnancy; BW: birth weight; rG-E: gene by environment correlation; MZ: monozygotic twins; DZ: dizygotic twins.

Determination of causal connections between parental behaviors and child outcomes is one of the main challenges facing the fields of developmental psychology and psychopathology. Due to the inability to experimentally control many important environmental stimuli, most research methods rely only on correlational data. However, simple epidemiological correlations between parents and children are ambiguous about causation (review in Rutter, 2000). Such associations may represent a multitude of different relations, including the presence of a third factor influencing both the parental and child behaviors. Because the theories and claims about causal processes shape and guide public policy and intervention efforts, determination of underlying mechanisms is a crucial research endeavor.

One of the main limitations of studying familial and environmental influences and child development is that the parents are providing both the environment and the genes to their offspring. What appears to be an 'environmental' family influence on children may be due to genotypic factors which influence the parental behaviors, are passed to their children, and in turn affect the children's behavior. The situation in which a common genetic component influences a parental characteristic or behavior (measured as the environment) and the outcome in the child is referred to as a passive gene by environment correlation (rG-E) (Eaves, Last, Martin, &

Jinks, 1977; Plomin, DeFries, & Loehlin, 1977; Scarr & McCartney, 1983). A correlation would arise between the environment and the child measure, but the environment is only an epiphenomenon representing the genetic risk and does not influence the children (Rutter et al., 1997).

Although rG-E confounds all epidemiological and psychological correlations between adult characteristics and family environments with child outcomes, 'the effects of passive gene-environment correlations have received surprisingly little attention in the research literature and their study constitutes a major research priority' (Rutter et al., 1997, pp. 344–345). Several lines of research illustrate the need to explore this phenomenon, especially in studying the intergenerational transmission of psychological disorders: (1) parental psychopathology is the best indicator of risk for the same disorders in children; (2) genetic influences are involved in these parental disorders which are likely to be relevant to the childhood forms; and (3) parental psychopathology is correlated with parenting practices and family relationships which are also risk factors for childhood psychopathology (Rutter et al., 1997).

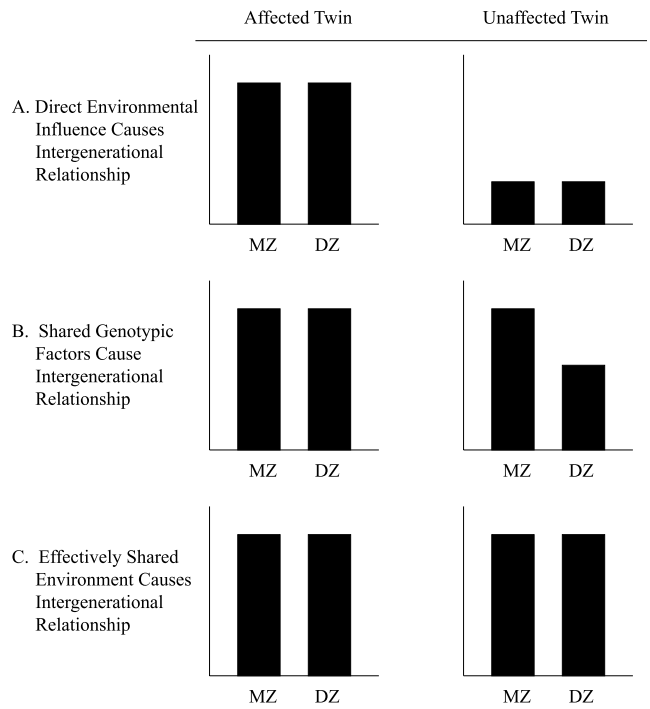
In addition to genetic transmission, parental and family traits may be associated with adjustment in children through various environmental processes. There may be a direct environmental connection, perhaps through social learning (e.g., parents may

model the psychopathology for the children). This situation may occur even if the parental behavior is influenced by genetic factors because the mediating mechanisms of risk factors are independent of origins of the risk (Kendler & Karkowski-Shuman, 1997; Rutter, Silberg, & Simonoff, 1993; Rutter, Pickles, Murray, & Eaves, 2001). The association between the characteristics in the two generations may be spurious, however, because of environmental confounds which cause both the adult and child characteristics (e.g., poverty may cause both the parents' behavior and the child's adjustment). Certainly these environmental and genetic processes are not mutually exclusive. Ultimately, all confounds, including both shared genetic and environmental factors, need to be considered when studying the covariance between parental variables and child outcomes.

Researchers have claimed that behavior genetic studies will help identify the salient environmental influences in human variation (Heath, Kendler, Eaves, & Markell, 1985), particularly with child/adolescent adjustment and psychopathology (Plomin, 1994; Reiss, Plomin, & Hetherington, 1991). This paper initially reviews how the Children of Twins (COT) design, a design which is not as well known in the developmental psychological literature, may elucidate the role that specific environments play in the etiology of psychological and behavioral phenomena. The association between smoking during pregnancy (SDP) and child birth weight (BW) will be investigated to (a) provide an illustrative example of a new analytical approach to the COT design which focuses on quantifying the processes involved with intergenerational relationships and (b) underscore the strengths and limitations of the design.

*Children of Twins designs*

*Children of discordant twins.* The COT design is perhaps best known for the study of unexpressed genetic predispositions in disorders such as schizophrenia (Fischer, 1973; Gottesman & Bertelsen, 1989). The children of schizophrenic parents are at higher risk for developing the disorder than the general population, but environmental or genetic processes may mediate this risk. In order to elucidate these mechanisms, researchers compare the rates of schizophrenia in the offspring of discordant pairs of twins. Figure 1 includes the rates of a disorder in the offspring of the affected and unaffected monozygotic (MZ) and dizygotic (DZ) cotwins, which are associated with three prototypical patterns of intergenerational transmission. A comparison between the children of the affected and unaffected MZ cotwins is the initial step in trying to understand the processes through which the risk is mediated. A lower prevalence of the disorder in the offspring of the unaffected MZ cotwins than the affected MZ cotwins would support a causal environmental as-



**Figure 1** Rates of child disorders in families of discordant MZ and DZ twins resulting from three patterns of intergenerational transmission

sociation between parental and child schizophrenia because the children of the unaffected MZ cotwins were not exposed to a parent with schizophrenia (Pattern A). In contrast, if the rates of the disorder in the offspring of the affected and unaffected MZ cotwins were equal to each other, the causal role of the parental psychopathology would be undermined (Gottesman & Bertelsen, 1989).

Equivalent rates of the disorder in children of discordant MZ twins illustrate that the disorder in the parents does not have a specific influence on the children, but it does not elucidate the paths responsible for the higher rates of the disorder in children of schizophrenic parents. However, a comparison of the rates in the children of the unaffected MZ and DZ cotwins assists in highlighting the factors responsible for the epidemiological relation between the two generations. Higher rates of schizophrenia in the children of the unaffected MZ cotwins than in children of unaffected DZ cotwins suggest that genetic factors account for some of the intergenerational covariation (Pattern B). Genetic factors are implicated because children from unaffected MZ cotwins are genetically related to the affected aunt/uncle as a first-degree relative whereas children from unaffected DZ families are genetically related to the affected aunt/uncle as a second-degree relative. If the rates were similar for the children in unaffected MZ and DZ families, shared environmental factors would be of most import (Pattern C).

For both schizophrenia (Fischer, 1973; Gottesman & Bertelsen, 1989) and manic depressive disorders

(Bertelsen & Gottesman, 1986), the risk for developing the diseases was the same for the offspring of the affected and the unaffected MZ twins, illustrating that being raised by an affected parent is neither necessary nor sufficient for producing either disorder. Likewise, for both disorders, the concordance rates among the children of unaffected MZ cotwins were higher than the rates among the children of unaffected DZ cotwins. Thus, the data support the role of genetic factors in the transmission of schizophrenia and bipolar depression from parent to offspring. Neither direct environmental effects of the parental psychopathology nor shared environmental processes could account for the transmission.

Although the COT design has illustrated the importance of genetic predispositions for developing schizophrenia and bipolar disorder using adult offspring of twins, researchers (Labuda, Gottesman, & Pauls, 1993; Rutter et al., 2001) have noted that the COT design may be particularly useful in evaluating environmental risk factors during childhood and adolescence. To date, only a few studies have utilized the COT design to study intergenerational associations between environmental variables and child outcomes, most notably birth weight.

Magnus, Berg, and Bjerkedal (1985) employed the COT design to study the relation between maternal characteristics and child BW. In order to explore the possible explanations for the intergenerational correlation between maternal BW and child BW, the authors studied the offspring of adult MZ twins who were discordant for BW (the adult twins had differed by more than 300g at their birth). No differences between the weights of the cotwins' offspring were found when they were grouped according to birth order or the magnitude of the BW difference, suggesting that maternal BW does not have a direct environmental impact on the offspring's BW. Due to the fact that the offspring of DZ twins were not included in the study, the study was unable to delineate between the role of shared environmental influences or genetic factors in explaining the covariance between the two generations.

This limitation was addressed in a study of the processes responsible for the association between SDP and BW which included MZ and DZ twins discordant for SDP (Magnus, Berg, Bjerkedal, & Nance, 1985). The concordance rate for SDP among MZ twins was higher than the concordance rate of DZ twins, suggesting that genotypic factors influence SDP. Although genetic factors influence maternal SDP, the offspring of MZ twin mothers who smoked weighed on average 127g less than the offspring of the MZ cotwins who did not smoke during pregnancy. The results support the hypothesis that SDP has a direct effect on BW via environmental processes.

*MZ Half-Sib Method.* The family structure of twins and their multiple offspring also permits analytical

strategies other than the comparison of means between the offspring of discordant twins. Nance and Corey (1976; Nance, 1976; Nance, Corey, & Boughman, 1978) proposed a nested analysis of variance approach to the study of offspring of monozygotic twin pairs, referred to as the MZ Half-Sib method. The analyses estimate a number of latent environmental and genetic parameters responsible for variation in offspring characteristics. The design does not include direct measures of the environment so the reader is referred to the cited papers for additional information on this analytical approach and the advantages of including multiple children of each cotwin (also see the discussion).

### *Overview of the existing Children of Twins studies*

The comparison of offspring from discordant twins provides insight into whether environmental or genotypic factors account for the association between parental characteristics and child adjustment. However, the study of the children of discordant twins is limited because the design considers the salient environment to be dichotomous, and many psychological phenomena are distributed continuously. Furthermore, most of the existing analyses have relied only on significance testing, with little emphasis on the magnitude of the different processes explaining the correlation between the generations. Therefore, the study of intergenerational relations with the COT design needs an analytic approach which considers variation in ordinal or continuously scaled environmental risk factors and provides estimates of the strength of the causal processes which co-occur in intergenerational relationships. This paper will present an analytical model of the COT design with these characteristics, and the quantitative approach will be used with SDP and BW to illustrate how the analyses disentangle and quantify the intergenerational processes. Utilizing a 'real' example frequently highlights difficulties with the models which may not occur with simulated data (e.g., Eaves, Last, Young, & Martin, 1978), and SDP is associated with a number of later child characteristics.

### *Maternal smoking and child outcomes*

Numerous studies across various countries and social classes have revealed associations between SDP and a wide range of child outcomes, including BW (e.g., Fried, 1993), cognitive abilities (Fried, 1993; Lassen & Oei, 1998; Sexton, Fox, & Hebel, 1990), externalizing behaviors in childhood (e.g., Brook, Brook, & Whiteman, 2000; Orlebeke, Knol, & Verhulst, 1997) and criminal behavior in adult males (Brennan, Grekin, & Mednick, 1999). The correlation between SDP and child characteristics highlights the difficulty in determining causal connections between parental behavior and child characteristics. Smok-

ing may have a direct causal influence on the child through biological mechanisms in the developing fetus (Fergusson, Woodward, & Horwood, 1998), or maternal SDP may merely be an indicator of other conditions which are actually responsible for the child characteristics. For example, socioeconomic factors, such as extreme poverty, may be associated with both higher rates of SDP and externalizing behaviors (Rantakallio, Laara, Isohanni, & Moilanen, 1992). Women who smoke during pregnancy are also 5 times more likely to have a current psychiatric disorder compared to the general population (Flick et al., 2001). Most studies illustrate an 'independent' association between maternal smoking and the outcome variable in the offspring by statistically controlling for confounding variables that may account for the correlation, but the association may nevertheless be the result of unmeasured or imperfectly measured confounds. A number of researchers (Fergusson, 1999; Fergusson et al., 1998; Sexton et al., 1990) have noted that there may be a genetic confound which explains the intergenerational relation between smoking and characteristics of the offspring. Analyzing the covariation between generations using the COT design can help identify the processes through which maternal SDP is associated with child BW and provides a descriptive example of the design and analytical model.

## Method

### Participants

Questionnaire data was collected in two population-based samples of adult twins. The first sample was ascertained through the Medical College of Virginia Twin Registry (referred to as the Virginia Sample), a sample obtained through birth records from 1915 to 1980 and matched with census and department of motor vehicle information (Corey et al., 1991). The second sample was recruited from the Norwegian Twin Panel (Norway Sample), a collection of adult same-sex twins born in Norway between 1915 and 1960 where at least one of the twins' addresses could be found using census data (Magnus, Berg, & Nance, 1983).

Zygosity was determined by self-report questionnaires which were mailed to the twins to determine whether they wanted to participate in research studies (Magnus et al., 1983). Participating twins and their spouses were subsequently sent a general health survey which ascertained general medical conditions, medication use, drug and alcohol use, and demographic information. The females, whether they were the twins or the spouses of twins, were also sent a questionnaire about their reproductive history. This questionnaire included questions about each pregnancy, such as birth complications, alcohol and drug use during pregnancy, medication use, and related medical conditions.

The Virginia Twin Registry Sample comprises 11,018 adults, including 7,836 twins and 3,182 spouses of twins (5,339 males and 5,689 females). Females in the

Virginia Sample reported 5,120 pregnancies which resulted in a live birth (50.2% Male and 48.8% Female) and which were the result of their current marriage (miscarriages, stillborns, and pregnancies from earlier marriages/partners were deleted). The Norway sample included 6,357 twins and 3,308 spouses (4,554 males and 5,111 females). The females reported 6,261 pregnancies that resulted in live births (46.7% Male and 53.3% Female) from their current marriage.

Analyses will be conducted on two subsets of the data. The first subset of the data, which includes parents and their first-born child, will be used to provide a preliminary view of the nature and the overall magnitude of the association between SDP and BW while controlling for other factors. The subset only includes the first child in each family because the models for the COT design described in this paper will only incorporate the first-born child of each family. The analyses are restricted to the first child in order to provide a succinct example of the rationale for the COT design. The subset has 4,150 families where either a twin or their spouse reported having a child. The mothers reported that 50.1% of the first pregnancies were females. The second subset includes sets of female twins ( $N = 1,004$ ) of known zygosity, in which at least one of the twins reported having a child. The subset includes 1,375 individual females with information about smoking during their first pregnancy and 1,435 reports of birth weight. Due to missing values and incomplete twin pairs, sample sizes will be presented with each analysis.

### Measures

Zygosity was determined by a 13-question survey, including items about physical characteristics and difficulty discriminating the twins, which has been shown to be over 95% accurate (Kasriel & Eaves, 1976). Smoking was measured in both samples on a 4-point Likert scale ('None', 'Less than 10 cigarettes per day', '10–20 cigarettes per day', and 'More than 20 cigarettes per day'). Men and women were asked about their current smoking habits, and the women also reported the average amount of cigarettes they smoked during each pregnancy. Women's alcohol consumption during pregnancy was based on the participants' response to the question, 'Did you drink beer during your pregnancy?' The four responses were 'No', 'Less than a bottle per day', '1–2 bottles per day', and 'More than two bottles per day.' The smoking and alcohol variables will be considered continuous variables for the analyses in this paper.

Self-report measures of adult height and weight were converted into Body Mass Index (BMI) scores in order to get measures of the mothers' and fathers' physical size. Gestational age is the number of days early or late that the child was born. If the child was born 'on time' then they received a score of zero. If the child was born 5 days early the gestational age was  $-5$ . Pregnancy number is the birth order of the child, including those from previous marriages and those ending in miscarriages and abortions. The child's BW, which was reported by the mothers, was converted into metric for the analyses.

Table 1 includes the mean, standard deviation, and sample sizes for the variables in subset of parents and

**Table 1** Means, standard deviations, and effect sizes of family-level and pregnancy-specific variables

Variable	Sample						$d^a$
	Virginia			Norway			
	<i>M</i>	<i>SD</i>	<i>N</i>	<i>M</i>	<i>SD</i>	<i>N</i>	
Family-level variables							
Father's Body Mass Index <sup>b</sup>	25.50	3.48	1,566	23.99	2.50	2,052	.51
Mother's Body Mass Index <sup>b</sup>	23.49	4.86	1,691	22.16	2.74	2,057	.35
Father's General Smoking <sup>c</sup>	.77	1.16	1,581	.70	.93	2,047	.07
Mother's General Smoking <sup>c</sup>	.47	.92	1,809	.51	.77	2,102	-.05
Pregnancy-specific variables							
Mother's Smoking <sup>c</sup>	.35	.76	1,776	.39	.63	2,218	-.06
Mother's Drinking <sup>c</sup>	.10	.33	1,787	.20	.40	2,245	-.27
Gestational Age <sup>d</sup>	1.11	13.32	1,560	.35	11.95	2,077	-.12
Mother's Age at Childbirth	23.65	4.23	1,704	24.73	4.07	2,184	-.26
Birth Weight (Kilograms)	3.32	.54	1,810	3.44	.55	2,340	-.22

Note: <sup>a</sup>The effect size  $d$  is a measure representing the difference between the two samples in terms of the pooled standard deviation. <sup>b</sup>Measure of physical stature which combines height and weight. <sup>c</sup>Measured on a 4-point Likert scale. <sup>d</sup>Measured in day, centered and due date.

their first-born children, delineated by country. An effect size statistic ( $d$ ), which represents the difference between the two samples in terms of the pooled standard deviation, was calculated to illustrate the magnitude of the difference between the means of the samples. The fathers and mothers in Virginia were physically larger than those in Norway ( $d = .51$  and  $.35$ , respectively), but mothers in Norway reported more drinking during pregnancy than those in Virginia ( $d = -.27$ ). Finally, mothers in Norway reported a higher age at childbirth for their first child and giving birth to heavier children than mothers in the Virginia sample ( $d = -.26$  and  $-.22$ ).

## Analyses

Regression analyses will provide standardized and unstandardized values of the relation between the SDP and BW, test whether the association between SDP and BW is linear or quadratic, and control for familial and pregnancy-specific factors which are known to relate to BW. These regression analyses represent the standard statistical method for controlling for measured environmental confounds. A regression analysis of the subset of female twins of known zygosity provides an exact comparison for the results of the model fitting using the COT model.

For all of the COT analyses, the linear influence of the child's sex, the country (either US or Norway), and the sex by country interaction will be removed from BW to control for these factors. Additional covariates were not controlled in the analyses because they may mediate possible genetic and environmental confounds. Only the results of model fitting with a pooled sample of the Virginia and Norway datasets will be presented because there were no substantive differences in the size of the parameter estimates when the samples were analyzed independently.

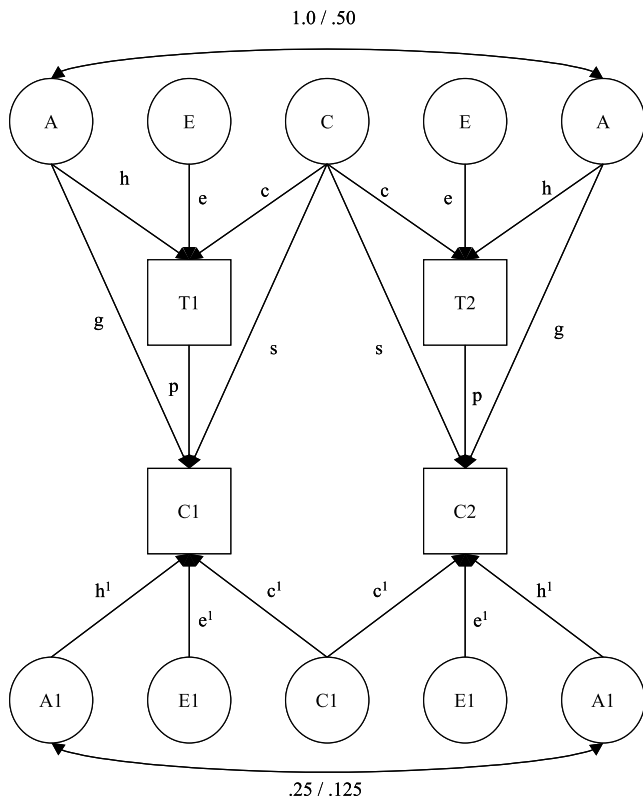
The correlations between SDP and the BW of the first-born child of each twin will be presented for MZ and same-sex DZ female twins. The difference between the MZ and DZ twin correlations for the same-trait, same-generation measures in the adults ( $r_{MZ, mom-mom}$  vs

$r_{DZ, mom-mom}$ ) estimates the genetic and environmental effects on SDP. This comparison is the same as in the standard univariate twin model; a higher correlation in the MZ twins relative to DZ twins implies that genetic factors influence the adult trait. The difference between the MZ cousin and DZ cousin correlations for the same-trait, same-generation measures in the children ( $r_{MZ, cousin-cousin}$  vs  $r_{DZ, cousin-cousin}$ ) estimates the genetic and environmental effects on BW. Cousins from MZ twin families share 25% of their genes, and cousins from DZ families share 12.5% of their genes. The difference in genetic relatedness between cousins in MZ and DZ families allows a comparison similar to the standard twin design, but the statistical power to estimate the genetic and environmental influences is lower.

The cross-generation, same-family correlations within MZ and DZ families estimate the same epidemiological relations between SDP and child's BW because the degree of genetic relatedness for parents and offspring (share 50% of their genes) does not depend on whether the parent is an MZ or DZ twin. In contrast, the comparison of the MZ child-aunt and DZ child-aunt correlations ( $r_{MZ, child-aunt}$  vs  $r_{DZ, child-aunt}$ ) estimates the genetic and environmental components of the intergenerational relationship. These cross-generation, cross-family correlations will be referred to as the 'avuncular relationship'.<sup>1</sup> In MZ twin families, aunts and nieces/nephews share 50% of their genes, but in DZ twin families, aunts and nieces/nephews share 25% of their genes. Therefore, a higher MZ avuncular correlation than DZ avuncular correlation suggests the importance of genetic factors in the intergenerational covariance between SDP and BW. Equal  $r_{MZ, child-aunt}$  and  $r_{DZ, child-aunt}$  suggest that environmental factors are responsible for the intergenerational association.

Figure 2 is a simple model of the COT design including only female twins and their children. Double-headed arrows represent correlations and single-

<sup>1</sup> For simplicity the relationship between the child and his or her aunt will be referred to as the avuncular relationship, in keeping with the terminology used in earlier behavior genetic research (e.g., Truett et al., 1994).



**Figure 2** Full children of twins model. *Note:* The squares represent twin 1 (T1), twin 2 (T2), child of twin 1 (C1), and child of twin 2 (C2). The paths estimate the genetic and environmental influences: *h* (genetic influence on parent trait), *e* (nonshared environmental influence on parent trait), *c* (shared environmental influence on parent trait), *g* (genetic path between the parent and child), *p* (direct environmental influence of parent trait on child), *s* (share environmental path between parent and child), *h'* (genetic influence on child trait), *e'* (nonshared environmental influence on child trait), and *c'* (shared environmental influence on child trait)

headed arrows specify a causal relationship between two variables (Loehlin, 1998). The squares T1 and T2 represent the phenotypic measures of the adult twins. The circles represent latent constructs since no direct measures of the environment or genes in the adult generation are included. The parental generation in the model is identical to the classic twin design (e.g., Neale & Cardon, 1992). The 'A' latent variable represents additive genetic effects. Therefore, the parameter connecting the twins' additive genetic variance components is the genetic relatedness of the twins and is set at 1.0 for the MZ twins and .50 for the DZ twins. The parameter (*h*) represents the influence of genetic component on the phenotype, and ( $h^2$ ) equals the percentage of the variance accounted for by genetic factors, referred to as the heritability. The 'C' latent variable represents the shared environment variance component, and its path coefficient (*c*) influences both phenotypes to the same extent. 'E' denotes the last latent construct in the parental generation, the nonshared environment. The (*e*) path estimate represents the influence of the environmental parameter that is unique to each twin. The variance components for the environmental latent var-

iables ( $c^2$ ) and ( $e^2$ ) are referred to as the shared environment and nonshared environment. As can be seen in the model, the correlation between twins can only be explained by either genotypic or shared environmental factors.

When the children of twins are included in the model, represented by the C1 and C2 squares, three intergenerational covariances are added to the classic twin study: between the children and the parents, between children and their aunt within MZ twin families, and between children and their aunt within DZ families. These covariances allow for the estimation of three intergenerational paths which account for the correlation between parents and their children. The first parameter (*g*) represents the genetic path between the parent and the children. Using standard path analysis rules (e.g., Loehlin, 1998), the path between a child and the aunt that incorporates this parameter equals ( $g$ )\*(genetic relatedness of the twins)\*(*h*). Because the path between the child and the aunt depends on the genetic relatedness of the twins, the (*g*) parameter quantifies differences in the avuncular relation between children of MZ and DZ twin families. Therefore, this parameter accounts for the genotypic factors which may influence both the parents and the offspring, a measure of passive rG-E.

The influence of environmental confounds is the second path through which the parent and child phenotypes are associated. A path due to shared environmental characteristics (*s*) estimates the influence of environmental characteristics which account for variation in both the parent and child generations. This parameter measures the degree to which the avuncular relationship is the result of environmental processes because the path representing the avuncular relationship, ( $s$ )\*(*c*), does not include the genetic relatedness of the twins. No difference in the avuncular relationship between MZ and DZ families suggests that shared environmental confounds are present. Finally, the parameter (*p*) represents a direct phenotypic influence from the mother's phenotype to the child's phenotype. This path estimates the link between the mother and the child while controlling for genetic and environmental intergenerational associations; it represents a direct, environmental, and causal relation between the two phenotypes.

The components and the path estimates in the child generation are similar to those found in the twin generation. The latent variable 'A1' represents the genetic component influencing child BW which is independent from the genetic component influencing maternal smoking. Since monozygotic twins share the same genes, their children will be genetically related to each other as half-siblings (sharing one-fourth of their genes) instead as typical cousins (sharing one-eighth of their genes). Therefore, the magnitude of the correlation between the two 'A1' components, .25 and .125, represents the genetic relatedness of 'social' cousins from MZ and DZ families. The latent component 'C1' represents shared environments that influence children's BW but are independent from phenomena that influence the parental generation. Finally, the 'E1' component represents an error function that accounts for environmental influences not shared with the parental generation or with the cousin.

**Table 2** Parameter estimates from simultaneous regression analyses of birth weight

Variable	Complete subset		Genetic subset	
	b	$\beta$	b	$\beta$
Country <sup>b</sup>	<b>101.12</b>	<b>.09</b>	<b>130.56</b>	<b>.11</b>
Father's Body Mass Index	<b>7.54</b>	<b>.04</b>	<b>9.87</b>	<b>.05</b>
Mother's Body Mass Index	<b>4.73</b>	<b>.03</b>	<b>11.01</b>	<b>.06</b>
Father's General Smoking	15.87	.03	20.95	.03
Mother's General Smoking	-14.10	-.02	-20.13	-.03
Mother's Smoking During Pregnancy	<b>-82.16</b>	<b>-.11</b>	<b>-115.92</b>	<b>-.13</b>
Mother's Drinking During Pregnancy	-22.65	-.02	-8.37	-.01
Gestational Age	<b>22.65</b>	<b>.51</b>	<b>21.92</b>	<b>.43</b>
Age of Mother at Birth	1.26	.01	8.71	.07
Sex of Child <sup>c</sup>	<b>-111.18</b>	<b>-.10</b>	<b>-110.21</b>	<b>-.10</b>

Note: b = unstandardized regression coefficient.  $\beta$  = standardized regression coefficient. The complete subset includes 2,561 families, and the genetic subset includes 1,657. Numbers in bold are statistically significant at the  $p < .05$  level. <sup>a</sup>Birth Weight was measured in grams for the regression analyses. <sup>b</sup>Amount children in Norway are heavier than the US. <sup>c</sup>Amount female children are lighter than male children.

A caveat of the COT model must also be addressed. Although all of the parameters are theoretically justified, the full model may be under-specified (i.e., under-identified) if the estimate for the shared environment (c) for the adult phenotype is negligible. If shared environmental influences do not influence the parental phenotype, then shared environmental influences cannot mediate the covariance between the parent and child phenotypes. When parameter (c) is zero, the shared environmental path between the generations (s) and the shared environment estimate in the children's generation ( $c^1$ ) are confounded – they both parameterize the covariance between the cousins based on shared environments. Therefore, one of these estimates will be dropped if the (c) parameter is insignificant.

The COT model will be fit to the raw data using Mx software (Neale, 1997) in order to account for missing values (the script and raw data matrix are available from the first author upon request). Using raw data enables all available information, such as the variances and covariances, to be utilized from incomplete pairs. Means are also estimated when using raw data. Because the structural equation modeling utilizes raw data instead of covariance matrices, typical measures of goodness of fit, such as RMSEA or AIC, cannot be utilized. Instead, models will be compared using differences in fit function ( $-2\text{LogL}$ ), which are distributed as a Chi Square, and the degrees of freedom. Three models will be fit to the data. A full model, which uniquely estimates all the means, variances, and covariances of the four variables in the two groups (total of 28 parameters), will initially be fit to the data. This will provide a comparison group for the COT models to determine whether the parameters adequately explain the covariance structure. The full COT model will then be fit to the data. Finally, a COT model without the ( $c^1$ ) path will be fit to examine whether all of the parameters can be estimated in the present example.

## Results

### Regression analyses

A regression analysis with 3,993 first-born children indicated that SDP is negatively related to BW when

it is the only predictor, decreasing BW by 93.5 grams per response category ( $\beta = -.12$ ). The linear effect of SDP accounted for 1.5% of the variance in BW, and the addition of the quadratic influence of SDP accounted for less than .10% of the variance of BW. The results suggested a linear association between SDP and BW. The influence of SDP was then included in a simultaneous regression equation with country, maternal and paternal BMI, maternal and paternal overall smoking, maternal drinking during pregnancy, gestational age, maternal age at pregnancy, and sex of the children. Table 2 presents the unstandardized and standardized estimates for the simultaneous regression analyses for the full subset of families and the families used in the genetic analysis. Even when controlling for other risk factors, the magnitude of the relation between SDP and BW was still substantial, albeit somewhat reduced (decrease of 82.16 grams per response category,  $\beta = -.11$ , in the full subset). Being born in Norway, having physically larger parents, having a longer gestational period, and being male were associated with higher birth weight. The analyses emphasize that the measured familial and pregnancy-specific factors, including the mother's general level of smoking, cannot fully account for the association between SDP and BW. The results support the claim that SDP is causally related to BW. In order to provide an exact comparison for the COT model fitting, a simultaneous regression analysis was conducted on the subset of female twins of known zygosity. The relation illustrates that SDP is negatively associated with BW in this subset ( $b = -115.92$ ,  $\beta = -.13$ ).

### Children of Twins model fitting

The correlations between the female twins and their first-born children for both MZ and DZ families are presented in Table 3. The difference in the correlations between the mothers' smoking for MZ twins ( $r_{\text{MZ, mom-mom}} = .55$ ) was higher than DZ Twins ( $r_{\text{DZ, mom-mom}} = .22$ ) which suggests that genetic

**Table 3** Twin and child correlations with sample sizes for female MZ and DZ twin families

Variables	1	2	3	4
1. Twin 1 SDP	–	.55 (227)	–.11 (453)	–.02 (232)
2. Twin 2 SDP	.22 (174)	–	–.11 (238)	–.20 (494)
3. Child 1 BW	–.14 (207)	–.04 (179)	–	.26 (245)
4. Child 2 BW	–.04 (180)	–.21 (219)	.18 (186)	–

Note: MZ twin family correlations are above the diagonal, and DZ twin family correlations are below. Child 1 is the first child of twin 1, and child 2 is the first child of twin 2. Sample sizes are in parentheses.

**Table 4** Unstandardized and standardized path coefficients for the COT model

Parameters	b	$\beta^a$
Genetic Influences on SDP (h)	<b>.49</b>	<b>.72 (.50–.77)</b>
Nonshared Environment on SDP (e)	<b>.47</b>	<b>.69 (.63–.75)</b>
Shared Environment on SDP (c)	.07	.10 (–.49–.48)
Genetic Intergenerational (g)	–.03	–.05 (–.38–.30)
Phenotypic Intergenerational (p)	<b>–.14</b>	<b>–.17 (–.31–.03)</b>
Shared Environmental Intergenerational (s)	.21	.38 (–.54–.54)
Genetic Influences on BW (h <sup>1</sup> )	.33	.59 (–.98–.97)
Nonshared Environmental on BW (e <sup>1</sup> )	.38	.69 (–.91–.90)
Shared Environment on BW (c <sup>1</sup> ) <sup>b</sup>	–	–

Note: Numbers in bold are statistically significant at the  $p < .05$  level. b = unstandardized path coefficient.  $\beta$  = standardized path coefficient. <sup>a</sup>95% confidence intervals are in parentheses. <sup>b</sup>Could not be estimated for this example.

factors influence SDP. The difference between the correlation between the cousins' birth weights ( $r_{MZ, \text{cousin-cousin}} = .26$  and  $r_{DZ, \text{cousin-cousin}} = .18$ ) suggests that there are some genetic influences on BW, but the differences between the two correlations is not large. The correlations between the mothers' smoking and their own children's BW in MZ families ( $r = -.11$  and  $-.20$  respectively for twin 1 and twin 2) and in DZ families ( $r = -.14$  and  $r = -.21$ ) illustrated the negative epidemiological relation which was highlighted in the entire sample with the linear regression analyses (weighted average  $r = -.16$ ). The differences in the correlations are due to sampling error and not to systematic factors because the designation of twin 1 or twin 2 was assigned at random. Finally, the correlation between a female's smoking and the BW of her sister's child highlighted the possible mechanisms involved in the intergenerational transmission. The  $r_{MZ, \text{child-aunt}}$  ( $r = -.02$  and  $-.11$ , weighted average =  $-.07$ ) appears to be no different than the  $r_{DZ, \text{child-aunt}}$  ( $r = -.04$  for both). The correlations suggest that genetic factors were not associated with the intergenerational relation. A series of COT models will more clearly illustrate the intergenerational processes involved.

The raw data for the analyses included 279 MZ families from Virginia, 111 DZ families from Virginia, 492 MZ families from Norway, and 152 DZ families from Norway where at least one twin had a child. The sample is limited to mothers who were from same-sex pairs of known zygosity. First, a full model that included unique estimates of the variances, covariances, and the means was fit to the data. This model provides a baseline because it estimates all of the covariances between the four variables ( $-2\log L$

= 4842,  $df = 2707$ , 28 parameters). The fit functions of the COT models were compared to the full model to determine whether the parameters adequately explain the observed covariance structure.

Two COT models were fit to the data: (1) the full COT model and (2) a model in which the shared environment estimate in the children's generation (c<sup>1</sup>) was dropped. The full COT model ( $-2\log L = 4867$ ,  $df = 2724$ , 11 parameters) estimated the 9 path parameters and 2 means (SDP in twin1 was constrained to be equal to SDP in twin 2 and BW in child 1 was constrained to equal BW in child 2). The COT model which dropped the estimate of the shared environment in the children's generation (c<sup>1</sup>) was then fit to the data ( $-2\log L = 4867$ ,  $df = 2725$ , 10 parameters). A comparison of the two models indicates that the full COT model is under-specified because the fit functions are identical (see explanation above). Therefore, the model with the shared environment parameter for BW (c<sup>1</sup>) fixed at zero was compared with the full model to determine whether the parameters found in the COT model significantly decreased the fit. The change in fit function ( $\Delta\chi^2 = 25$ ,  $\Delta df = 18$ ,  $p < .12$ ) was statistically insignificant and implies that the COT model adequately explains the observed covariance structure.

Table 4 summarizes the results of the model fitting and includes both the unstandardized and standardized parameter estimates for the model. The 95% confidence intervals are also given. Squaring the standardized estimates provides an estimate of the amount of variance accounted for by the path (Loehlin, 1998). The estimates suggest moderate genetic ( $h^2 = .52$ ) and the nonshared environment influences ( $e^2 = .47$ ) on SDP, with very minimal

influence of the shared environment ( $c^2 = .01$ ). The phenotypic pathway from SDP to BW indicated an incremental decrease of .14 kg/level of smoking ( $-139.67$  g/level of smoking, standardized =  $-.17$ ). This corresponds to the regression analyses on the subset of females of twins. Tracing the possible genetic intergenerational transmission required multiplying the genetic influence on SDP ( $h$ )  $\times$  the genetic intergenerational path ( $g$ ) =  $(.72 \times -.05) = -.04$ . The result was minimal and statistically non-significant. The influence of shared environmental influences related to SDP was also minimal and statistically nonsignificant:  $(c) \times (s) = (.10 \times .38) = .04$ . Thus, the intergenerational transmission via genetic processes and the shared environment could not explain the association. Although the estimate for genetic influences on BW, independent of smoking, was large, the confidence intervals around the estimate included zero. None of the parameters that were unique to the child generation were significant. This suggests that there was not enough power to estimate the three parameters simultaneously but does not imply that the variance of BW can be solely explained by the intergenerational paths.

## Discussion

The COT design can delineate the environmental and genetic mechanisms responsible for epidemiological correlations between environmental measures and child outcome variables. The COT model suggested that the intergenerational covariation between SDP and BW could not be accounted for by shared environmental factors or genetic factors. Rather, the direct, causal environmental path between the two variables explained the negative association. The finding of a causal connection between SDP and BW is consistent with other research designs. For instance, a dose-dependent relationship has been found in many studies (Ellard, Johnstone, Prescott, Ji-Xian, & Jian-ua, 1996; Meyer, Jonas, & Tonascia, 1976). A comparison of same-sex pregnancies during which the mother only smoked during one also has supported a causal connection between SDP and BW (Naeye, 1978). Likewise, mothers who stopped smoking during pregnancy have been found to give birth to heavier children than those who do not (Secker-Walker, Vacek, Flynn, & Mead, 1998). Therefore, the results of the COT model fitting support different methodological findings which suggest a causal link between the two variables while controlling for confounds which have heretofore limited the interpretation of SDP studies (Fergusson, 1999).

The study of the association between SDP and BW stresses two important advantages of the COT design. First, the analyses illustrate that the design is able to separate the mechanisms of risk from the sources of the risk – although SDP is influenced by

genetic factors its influence on BW is solely environmental (e.g., Magnus et al., 1985). Second, the results exemplify a quantitative approach that can quantify the underlying processes responsible for the intergenerational association. In fact, preliminary analyses of the association suggested that SDP was even more highly associated with BW than the epidemiological associations indicate because of a negative genetic association between the two variables (D'Onofrio et al., 2000). Therefore, because the COT design considers common genetic factors, it may actually reveal that environmental factors are more important than previously thought.

The results of the SDP and BW example are limited in several respects. The sample of female twins of known zygosity and their first-born offspring is small, limiting the statistical power to estimate many of the parameters in the offspring generation. The adult twins included in the analyses were born over a 65-year period, and cohort effects may have influenced the environmental and genetic parameters in the model. The data were also based on retrospective reports. Only the first child in each nuclear family was included in the analyses, and other studies have found differences in BW based on parity (Nance, Kramer, Corey, Winter, & Eaves, 1983). Finally, the SDP variable was considered to be a continuous variable, even though it was only measured on a 4-point Likert scale and the distribution of the scores was positively skewed. However, rescaling the SDP variable (results not shown) did not influence our results.

## Comparison to other behavior genetic designs

A number of different behavior genetic designs have been used to study the influence of genetic and environmental factors associated with specific measures of the environment (Rutter et al., 2001). The similarities and differences between the COT and other designs are explored below in order to compare the strengths and limitations of different approaches (see Neale & Cardon, 1992 for structural equation models for these designs). All of the designs, the COT included, suffer from two main limitations. Because the designs are necessarily non-experimental, they cannot determine definitively (a) whether the measured environment represents the true source of risk or is merely correlated with some other salient risk factor and (b) the direction of causation between environments and outcomes.

*Adoption studies.* Adoption studies provide a powerful design to detect environmental influences. In addition to studying intergenerational associations, the design is able to study gene by environment interaction and additional processes through which rG-E creates the covariance between parents and children. The COT model, as specified, cannot estimate either of these phenomena. However,

adoption studies are becoming increasingly rare due to societal changes and are limited by methodological problems (recent reviews in Rutter et al., 2001; Rutter, Silberg, O'Connor, & Simonoff, 1999). The study of MZ twins and their children is similar to an adoption study, but the 'natural' and 'foster' parents are genetically identical and share other cultural experiences which will make them similar (Eaves et al., 1978). However, including adult DZ twins in addition to MZ twins in the study helps to account for these experiences and distinguish between multiple pathways relating parents and children. The COT design offers many advantages over the adoption design because it does not suffer from some of the limitations in studying individuals that are adopted. Specifically, samples of adult twins and their children may be easier to obtain than adoption samples, especially samples which include children who are exposed to high-risk environments. The assumptions that there are no negative consequences of being adopted and that environmental processes operate similarly in adoptive and non-adoptive families are also not necessary in the COT design.

*Twin studies including specific measures of shared environment.* Although studies which incorporate direct measures of the environment into twin studies (e.g., Caspi et al., 2000; Kendler et al., 1992) remedy some of the limitations of the classical twin study, the design is limited by the assumptions made about rG-E in the design. The models may only partially control for genetic factors since they assume that the specified environments represent 'true' or 'pure' environmental risk factors (i.e., no rG-E) which are free from genetic influences (Caspi, Taylor, Moffitt, & Plomin, 2000; Kendler, Neale, Kessler, Heath, & Eaves, 1992). In contrast, the COT design specifically parameterizes the role of passive rG-E and accounts for the possibility that latent genetic and environmental factors may cause the association between an environmental risk factor and child outcome. Ultimately, classical twin studies which add an explicit measure of the environment are not able to delineate the processes involved in many intergenerational associations.

*Bivariate twin studies.* In order to study the relation between an environmental risk factor and an outcome, a bivariate behavioral genetic analysis can be conducted in which the environmental measure is considered a phenotype (e.g., Reiss, Neiderhiser, Hetherington, & Plomin, 2000). The COT and bivariate twin models which include measures of the environment have the same goals and are theoretically similar. In fact, the structural equation model presented here is a re-parameterization of the bivariate cholesky model (Neale & Cardon, 1992), a model commonly used in multivariate twin studies, except that a direct path has been drawn from the

parental phenotype to the child phenotype instead of through the nonshared environmental parameter. However, the bivariate twin design cannot study all of the possible environmental risk factors that are typically studied in developmental psychology because the model can only include environments for which twins can differ. As a result, putative family-level environmental phenomena such as divorce, socioeconomic status, family cohesion, etc., cannot be studied with the bivariate models because twins growing up in the same household are always concordant for these events. The COT differs from bivariate analyses because it is able to study the influence of family-level factors while controlling for genetic effects.

*Twin-family studies.* The basic twin study can be expanded to include measures of twins' parents (Eaves et al., 1978; Kendler et al., 1996; Meyer et al., 2000; Taylor, McGue, & Iacono, 2000), a design referred to as the twin-family design. The strength of this design lies in its ability to estimate environmental effects while controlling for genetic effects on both the parents and children (Rutter et al., 1997). However, the model includes several restrictions and methodological assumptions which limit the interpretation of the results (Rutter et al., 2001). The twin-family design must include identical measures for the parents and children and make the assumption that the same genetic (i.e., same genes) and environmental structure influences both generations. In comparison, the COT design also estimates environmental and genetic paths from specified environmental measures to child characteristics, but the design does not require the same phenotype to be studied in both generations, nor does it require the assumption that the genetic and environmental structure is similar for both children and adults. These differences permit the COT design to study intergenerational associations with different and sometimes fewer major assumptions.

*Cotwin control studies.* The cotwin control design, most notably with MZ twins, controls for latent factors that may be responsible for the correlation between an environmental risk and an outcome because it incorporates twins discordant for an environmental measure. The design controls for the effects of age, gestational influences, especially when the twins share the same chorion, and genetic factors (Davis, Phelps, & Bracha, 1995; Phelps, Davis, & Schartz, 1997). Likewise, the cotwin control design can control for environmental factors which may also be responsible for epidemiological associations because it is a form of the sibling control design (see Geronimus & Korenman, 1992 and Hoffman, Foster, & Furstenberg, 1993 for examples of how sibling control studies have helped to further elucidate the statistical association between teenage pregnancy and later negative consequences for the mother).

Yet, the cotwin control design is limited by a number of methodological problems which prohibit the use of the cotwin control design from being able to study many environmental risk factors. The difficulties in finding large samples of twins which are discordant for salient environmental factors limit the statistical power of the cotwin control study to draw definitive conclusions (e.g., Kendler & Gardner, 2001). In similar fashion to bivariate twins studies, the cotwin control design cannot study family-level variables. The COT design can be seen as an extension of the cotwin control design but provides the opportunity to study family-level risk factors.

### *Limitations of the Children of Twins design*

To date, there has not been a systematic review of the limitations of the COT design, and researchers must be cognizant of these issues before utilizing the design. These considerations will also be important in evaluating the results of the COT design to relations between parents and children in other samples (e.g., Reiss et al., 2000). Caution is warranted when interpreting the paths in the COT model because of several reasons. First, the design has low power to distinguish between the environmental processes responsible for intergenerational correlations compared to other behavior genetic designs, such as adoption studies (see Heath, Kendler, Eaves, & Markell, 1985 for a comparison of the statistical power of behavior genetic designs which study parent-child relations).

Second, as stated above, the design is based on the relations between variables in a correlational study and is therefore unable to make strong claims of causation like those based on a randomized control study. The association between the parent's behavior and the child outcome may be the result of effectively nonshared environments (Goldsmith, 1993; Turkheimer & Waldron, 2000) (e.g., environments that make twins dissimilar and are correlated with SDP could be responsible for the relationship between the parent and the child). The COT model is not able to estimate both a direct 'causal' path from the parental phenotype to the child phenotype and a path from the E parameter in the parental generation and the child's phenotype (Heath et al., 1993; Simonoff, 2000). The COT model could be drawn with an intergenerational path from the E parameter to the child phenotype instead of a direct path from the adult characteristic. The two models provide an identical fit to the data and are merely a re-parameterization of the estimates. However, the direct path ( $p$ ) in the COT model, as described in this paper, has a direct comparison to regression coefficients. Although the design can control for many latent factors, it cannot control all possible confounds.

Third, as the COT model is specified here, the environment is assumed to 'cause' differences in the

child instead of the other way around. Therefore, child effects on parenting are assumed to be negligible which may be unjustified for some situations, such as parenting and conduct disorder (e.g., Bell, 1977; Lytton, 1990). The assumption of the direction of effects may be warranted in the study of SDP and BW because it is a longitudinal design, but the assumption may be less defensible with cross-sectional data. Fourth, other processes through which environments are associated with genetic factors, such as active and evocative rG-E (Eaves et al., 1977; Plomin et al., 1977; Scarr & McCartney, 1983), are not included in the model. Active rG-E occurs when an individual selects environments based on genetically influenced traits (i.e., someone who is high on sensation-seeking will be more likely to participate in risky behaviors). Evocative rG-E occurs when genetically influenced traits elicit environmental responses from others. In the COT model presented here, the presence of active or evocative rG-E would increase the estimate of genetic factors in the child characteristic.

Fifth, violations of the equal environments assumption may unjustly increase the estimation of the role that genetic factors play in intergenerational relations. Two factors would need to be present for this to occur. MZ twins and their respective families would have to spend more time together than the families of DZ twins, and increased exposure between the two twin families would have to increase the association found in the avuncular relationship (e.g., between niece and aunt in SDP and BW in the present study). Therefore, measures of contact between the families should be included in COT studies in order to test the equal environments assumption and allow for statistical controls when necessary.

Sixth, the current COT model also assumes the absence of assortative mating, the situation in which mates select each other in a non-random fashion for the phenotype being studied. Assortative mating can confound correlations between mothers and their children through both environmental and genetic processes. For example, the higher likelihood of antisocial individuals marrying other antisocial individuals (Krueger, Moffitt, Caspi, Bleske, & Silva, 1998) may have an environmental influence on the children, such as being exposed to two parental models of antisocial behavior. Assortative mating may also cause an increase in genetic factors associated with a behavior or characteristic. We are currently working on quantitative approaches that will address many of these limitations.

Finally, the COT design may require a very specific sampling strategy, depending on the focus of the developmental research. The example of SDP and BW presented in the paper effectively measures all children at age zero. Samples will have to include children of similar ages in both twin families in order to study children's adjustment to environmental

influences such as parenting (e.g., the study of corporal punishment will require that both sets of twins have/had young children). Such samples may require large twin registries or databases, making it difficult to conduct COT studies for researchers without access to such resources. Developmental research examining the impact of parental characteristics such as IQ and divorce, as compared to parenting practices, may not require that both twins have children of similar age. Large samples of cousins are also required to accurately measure residual genetic influences on the child outcome variable because of the small differences in genetic relatedness between cousins from MZ and DZ families. However, researchers do not have to estimate all of the parameters in the child generation, including those related to genetic factors, if the research is solely focused on the intergenerational processes. The low statistical power of the half-sib method to estimate the magnitude of genetic factors does not influence the ability of the COT model to calculate the intergenerational paths.

#### *Future directions with the Children of Twins model*

The COT model can be expanded to include additional parameters and test other hypotheses about intergenerational relationships. By including measures of both parents a COT model could also test whether maternal or paternal behaviors are more influential (see Rose et al., 1980 for an example of the COT design's ability to enumerate maternal effects). Factors associated with mate selection could also be explored instead of assuming that assortative mating is zero. For instance, analyses including both parents would be able to examine whether the correlation between a maternal characteristic and a child characteristic is due to an increase in genetic loading for the trait because of the mother's selection of a mate. Analyses which include the spouses of the adult twins could study whether mate selection mediates the genetic association between parental factors and the children's adjustment.

Similarly, more than one child from each nuclear family can also be included in the model. Adding multiple children would increase the power to estimate the intergenerational paths and provide the opportunity to measure environmental variables which influence all of the children in the same family but which are independent of the parental variable (Nance & Corey, 1976; Nance et al., 1978). This parameter would provide another measure of the effectively shared environment. Likewise, the design may also include measured characteristics of the family (i.e., family cohesion or marital discord) to determine the extent to which these constructs influence the child through environmental processes and/or genetic transmission. This represents a crucial research endeavor because measures of the environment have been shown to include a genetic

component when studied within behavior genetic studies (Plomin & Bergeman, 1991; Reiss & Neiderhiser, 2000).

The COT design can also be combined with other extended twin designs, such as the twin-family design, to study intergenerational associations. These models provide a powerful estimate of complex genetic and environment influences and interactions without some of the assumptions inherent in the other extended twin designs (D'Onofrio, Eaves, Murrelle, Maes, & Spilka, 1999; Truett et al., 1994; Maes, Neale, & Eaves, 1997). A longitudinal COT study would be able to more clearly delineate the processes involved in children's adjustment to environmental influences and overcome many of the limitations inherent in cross-sectional COT studies. Finally, the role of genetic nonadditivity needs to be explored in behavioral genetic designs, including the COT model, which study the relations between parent characteristics and child outcomes. This may be especially pertinent in the study of SDP because the MZ correlation is more than twice the DZ correlation.

#### **Conclusion**

The main appeal and strength of the COT model is the ability to quantify the processes involved – both genetic and environmental – in intergenerational relationships. The design can strengthen claims about a causal relation between environmental variables and child outcomes or highlight confounds that are responsible for the association. The COT design overcomes the limitations of some behavior genetic studies which use a summary statistic for the environment (Wachs, 1983) by directly specifying the salient environment. The COT model also permits the study of family-level environmental risk factors. Although some behavior geneticists have discouraged the study of environments which siblings share (e.g., Plomin & Daniels, 1987), it is still unclear whether such traits are important for child development (Rutter et al., 2001). The COT design is unique because it is not limited by the same assumptions made by the other designs and may present fewer difficulties in obtaining the necessary samples. Extended twin studies, albeit with their own limitations, represent the next step in discriminating how risk mechanisms operate because they begin to illustrate the processes through which genes and environment act (Rutter et al., 1999).

This paper seeks to introduce developmental researchers to the underlying methodology, strengths, and weaknesses of the COT design. The design, like all research designs that are focused on revealing causal processes in the field of developmental psychopathology, is limited by a number of methodological difficulties, most notably those involved with obtaining appropriate samples. However, the

authors feel that the ability to delineate the risk mechanisms from the source of the risk and quantify the underlying processes makes the COT design a particularly powerful tool for studying associations between environmental measures and outcomes. These benefits especially apply when genetic factors have been found to influence both constructs. For example, the COT design may be utilized to study the influence of environmental factors which are frequently studied by the field of developmental psychology, such as parenting practices (Kendler, 1996; Wade & Kendler, 2000), parental psychopathology (Faraone, Tsuang, & Tsuang, 1999), divorce (Jockin, McGue, & Lykken, 1996; McGue & Lykken, 1992), and maternal drug use during pregnancy (Magnus et al., 1985). The question remains whether the correlation between such environmental antecedents and childhood behavioral outcomes are due to a direct environmental influence, other environmental factors, or a genetic factor, and the COT model provides a useful method to discriminate among them.

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