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# The Twin and Offspring Study in Sweden: Advancing our understanding of genotype–environment interplay by studying twins and their families

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## The Twin and Offspring Study in Sweden: Advancing Our Understanding of Genotype-Environment Interplay by Studying Twins and Their Families

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**Abstract:** The Twin and Offspring Study in Sweden (TOSS) is a study of 909 pairs of twins who are parents and includes the twins, their adolescent child and their spouse or partner. The TOSS was designed to address three key questions: (1) what are the genetic and environmental influences on parenting for a sample of twins who are parents; (2) what are the genetic and environmental influences on adult family relationships; and (3) how do family relationships impact the adjustment of adults. Because of the inclusion of the children of twins as well as the twins themselves, the TOSS is able to begin to specify the types of genotype-environment correlation, especially when paired with other studies examining children who are twins. Findings from the TOSS have helped to clarify the types of genotype environment correlation involved in parenting and other family relationships, have helped to specify how individual characteristics of parents influence their parenting, and how such individual characteristics can explain genetic influences on family relationships. Future directions for analyses using the TOSS include additional specification of genotype-environment correlation, examination of genotype  $\times$  environment interaction and the analysis of specific genes for associations with the environmental constructs measured in TOSS and specific gene  $\times$  specific environment interactions.

**Keywords:** twin parents; children of twins; genotype-environment correlation; family relationships

### The Twin and Offspring Study in Sweden

There has been an increasing focus on the interplay between genes and the environment in understanding the development and adjustment of individuals throughout the lifespan. In part, the growth in this area of research has been driven by the rapid advances in molecular genetics combined with the methodological advances in behavioral genetics that facilitate the ability to examine moderation using a twin/sibling design (Caspi et al., 2002; Plomin & Crabbe, 2000; Purcell, 2002; Purcell & Koenen, 2005; Purcell & Sham, 2002). These advances have led to more genetically informed studies adding and/or examining measures of environment to their designs and to nongenetic studies adding genetic indices, most commonly by collecting DNA. The coupling of well measured environment and a genetically informed design is critical to advancing our understanding of gene-environment interplay.

As a result of this focus on gene-environment interplay and the accompanying flurry of studies in this area, our understanding of how genes and environment interact has rapidly advanced. We now know that early life stress has a differential impact on child and adult functioning depending on the form of one or more specific genes (e.g., Caspi et al., 2002; J. Kaufman et al., 2004; J. Kaufman et al., 2006), that parent-adolescent relationships during adolescent moderate the heritability of antisocial behavior but not depressive symptoms (Feinberg, Button, Neiderhiser, Reiss, & Hetherington, 2007), and there even has been one report of a specific gene moderating the effects of an intervention in toddlers (Bakermans-Kranenburg, Van IJzendoorn, Pijlman, Mesman, & Juffer, 2008). One key component of gene-environment interplay that has received much less attention, yet may be ubiquitous, is genotype-environment correlation.

Genotype-environment correlation (*rGE*) occurs when an individual's genes and environment are correlated. Typically, three types of *rGE* have been described: passive, evocative/reactive and active (Plomin, DeFries, & Loehlin, 1977; Scarr & McCartney, 1983). Passive *rGE* is due to the fact of parents and children sharing both genes and

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environment, evocative *rGE* occurs when the environment responds (or the child evokes) to genetically influenced characteristics of the child and when an individual actively selects an environment correlated with his or her genotype active *rGE* is indicated. Outside of an experimental setting it is difficult to distinguish between evocative and active *rGE*, so they are most often considered together as evocative. In the context of a behavioral genetic design, finding genetic influences on measures of the environment, like life-events (Plomin, Pedersen, Lichtenstein, McClearn, & Nesselrode, 1990), parent-child relationships (e.g., Bussell et al., 1999), peer group characteristics (e.g., Manke, McGuire, Reiss, Hetherington, & Plomin, 1995), or marital quality (Spotts, Neiderhiser, Towers et al., 2004) is evidence of *rGE*. What is not always clear is what type of *rGE* is operating or what specific characteristics may account for the genetic influences. Understanding these mechanisms is crucial for advancing our ability to use findings from behavioral genetics to inform intervention research and practice.

#### *The TOSS Study: Research Questions and Method*

The Twin and Offspring Study in Sweden (TOSS) is a study of adult twins and their families. The primary objectives of TOSS were focused on understanding how family relationships influence the mental health of men and women who were parents of at least one adolescent, how these relationships were influenced by genetic and environmental factors, and specifying types of genotype-environment correlation (*rGE*). These aims were guided, in part, by findings from the Nonshared Environment in Adolescent Development (NEAD) study, described in detail elsewhere (Neiderhiser, Reiss, & Hetherington, 2007; Reiss, Neiderhiser, Hetherington, & Plomin, 2000, and in this special issue, Reiss, 2008). NEAD found a consistent pattern of evidence for genetic influences on family relationships and a sizable genetic correlation between family relationships and adolescent adjustment. As will be described in more detail below, through the use of this unusual and carefully measured sample of twins and their families we have been able to make important advances in our understanding of how marital and other social and family relationships impact the mental health of men and women, in the overlap among different types of family relationships, and in developing a model to distinguish between passive and evocative genotype-

environment correlation using the full children-of-twins design.

The TOSS was designed to address three key questions, all centered on understanding, identifying and specifying correlations between genotype and environment. (1) What are the genetic and environmental influences on parenting for a sample of *twins who are parents* of an adolescent child? In order to address this first question the measurement and recruitment of the sample was matched as closely as possible to that of the NEAD study, as noted above. In this way we could examine finding for twin parents in conjunction with findings for twin children (as in NEAD). (2) What are the genetic and environmental influences on other adult twin family relationships? The key other family relationship to be examined is that between the spouses. At the time of data collection for the first cohort of TOSS, there were no published studies of genetic influences on marital relationships other than for pair bonding or the likelihood of divorce/remarriage. (3) How do family relationships impact the adjustment of middle-aged adults? The key component of this third question was whether the patterns of associations between family relationships and adult adjustment would be similar to those for adolescents with the bulk of the covariation accounted for by genetic influences. We were also interested in whether different family relationships (i.e. parent-child and marital) would show a different pattern of findings in influencing the adjustment of these adult twins. Two additional questions were possible with the addition of cohort 2. First, are the patterns of findings different for men and women and second, what are the influences on the adolescent children's adjustment?

*Sample Description.* The TOSS sample includes 909 twin pairs who are mothers (559 pairs) or fathers (350 pairs) of at least one adolescent child (254 MZ and 285 DZ twin mother pairs and 128 MZ and 183 DZ twin father pairs), their long-term partner or spouse, and one adolescent child of the twin parent. The recruitment of this complex twin family sample was possible by using the Swedish Twin Registry. The TOSS consists of two cohorts collected approximately 3 years apart. The first cohort consisted of 326 pairs of twin mothers drawn from female-female twin pairs born between 1926 and 1966. We extended this sample by adding a second cohort of twin mother and twin father families. The second cohort was drawn from same-sex twin pairs born between 1944 and 1971. Each member of the

twin pair was involved in a long-term relationship with a partner residing in the same home. For inclusion in our sample, each twin was also required to have an adolescent child, ranging in age from 11 to 22 years (mean child age =  $15.7 \pm 2.4$  years), the same sex as the co-twin's child (49% males) with no more than a four-year age difference between the cousins. Twin fathers were slightly older than twin mothers, with average ages of 47.0 ( $\pm 4.7$  years) and 43.6 ( $\pm 4.6$  years) for fathers and mothers, respectively. Although it was not a requirement for inclusion, 96% of the spouse/partners were biologically related to the adolescent. These inclusion criteria were necessary to ensure that the current living experiences of each of the twin parents were comparable to his or her co-twin and their family members (see Reiss, Cederblad et al., 2001 for a detailed description of the study rationale for cohort 1). Participants are mostly middle class, and consistent with the population of Sweden, are in principle 100% Caucasian.

Because the original 326 pairs of twin mothers were recruited and assessed 3 years earlier than the 350 pairs of twin fathers and additional 233 pairs of

twin mothers from cohort 2, we systematically examined cohort effects prior to combining them for analysis. For the vast majority of the measures examined in TOSS (89%) there were no significant and meaningful differences between the cohorts.

*Measurement.* As noted above and in Reiss et al. (2001), the focus of TOSS is on family relationships and adjustment of adult twin parents. The measurement package reflects this focus by assessing five broad categories of constructs: parent and child relationships with current family, parent's social experiences, parent adjustment, child adjustment, and individual attributes of family members. We also assessed twin specific factors and demographics. Table 1 lists the constructs and measures, including the respondent. In many cases the respondent reports about themselves and about other family members. For example, parents report on their own depression and also report on the child's depression. We have also collected DNA samples for all twins participating in TOSS and all family members who participated as part of cohort 2.

Table 1.  
*Summary Of Measures Used In The TOSS.*

	TWIN	SPOUSE	ADOLESCENT
<b>INDIVIDUAL ATTRIBUTES OF FAMILY MEMBERS</b>			
Sense of coherence (Antonovsky, 1983)	x	x	
Mastery (Pearlin, Menaghan, Lieberman & Mullan, 1981)	x	x	
Karolinska Scales of Personality: Aggression scales (Schalling & Edman, 1993)	x	x	
Swedish University Scales of Personality			x
Attachment style (Simpson, Rhodes & Phillips, 1996)	x	x	
Temperament and Character Inventory (Cloninger, Przybeck, Svrakic, & Wetzel, 1994)	x	x	x
Vocabulary test (Dureman, Keebon & Österberg, 1971)	x	x	x
Hansson Activity Inventory (developed for TM study)	x	x	x
Extraversion & Neuroticism (short form)	x	x	x
<b>PARENT'S SOCIAL EXPERIENCES</b>			
<b>1. Stress buffered by social support</b>			
Life events (Plomin et al., 1990)	x	x	
Social support (Henderson, Hetherington, Mekos, & Reiss, 1996)	x	x	
Socioeconomic status (P. Lichtenstein, Harris, Pedersen, & McClearn, 1992)	x	x	
Socioeconomic status during childhood (P. Lichtenstein et al., 1992)	x		
Parental Bonding Instrument (Parker, Tupling, & Brown, 1979)	x		
<b>PARENT AND CHILD RELATIONSHIP WITH CURRENT FAMILY</b>			
<b>1. Marital processes</b>			
Dyadic Adjustment Scale (Spanier, 1976)	x	x	
Marital Instability Scale (Booth, Johnson, & Edwards, 1983)	x	x	
Marital Adjustment Test (Locke & Wallace, 1987)	x	x	
<b>2. Parenting processes</b>			
Expressed emotions (Hansson & Jarbin, 1997)	x	x	x
Child Monitoring (Hetherington & Clingempeel, 1992)	x	x	x
Child Rearing Issues: Discipline (Hetherington & Clingempeel, 1992)	x	x	x
Child Rearing Issues: Parent-Child Agreement (Hetherington & Clingempeel, 1992)	x	x	x
Parent Child Relationship (Hetherington & Clingempeel, 1992)	x	x	x
Expression of Affection (Hetherington & Clingempeel, 1992)	x	x	x

<b>3. Characteristics of the family system</b>			
Family environment scale (Moos & Moos, 1981)	x	x	x
Lund family climate (Hansson, Ryden, & Johnsson, 1994)	x	x	x
<b>4. Child Relationship with Siblings &amp; Peers</b>			
Sibling Inventory of Behavior (Hetherington & Clingempeel, 1992)			x
Network of Relationship Inventory (Hetherington & Clingempeel, 1992)			x
<b>CHILD'S ADJUSTMENT MEASURES</b>			
Self-esteem and competence (Harter, 1982)			x
Optimism, "Ladder of life"	x	x	x
Child Behavior Checklist (Achenbach, 1994)	x	x	x
Children Depression Inventory (Kovacs, 1983)	x	x	
Center of Epidemiological Studies, Depression Scale (CES-D)			x
Physical Symptoms Inventory (developed for TM study)			x
Height and weight (developed for TM study)			x
Alcohol and Drug Use			x
Eating Disorders	x	x	x
Relational Aggression			x
Child Aggression (Olweus, Mattsson, Schalling, & Low, 1988)			x
Phobia			x
Child puberty (Peterson, Crockett, Richards, & Boxer, 1988)	x	x	x
Child health (developed for this study)	x		
<b>PARENT ADJUSTMENT MEASURES</b>			
<b>1. Depression and anxiety</b>			
SCID: Screening questionnaire for Axis I diagnoses: anxiety and mood disorders (Spitzer, Williams, Gibbon & First, 1992)	x		
Center for Epidemiological Studies Depression scale (Radloff, 1977)	x	x	
Beck Anxiety Inventory (Beck & Steer, 1993)	x	x	
Parent ADHD Measure	x	x	
Phobias and fears (Fredrikson, Annas, Fischer & Wik, 1996)	x	x	
Karolinska scales of psychic and somatic anxiety (Schalling & Edman, 1993)	x	x	
<b>2. Legal drug use</b>			
Alcohol and Drug Use	x	x	
<b>3. Quality of life/Positive Adjustment</b>			
Quality of life (Kajandi, Brattlof & Soderlin, 1983)	x	x	
Perceived competence (Messer & Harter, 1986)	x	x	
Optimism, "Ladder of life" (developed for TM study)	x	x	x
<b>4. Physical health</b>			
Physical health (Reiss et al., 2001)	x	x	
SF-36	x	x	
Height & Weight	x	x	
<b>TWIN MEASURES</b>			
Zygoty (Nichols & Bilbro, 1966)	x		
Relationship between twins (developed for TM study)	x		
Adult Sibling Relationship (Lanthier & Stocker, 1992)	x		
<b>DEMOGRAPHIC MEASURES</b>			
Marital History (developed for TM study)	x	x	
Household composition (developed for TM study)	x	x	
Demographic Questionnaire (developed for TM study)	x	x	

### Results to Date

Consistent with the study objectives, there are three key areas that have been examined using one or both cohorts of TOSS. To date, reports from TOSS have made the most significant contribution by specifying and advancing our understanding of *rGE*. These reports, described in more detail below, have examined parent-child and marital relationships and the interrelationships among family relationships. A

second set of reports from TOSS have helped to clarify how individual characteristics like temperament and personality as well as family relationships covary with the adjustment of adults for genetic and environmental reasons. Similarly, the degree to which individual characteristics can explain genetic influences on family relationships – specifying how *rGE* operates – has been a focus of a

number of reports from TOSS. Each of these key sets of findings will be described in more detail below.

*Understanding Family Relationships.* Building on studies that found evidence for genetic influences on parent-child relationships in studies of twin children (e.g., Elkins, McGue, & Iacono, 1997; Plomin, Reiss, Hetherington, & Howe, 1994; Rowe, 1981) and on the few studies of twin parents (e.g., Kendler, 1996; Losoya, Callor, Rowe, & Goldsmith, 1997; Plomin, McClearn, Pedersen, Nesselrode, & Bergeman, 1989) TOSS sought to examine genetic and environmental influences on parent-adolescent relationships. One such report examined twin women's remembered parenting as indexed by the Parental Bonding Instrument and found that only remembered parental warmth showed genetic influences with parental authoritarianism and protectiveness explained by environmental influences only (Paul Lichtenstein et al., 2003). We also found that some of the genetic influences on remembered parental warmth could be explained by genetic influences on optimism, aggression and humor in the adult twins, suggesting that part of this finding may be due to recall biases correlated with personality characteristics. A similar study examined possible personality correlates of parenting in both twin women and men with a focus on current parenting (Ulbricht, 2006). In this report we found significant and moderate genetic correlations between personality of mothers and fathers, indicating that although personality explains some of the genetic variance on parenting, other genetically (and environmentally) influenced factors are also involved.

A key focus of TOSS is to disentangle passive *rGE*, or correlations between genes and environment due to parents and children sharing both genes and environment, from evocative *rGE*, correlations due to genetically influenced characteristics of the child evoking responses from the environment. In two reports on this topic – one focused on mothering and one on fathering – we found that parent-adolescent positivity and negativity was due to both passive and evocative *rGE* and that there was little evidence of *rGE* for parental monitoring (Neiderhiser, Reiss, Lichtenstein, Spotts, & Ganiban, 2007; Neiderhiser et al., 2004). There were some differences in the patterns of findings for mothers and fathers and by reporter, but taken as a whole the results indicated that both passive and evocative *rGE* were important for parent-adolescent relationships, but less so for monitoring. In these reports, the ability to distinguish between

passive and evocative *rGE* was due to comparing findings from two different samples, NEAD (Neiderhiser, Reiss, & Hetherington, 2007) and TOSS. A more elegant and rigorous approach to distinguishing between passive and evocative *rGE* is provided by an Extended Children of Twins (ECOT) approach. This approach takes advantage of the complex children of twins design of TOSS – including data from twin parents and their children – and also extends the examination of *rGE* to include child adjustment. A recent report describes the model and describes findings using maternal emotional overinvolvement and adolescent internalizing as an example (Narusyte et al., in press). We found clear evidence of evocative *rGE* with no evidence of passive *rGE* or direct environmental influences of maternal overinvolvement on adolescent internalizing behavior. This report is especially exciting as it presents a strategy that can be extended to other studies and samples and allows for the examination of data from parents and from children within the same model. A next step is to also incorporate the data from the other parent into the model, thereby enabling the estimation of assortative mating effects and also taking full advantage of all of the data collected in TOSS.

Another set of reports from TOSS has provided the most comprehensive description to date of genetic and environmental influences on marital relationships, the role of individual characteristics in explaining these genetic and environmental influences and the etiology of the associations between marital relationships and the adjustment of women. Specifically, we found evidence for genetic influences on marital quality in twin women – a finding that was consistent across both wife and spouse reports – although the majority of variance in marital quality could be explained by nonshared environmental factors (Spotts, Neiderhiser, Towers et al., 2004). In order to better understand the possible sources of the genetic and environmental influences on marital quality, personality characteristics of the twin women and their spouses were examined. We found that wives' personality characteristics, but not their spouses', accounted for genetic and nonshared environmental variance in the wives' marital satisfaction (Spotts, Lichtenstein et al., 2005). These findings, taken together, provide clear evidence for the importance of *rGE* because of the genetic influences found for marital quality as reported by the twin women and their spouses and by the ability to

account for some of the genetic influence through the personality characteristics of the wife – evocative *rGE*.

We have just begun to integrate the findings of *rGE* for parenting and marital relationships by considering the overlap of family systems and whether these may be best explained by similar genetically influenced characteristics or factors within the family members. This report found that genetic factors explained nearly half of the covariance between marital satisfaction and parenting for both mothers' and fathers' self-reported warmth and negativity and somewhat less for observational ratings of maternal and marital warmth, but did not contribute to the association between observational ratings of maternal and marital negativity (Ganiban et al., 2007). These findings support evidence of *rGE* for both warmth and negativity in marriage and parenting and suggest that both may be influenced by the same genetically influenced characteristics of the twins.

*Understanding Adult Adjustment.* The importance of understanding genetic and environmental influences on family relationships and in specifying the type of *rGE* is in how this then relates to healthy adjustment in children and adults. In TOSS we have clear evidence that marital relationship quality is correlated with depression and positive adjustment in women due to correlated genetic and nonshared environmental factors (Spotts, Neiderhiser, Ganiban et al., 2004; Spotts, Pederson et al., 2005). These findings help to highlight a key aspect of TOSS – we have found more consistent evidence for the importance of the nonshared environment (factors that make family members different) than has been reported to date. The findings from Spotts et al. (2004; 2005) suggest that nonshared environmental influences become more important when adult twins are examined with their families. The spouse and the child both are sources of nonshared environmental influences, and have an important influence on the adjustment of the twins. These influences are indicated by the significant nonshared environmental correlations between marital quality and the adjustment of women (Spotts, Neiderhiser, Ganiban et al., 2004; Spotts, Pederson et al., 2005). There was an effort in TOSS to systematically identify the sources of nonshared environmental influences by examining spouses' personality and other characteristics, life events and current family environment as nonshared environmental influences on the twin women's adjustment (Towers, 2002). The findings indicated that nonshared environmental influences of all three

sets of factors were important in influencing the adjustment of twin women.

There is also evidence in TOSS for the importance of the personality of twin women in influencing their own mental health for primarily genetic reasons. Specifically, we have found that temperament was associated with depressive symptoms and that the bulk of this association could be explained by genetic influences (Yuh et al., 2008). In addition, in a different analysis internalized aggression was found to be associated with depressive symptoms and this association was also mediated primarily by genetic factors (Haddad et al., 2008). Both of these reports underscore the importance of considering the characteristics of the individual when examining the adjustment, at least in adults, as these factors appear to be due to genetic influences that are correlated with genetic influences on adjustment.

#### *Future Directions for TOSS*

One of the most exciting aspects of TOSS is the ability to identify and specify types of *rGE*. There are few studies that can do this and none that are able to distinguish between passive and evocative *rGE*. Now that we have developed a model that is able to use the ECOT to disentangle evocative and passive *rGE* and direct environmental influences on child adjustment we hope that others will be able to incorporate this approach into their own research. An important limitation of this, however, is the need for a specialized sample that includes twin parents and their children and, to take full advantage of the ECOT, an appropriately matched sample of children who are twins. Nonetheless, we look forward to applying this model to a number of key associations between family factors and adolescent adjustment. As noted above, an important part that is missing from the current version of the ECOT is the inclusion of spouses in the model. Including the spouse will allow for the full range of genetic influences on the child to be estimated and will also permit the examination of the impact of assortative mating.

Another future direction of analyses using the TOSS sample is to examine genotype  $\times$  environment interaction. Given our moderate sample size of 900 pairs of twin families, it is the extensive and careful measurement of environmental influences, especially family environmental influences, that provides a real advantage here. As indicated in the measures table, we have extensively measured parenting, marriage, social support, life events, and adult twin relationships

in TOSS. Thus, considering these well measured environments as moderators of heritability is an important next step.

We have also collected DNA for participants in TOSS. Analyses of these data are currently underway. Again, the key advantage we have with the TOSS sample is the well characterized environment and the ability to examine *rGE* and GxE by examining specific genes and specific environments. A recent report has underscored the importance of considering *rGE* when examining GxE (Jaffee & Price, 2007) and in TOSS we are in a unique position to consider both.

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## 瑞典的双生子与子代研究： 通过双生子及其家庭来增加对遗传与环境互动的了解

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**摘要：**双生子及子代研究（TOSS）收集了 909 对双生子及他（她）们的配偶和他（她）们的青少年子女的数据。设计该项目是为研究以下三个问题：1）遗传与环境是如何影响双生子父母的养育方式的？2）遗传与环境是如何影响成年人的家庭关系的？3）家庭关系是如何影响成年人的心理调适的？由于此研究包括了双生子及其子女，该设计可以与其他研究相比较来具体地分析遗传与环境的关联。此研究的结果有助于厘清遗传与环境在养育方式和家庭关系中的型态，同时也澄清了父母个人特征是如何影响他（她）们的养育方式，以及父母的个体特征是如何帮助解释了遗传对家庭关系的影响。此研究今后将进一步分析遗传与环境的关联与互动，以及候选基因与环境的关联与互动。

**关键词：**双生子父母；双生子儿童；遗传与环境关系；家庭关系

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