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Why aren't identical twins linguistically identical? Genetic, prenatal, and postnatal factors*

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Results of behavioral and molecular studies clearly demonstrate that genetic factors play an important role in the rate of language acquisition and linguistic proficiency attained by children and adults for both normal and impaired people (for a review, see Stromswold, 1998; Stromswold, 2001). In addition to heritable factors that influence both nonverbal and verbal abilities, there appear to be genetic factors that influence verbal abilities but not nonverbal abilities. Furthermore, some studies suggest that different genetic factors are involved in different aspects of language (e.g., written vs. spoken language, lexical vs. syntactic abilities). That said, it is also clear that identical (monozygotic, MZ) twins, who are generally assumed to have identical genetic endowments and identical environments, do not always have identical language systems. This paper discusses how genetic factors and pre- and post-natal environmental factors, and interactions among these factors could result in MZ cotwins having substantially different linguistic abilities. Empirical methods that tease apart the effects and interactions of genetic and pre- and post-natal environmental factors are proposed.

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1. Twin Studies of Language

The most common method used to tease apart the relative importance of environmental and genetic factors for language development is to determine whether identical (monozygotic, MZ) cotwins are

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linguistically more similar to one another than fraternal (dizygotic, DZ) cotwins. Roughly speaking, the logic of twin studies is as follows: MZ and DZ twins share essentially the same pre- and postnatal environment, whereas MZ twins share 100% of their genetic material and, on average, DZ twins share only 50% of their genetic material. Therefore, if MZ twin pairs' linguistic abilities are more similar than DZ twins, this suggests that genetic factors play a role in language. If, on the other hand, MZ twin pairs are no more similar to one another than DZ twin pairs, this suggests the heritability of language is negligible. Putting aside the possibility of interactions and correlations between genetic and environmental factors (see section 6), the variation in linguistic abilities in a population (the phenotypic variance) is due to genetic variance plus environmental variance. Heritability is a measure of the proportion of the phenotypic variance that is due to genetic variance. In twin studies, environmental factors that may contribute to phenotypic variance are divided into those environmental factors that co-twins do and do not share and those cotwins do not share. Shared environmental factors include, for example, the linguistic input children receive (assuming parents of twins speak the same way to both cotwins). Nonshared environmental factors include, for example, illnesses or accidents that only one cotwin experiences.

1.1 Concordance rates for language disorders

One way to determine whether MZ cotwins are linguistically more similar than DZ cotwins is to compare the concordance rates for developmental language disorders in MZ and DZ twin pairs. Twins are concordant for a language disorder if both cotwins are impaired. Twins are discordant for a language disorder if one cotwin is impaired and the other is not. If the concordance rate for language disorders is significantly greater for MZ than DZ twins, this suggests that genetic factors play a role in language disorders such as dyslexia and specific language impairment. If there is no significant difference in the concordance rates for MZ and DZ twins, this suggests that genetic factors play little role in developmental language disorders.

Meta-analyses of 10 twin studies of written or spoken language disorders have revealed that for MZ twins, proband-wise concordance rates range from 35% to 100% (mean rate = 80%), whereas for DZ twins, concordance rates ranged from 31% to 68% (mean rate = 46%, for details see Stromswold, 2001). In all 10 studies, concordance rates are greater for MZ than DZ twin pairs, with the differences being significant in all but one study. When the twin pairs from the studies are pooled together, the overall concordance rate is significantly higher for MZ twins (80%) than DZ twins (46%). In the 5 twin studies of written language disorders, MZ concordance rates range from 33% to 100% (mean = 76%), and DZ concordance rates range from 31% to 50% (mean = 41%), with the overall concordance rate for MZ twins (75%) being significantly greater than for DZ twins (43%). For the 5 twin studies of spoken language disorders, MZ concordance rates range from 70% to 96% (mean rate 84%) and DZ concordance rates range from 42% to 69% (mean 52%), with the overall concordance rate for MZ twins (84%) being significantly greater than for DZ twins (50%).

One can obtain an estimate of the role of heritable factors for a disorder by doubling the difference in MZ and DZ concordance rates for a disorder. For example, if the concordance rate for spoken language impairments is 84% for MZ twins and 50% for DZ twins, the heritability for spoken language impairments is 68%. An estimate of the role of shared environmental factors is obtained by subtracting the heritability estimate from the MZ concordance rate. Artifacts such as systematic rater bias (i.e. the tendency of parents or experimenters to give similar scores to cotwins) may inflate estimates of shared environmental factors. An estimate of the role of non-shared (twin-specific) environmental factors is obtained by subtracting the MZ concordance rate from 100 (100-84% = 16%). The value of non-shared environmental factors includes variance due to measurement error and contrast effects of rater bias that may inflate differences between twin scores. Thus, for spoken language impairments, environmental factors shared by cotwins and environmental factors experienced by only one cotwin each play a modest, but equal role in determining whether a person will have a spoken language impairment (shared environment = 84%-68% = 16%; nonshared environment = 100-84% = 16%).

The twin study method assumes that, like nontwin siblings, DZ twins share, on average, 50% of their genetic material. Thus, to the extent that language disorders are due solely to genetic factors, we would expect the concordance rates for DZ twins to be similar to those of nontwin siblings. In 10 family

aggregation studies of spoken language disorders that reported impairment rates for siblings, Stromswold (1998) found that the rate of impairments among language-impaired children's siblings ranged from 15% to 49% (mean 30%). Thus, consistent with language disorders being largely the result of heritable factors, the impairment rate for nontwin siblings is quite similar to the overall DZ pair-wise concordance rate for spoken language disorders (26%).[1] The finding that proband-wise concordance rates are 30 to 35 percentage points higher for MZ twins than DZ twins indicates that genetic factors play a major role in developmental language disorders. However, if MZ twin pairs have exactly the same genetic and environmental makeup, why are the mean and overall concordance rates for MZ twins between 76% and 84%, with only one of the 10 studies reporting 100% concordance in MZ twins? Broadly speaking, the finding that a non-trivial percentage of MZ twins are discordant for language disorders suggests that (1) some of the supposedly MZ twins were actually DZ twins; (2) MZ twins don't have perfectly identical genetic and/or environmental backgrounds; (3) the expressivity or penetrance of language disorders is incomplete (some people have the genotype for language disorder, but do not have a clinically-apparent impairment); and/or (4) researchers failed to diagnose language disorders in some of the MZ cotwins.

1.2 Comparisons of normal twins' linguistic abilities

One drawback of twin concordance studies is that they can only be used to study twins who suffer from a language impairment, and it appears that the overlap in heritable factors that influence language development and linguistic proficiency in language impaired people versus non-language impaired people is far from perfect (Stromswold, 2001). A second drawback is that they take what is likely a continuous variable (linguistic ability) and artificially categorize people as either impaired or not impaired. Perhaps the lack of 100% concordance for MZ twins reflects the fact that inevitably there will be cases in which one MZ cotwin scores just a few points higher than his or her twin, but this small difference is enough to have one twin be labeled "normal" and the other impaired. In cases where the data obtained are more or less continuous (e.g., scores on language tests, age of acquisition of linguistic milestones, etc.) rather than dichotomous (presence or absence of a language disorder), one can address both problems by comparing how similar normal MZ and DZ cotwins' scores are on measures of language development or linguistic ability.

In meta-analyses of 8 studies of typically-developing twins' vocabulary development, Stromswold (2001) found that the MZ correlations were greater than DZ correlations in all 8 studies, and that the mean weighted correlation coefficient was .93 for MZ twins (as compared to .76 for DZ twins). For phonemic awareness, the MZ correlation coefficient was .90 (compared to .56 for DZ twins). For articulation, the weighted correlation coefficient was .92 for MZ twins and .85 for DZ twins. Stromswold (2001) reported the results of 12 twin studies in which 36 tests of morphosyntax were administered. For 33 of these tests, the correlation coefficients were larger for the MZ twins than the DZ twins, although the difference was only significantly greater for 12 of the 36 tests. For reading, the mean correlation coefficient for MZ twins was .86 (as compared to .66 for DZ twins). For spelling, the mean correlation coefficient was .78 for MZ twins (as compared to .48 for DZ twins).

Falconer (1960; 1989) devised a simple method for estimating the effect of genetic factors and environmental factors from MZ and DZ correlation coefficients. Falconer's estimate of heritability is calculated by doubling the difference between the MZ and DZ intra-twin correlation coefficients. The role of shared environmental factors is computed by subtracting Falconer's heritability estimate from the MZ correlation coefficient and the role of non-shared environmental factors is calculated by subtracting the MZ correlation from one. Using these formulas, we can estimate, for example, that heritable factors account for approximately 34% of the variance in vocabulary size, environmental factors that both

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[1] Affectedness rates for nontwin siblings are compared with pairwise twin concordance rates because the method for calculating affectedness rates for nontwin siblings (# affected siblings/total number of siblings) is more similar to the method for calculating pair-wise twin concordance rates (number of concordant twins/total number of twins) than the method for calculating proband-wise twin concordance rates (number of affected twins who are members of concordant twin pairs/total number of affected twins).

cotwins experience account for 59% of vocabulary size, and environmental factors that only twin experiences accounts for a mere 7% of twins' vocabulary. The finding that, for a wide-range of linguistic tasks, normal MZ twins perform more similarly to one another than do DZ cotwins suggests that heritable factors play a substantial role in the linguistic abilities of normal people. On the other hand, the finding that MZ twin scores were neither identical nor perfectly correlated for any of the 60 plus linguistic tests that Stromswold (2001) suggests that at lease some of the assumptions that underlie the twin method are questionable.

1.3 Why aren't MZ cotwins' linguistically identical?

If we assume for the moment that the results summarized in sections 1.1 and 1.2 are not solely due to the misclassification of MZ and DZ twins (i.e., calling MZ twins DZ or vice versa) or measurement error, there are at least 3 types of reasons why MZ cotwins might actually have (measurably different) linguistic abilities.

1) MZ cotwins are not genetically identical
2) MZ cotwins are not epigenetically identical
3) MZ cotwins have different prenatal, neonatal or postnatal environments

Furthermore, interactions within and among these 3 types of factors may either accentuate or attenuate behavioral (phenotypic) differences in MZ twin pairs. In section 2, we review mechanisms that could cause MZ cotwins to be genetically or epigenetically different from one another. Section 3 discusses differences in the perinatal environments experienced by twins versus singletons and MZ versus DZ twins concentrating on perinatal factors that could result in MZ cotwins being different from one another. In section 4, we discuss how these perinatal factors could preferentially impact language development. Section 5 reviews postnatal factors that may affect language development. In section 6, we discuss ways in which prenatal and postnatal environmental and genetic factors may interact with one another, concentrating on interactions that could result in MZ cotwins developing different linguistic systems. We conclude in section 7 with a discussion of possible ways of teasing apart the effects of genetic, prenatal and postnatal environmental factors.

2. Genetic and Epigenetic Differences

2.1 Twin types

DZ twins result when two ova are fertilized by two different sperm in the same menstrual cycle. The result is two zygotes that are, on average, genetically no more similar to one another than zygotes of non-twin, full siblings. MZ twins, on the other hand, result when a single zygote (that originates from the fertilization of one ovum by a single sperm) divides in two. There are 3 distinct types of MZ twins, and these differences may have genetic and perinatal environmental (see section 3) implications. MZ gestations may be dichorionic-diamniotic (two placentas, two amniotic sacs), monochorionic-diamniotic (one placenta, two amniotic sacs), or monochorionic-monoamniotic (one placenta, one amniotic sac). Dichorionic-diamniotic MZ twins occur when the zygote splits during the first 3 days following fertilization. This type of MZ twinning accounts for about 20-25% of all MZ twins. When the inner cell mass splits after blastocyst formation but before the formation of the amniotic sac (at 8 days after fertilization), the result is monochorionic-diamniotic MZ twins which account for about 70-75% of MZ twins. When division occurs after the formation of the amniotic sac, but before the establishment of the embryonic axis (at approximately 15 days after fertilization), the result is monochorionic-monoamniotic MZ twins which account for about 1-5% of all MZ twins. (For a succinct and accessible summary of twinning, see Redline, 2003.)

2.2 Genetic differences

Although most MZ twins are karyotypically identical, if chromosomal nondisjunction occurs just before or at the time of twinning, MZ twins will have different karyotypes. When this happens, the MZ twins are said to be heterokaryotic (Lejeune, 1963). Reports of heterokaryotic MZ twins in which one

twin is normal and the other is affected with Trisomy 21 (Down Sydrome) or Turner Syndrome (X0 Females) date back to at least the early 1960s (Lejeune, 1963), Another way that MZ twins may have different genotypes is if a spontaneous mutation occurs either before or after the zygote has split. In most cases, the MZ cotwin would be a genetic mosaic with some, but not all, of the twin's cells exhibiting the mutation. A very early mutation will affect a greater proportion of the cells in the fetus, and will result in generalized mosaicism with most of the tissues affected. A mutation which occurs later (e.g., at the blastocyst stage) will affect a smaller proportion of the cells in the fetus, and the abnormal cells may be restricted to a certain area or tissue type (e.g., the central nervous system). When MZ splitting occurs earlier (e.g., as in dichorionic MZ twins), there is a greater chance that MZ cotwins will have different spontaneous mutations. Very late splitting may mean that the "handedness" of the embryo has already been determined prior to twinning. Sommer and colleagues (2002) have argued that late splitting is associated with MZ twins who are discordant for handedness and language lateralization. Nance (1990) has argued that if the inner cell mass splits unequally, there will be different number of founder cells for the two cotwins and this can result in phenotypic differences.

2.3 Epigenetic differences

Epigenetic processes refer to processes that result in alterations in gene expression that are stable, but are not transmitted to offspring. Epigenetic processes, such as methylation and gene silencing (e.g., X chromosome inactivation or imprinting[2]) are part of normal development and cell proliferation. In addition to playing a crucial role in early development, epigenetic processes occur throughout development as random events or in response to environmental factors (Jaenisch & Bird, 2003). Epigenetic processes are responsible for some cases of phenotypic discordance in MZ twins. For example, Tsujita and colleagues (1998) compared the DNA of schizophrenia-discordant MZ twins and found two loci that were clearly different. These differences were consistent with either differences in methylation patterns or with a very small mutation in one of the twins. Recently, Petronis et al. (2003) compared the 5' regulatory region of the dopamine 2 receptor gene in one pair of MZ twins who were concordant for schizophrenia and one pair of MZ twins who were discordant for schizophrenia. They found that the methylation patterns were more similar in the concordant twin pair than in the discordant twin pair, suggesting that the differences in methylation patterns are (at least partially) responsible for the phenotypic differences in MZ twins.

X-inactivation is the process in females whereby every second X chromosome in a cell is randomly inactivated to create cellular mosaics of paternal and maternal X chromosomes. Due to its stochastic nature, differences in X chromosome inactivation patterns are one source of phenotypic discordance in female MZ twins. There have been cases reported of MZ female twins who are carriers for X-linked red-green color blindness (Jorgensen et al., 1992), Duchenne muscular dystrophy (Lupski, Garcia, Zoghbi, Hoffman, & Fenwick, 1991; Richards et al., 1990) and Fragile X syndrome (Kruyer et al., 1994; Willemsen, Olmer, De Diego Otero, & Oostra, 200), in which one twin is affected and the other is not. In each case, the affected twin had more inactivation of paternal than maternal X chromosomes. Some studies have reported that non-random or skewed X chromosome inactivation patterns are more frequent in MZ twins than in DZ twins or singletons (Goodship, Carter, & Burn, 1996; Trejo et al., 1994). Recent findings by Fisk and colleagues (1999) suggest that X-inactivation occurs after monochorionic twinning, which means that differential X inactivation could result in even MC cotwins being discordant for X-linked traits.

3. Perinatal environmental differences in twins

[2] A maternally imprinted gene is switched off when it is transmitted via the ovum, whereas a paternally imprinted gene is switched off when it is transmitted via the sperm. Because MZ twins get the same genes from the ovum and sperm, imprinting cannot account for phenotypic discordance in MZ twins. Hence, we will not discuss imprinting further.

3.1 Twins' language development

Day (1932a; 1932b) first compared the language abilities of twins and singletons and found that with respect to vocabulary, grammatical complexity of utterances, and mean length of responses, 2- to 5-year old twins were linguistically delayed relative to singletons. Day also found that twins' language impairments were greater than their cognitive impairments, suggesting that twins' delays are somewhat specific to language. Subsequent studies by Koch (1966), Mittler (1969; 1970; 1976) Conway et al. (1980), Hay and O'Brien (1983), Rutter and Redshaw (1991), and Dale et al. (2000) have confirmed that language development is slower in twins than singletons. Even when impaired twins are excluded, twins' language development appears to be about 2 to 3 months delayed relative to that of singletons, suggesting that the genetic makeup and/or environment of twins and singletons differ.

Twin studies are usually used to explore whether genetic factors affect a phenotypic trait, but it is equally valid to use twin studies to examine how environmental factors influence a trait. In traditional twin studies, estimates of the phenotypic effects of shared and nonshared environmental factors completely conflate the role of prenatal and postnatal environmental factors. The (often unspoken) assumption in twin studies of language is that when one refers to the role of environmental factors, one is referring to postnatal factors such as the quantity or quality of adult linguistic input that children receive. However, it has long be noted that twins suffer from more pre- and perinatal complications than singletons, and MZ are at greater risk for many of these complications than DZ twins (e.g., Lenneberg, 1967). Overall, the perinatal mortality rate for twins is 3-7 times higher than that for singletons (Sherer, 2001). Much of the increased morbidity and mortality in twins is due to the rate of premature birth being at least 4-5 times higher in twins than singletons, and the rate of fetal growth restriction being at least 3-7 times higher in twins than singletons. Only MZ twins can share a placenta or amniotic sac, and as is discussed below, sharing a placenta or amniotic sac confers certain special risks during the perinatal period.[3] The result is that monochrorionicity-monoamniotic MZ twins have higher perinatal morbidity and mortality rates that monochorionic-diamniotic MZ twins who have higher morbidity and mortality rates than dichorionic-diamniotic MZ twins who have higher morbidity and mortality rates than DZ twins who are always dichorionic-diamniotic (Dube, Dodds, & Armson, 2002; Hatkar & Bhide, 1999; Sherer, 2001; Victoria, Mora, & Arias, 2001). In this section, we discuss some of the special risks twins face during the prenatal, intrapartum and neonatal periods, concentrating on factors that are more likely to affect MZ than DZ twins, and that can affect one member of a twin pair more than another.

3.2 Intrauterine growth restriction and low birth weight

In the US, twins are approximately 10 times more likely to be born at low birth weights (LBW, birth weights of less than 2500 grams) than singletons, with over half of all twins being LBW (Center for Disease Control, 1999; Guyer et al., 1999; MacDorman & Atkinson, 1999). Furthermore, MZ twins tend to weigh less at birth than DZ twins of the same gestational age (Ananth, Vintzileos, Shen-Schwartz, Smulian, & Lai, 1998; Senoo et al., 2000; Victoria et al., 2001). Twin fetuses without additional complications typically grow as well as singletons during the first two trimesters of gestation (Fliegmer & Eggers, 1984). Beginning at between 28 to 32 weeks gestation, however, the rate of growth decreases for twins relative to that of singletons. Because monochronionic MZ twins share a placenta, monochorionic

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[3] There are reports in the literature of the two placentas in dichorionic twins fusing (e.g., Souter et al., 2003). In their study, van Dijk and colleagues (1996) found that 8% of DZ twins and 21% of non-identical triplets have two genetically dissimilar cell lines in their blood, but one cell line in their solid tissues. This phenomenon, known as blood chimerism, is the result of transplacental vascular anastomoses in conjoined placentas, which allow fetal blood cell precursors to migrate from one twin to the other. The high rate of blood chimerism in DZ twins suggests that fused placentas are not as rare as previously thought, and raises the possibility that some of the special risks previously thought to affect only twins that share a placenta (i.e., monochorionic MZ twins) could in theory affect dichorionic DZ and MZ twins as well. The other implication of van Dijk and colleagues' finding (1996) is that twins who share a placenta should not necessarily be assumed to be MZ and, ideally, zygosity should be determined by karotyping solid tissue and not blood (Redline, 2003; Souter et al., 2003).

MZ twins also tend to be lighter than dichorionic MZ twins, even correcting for the degree of prematurity (Ananth et al., 1998; Senoo et al., 2000; Victoria et al., 2001). Bryan (1993) points out that the birth weight differences for monochorionic versus dichorionic twins cannot be completely due to effect of sharing a placenta because dichorionic MZ twins are also lighter than DZ twins (Corney, Robson, & Strong, 1972). He suggests that the difference in birth weights for MZ & DZ dichorionic twins could reflect reduction in cell mass in MZ twins due to the division of a single zygote into two embryos. [4] Fetuses with velamentous cord insertion[5] weigh less than fetuses with central cord insertion (Loos, Deroma, Deroma, & Vlietincka, 2001). Because velamentous cord insertion occurs more commonly in dichorionic MZ twins than dichorionic DZ twins (Loos et al., 2001), this is another possible reason why MZ dichorionic twins weigh less than DZ dichorionic twins.

Intra-twin pair variation in birth weight is greater in monchorionic MZ twins than dichorionic MZ twins for several reasons. The first reason is that, in monchorionic MZ twins, where each twin's cord is inserted affects what proportion of the placenta is allocated for that twin. The monchorionic MZ twin whose umbilical cord is located more centrally receives more than his or her fair share of the placental resources. The second reason is that 80% of monochorionic placentas have inter-fetal vascular connections that allow blood to be shunted from one twin to another (Machin, 2001). These anastomoses mean that one twin may 'steal' the other twin's blood (see section 3.3). A third reason is that during twinning, the splitting of the inner cell mass may be unequal, with fewer founder cells in the smaller twin (Nance, 1990).

Studies of children who were born at term but were small for gestational age (SGA, birthweights of less than 2500 grams for full term babies) show that, although such children typically have IQs that fall in the normal range, they tend to have lower IQs than normal birth weight (NBW, birthweights of 2500 grams or more) full-term children (Hay, Catz, Grave, & Yaffe, 1997). In particular, SGA full-term children are at greater risk for language and learning disorders that first manifest themselves during the elementary school years (Low et al., 1992; Walther, 1988). Breslau and colleagues (1996; 2000) have compared the linguistic skills of NBW and SGA full-term children. Multivariate regression analyzes revealed a significant positive relationship between birthweight and performance on a variety of linguistic tasks, and this relationship held even at birthweights above 3000 grams. Given the relationship between birth weight and linguistic performance and the large birth weight discrepancies found in some MZ twins, it is not surprising that some MZ twins are linguistically discordant.

3.3 Placental vascular anastomoses

Eighty percent of monochorionic MZ twins have placental vascular anastomoses, and approximately 15% of monochorionic MZ twins suffer from clinically significant twin-twin transfusion syndrome in which one twin acts as the donor and the other acts as the recipient of fetal blood (Machin, 2001). In twin-twin transfusion syndrome, donor and recipient twin suffer different complications, but the overall mortality rates are similar for donor and recipient (Dube et al., 2002; Hatkar & Bhide, 1999; Sherer, 2001). Donor twins suffer from anemia which can lead to fetal growth restriction, cellular malnutrition and hypoxic/ischemic injuries (particularly of the brain), whereas recipient twins suffer from polycythemia (too many red blood cells) which can result in sluggish blood flow which increases the chance of thrombotic injuries (particularly of the brain) and hyperbilirubinemia (from the breakdown of excess red blood cells). Diminished blood flow to the donor twin can further increase the risk of hypoxic/anoxic injuries, whereas the increased blood flow to the recipient twin can result in congestive heart failure that secondarily can cause neural injuries.

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[4] Alternatively, Bryan (1993) suggests that the lower birth weight of MZ twins could reflect the positive effect of antigenic differences between DZ cotwins on intrauterine growth or the fact that mothers of DZ twins tend to be taller and heavier than MZ twins (MacGillivray, 1986).

[5] Normally, blood vessels run from the placenta to the fetus via the umbilical cord. In velamentous insertion, the vessels travel across the amniotic membranes before they come together into the umbilical cord.

3.4 Amniotic factors

Diamniotic twins may have different perinatal experiences by virtue of the fact that the cotwins do not share an amniotic sac. Thus, amniotic differences could account for some of the discordance in the 99% of MZ twin pairs who are dichorionic. When twins have separate amniotic sacs, one member of the twin pair can have too little amniotic fluid, which is associated with fetal deformities (Hatkar & Bhide, 1999; Luke & Keith, 1990; MacGillivray, 1986; Machin, 2001; Sherer, 2001). In twin-twin transfusion syndrome, for example, the donor twin will typically have too little amniotic fluid and the recipient twin will have too much amniotic fluid (which can cause uterine irritability and preterm labor). Twins who share an amniotic sac have exactly the same exposure to toxins and infections, whereas twins with separate amniotic sacs may have different exposures to toxins and inflections (e.g., Arai et al., 2002). Because intrauterine infection is a major risk factor for developmental disorders (O'Shea & Dammann, 2000; O'Shea, Klinepeter, Meis, & Dillard, 1998; Wilson-Costello et al., 1998), this could account for some of the neurodevelopmental discordance in MZ twins.

3.5 Intrapartum complications

Complications are more common in twin deliveries than in singleton deliveries, and, for both MZ and DZ twins, the second born twin is at greater risk for neurodevelopmental disabilities such as cerebral palsy (Bryan, 1993). Vaginal deliveries are most straightforward when the head of the baby is facing the birth canal (vertex presentation). Between one quarter to one third of all twin gestations are non-vertex at the time of delivery as compared to less than 5% of singletons (Chervenak, Johnson, Youch, Hobbins, & Berkowitz, 1985; Piekarski, Czajkowski, Maj, & Milewczyk, 1996). Perinatal morbidity and mortality rates are higher with non-vertex deliveries than vertex deliveries (Cetrolo, 1986; Chervenak et al., 1985; Piekarski et al., 1996). Non-vertex presentation is a risk factor for neurodevelopmental disorders such as cerebral palsy (Bryan, 1993), but some researchers have suggested that fetuses with neurodevelopmental abnormalities are unable to turn in the womb, and hence breech presentation is merely a marker for these abnormalities (Kuban & Leviton, 1994). It is not clear whether the incidence of nonvertex presentation is higher in MZ twins than DZ twins.

With velamentous umbilical cord insertion, fetal vessels can tear when the amniotic membranes rupture or they can be compressed during labor (Benirschke & Kim, 1973). Because velamentous insertion occurs more commonly in MZ gestations than in DZ gestations than in singleton gestations (Loos et al., 2001), vasa previa and exanguination are more frequent complications in delivery of MZ than DZ than singleton pregnancies. If the umbilical cord enters the birth canal before the baby (umbilical cord prolapse), the cord is compressed, and blood flow to the baby is diminished, which can result in hypoxic/ischemic brain injuries. Because of the increased incidence of non-vertex presentation, rupture of the membranes of one twin before that twin's presenting part has entered the pelvis, and the presence of two umbilical cords, umbilical cord prolapse is more common in twin pregnancies than in singleton pregnancies. In addition, compared to dichorionic twins (which may be DZ or MZ), monochorionic twins (i.e., MZ twins) are at greater risk for hypotensive events, particularly during the delivery of the second twin. The reason is that, during the delivery of the first monochorionic twin, the blood in the second twin may drain into the first twin. In effect, the second twin exanguinates. The resulting hypotension can cause an extreme anoxic and acidotic environment. Lastly, compared to diamniotic twins (which are more likely to be DZ than MZ), monoamniotic twins (which are always MZ) are at greater risk of fetal interlocking, umbilical cord entanglement, and, after the membrane ruptures, cord prolapse and compression.

3.6 Premature birth

According to older studies, the rate of preterm birth (delivery prior to 37 weeks gestation) is approximately 30% for twin gestations and about 8% for singleton gestations (MacGillivray, Campbell, & Thompson, 1988). However, the rate of premature delivery is increasing particularly for twins, and in the late 1990s in the United States, 11% of singletons and 55% of twin were born prematurely (Center for Disease Control, 1999; Guyer et al., 1999; MacDorman & Atkinson, 1999). Monochorionic twins are

born very preterm (before 32 weeks gestation) twice as often as dichorinoic twins (Sebire, Snijders, Jighers, Sepulveda, & Nicolaides, 1997) and male MZ twins are more likely to be premature than female MZ twins, whereas there doesn't appear to be male/female differences for same-sex DZ twins (Bryan, 1993).

A large body of research has documented that, as a group, children who are born prematurely reach speech and language developmental milestones later, perform more poorly on a wide range of speech and language tests, and are more likely to be diagnosed with speech and language disorders than their full-term peers (Barlow & Lewandowski, 2000; Bowen et al., 1993; Briscoe, Gathercole, & Marlow, 1998, 2001; Fawer, Bsenier, Forcada, Buclin, & Calame, 1995; Goldstein, Waldrep, VanPelt, & O'Shea, 2000; Grunau, Kearney, & Whitfield, 1985; Hack et al., 1991; Hack et al., 1994; Halsey, Collin, & Anderson, 1996; Herrgard, Luoma, Tuppurainen, Karjalainen, & Martikainen, 1993; Hindmarsh, O'Callaghan, Mohay, & Rogers, 2000; Jennische & Sedin, 1999; Koeppen-Schomerus, Eley, Wolke, Gringras, & Plomin, 2000; Kok, Lya den Ouden, Verloove-Vanhorick, & Brand, 1998; Luoma, Herrgard, Martikainen, & Ahonen, 1998; Menyuk, Liebergott, Schultz, Chesnick, & Ferrier, 1991; Ornstein, Ohlsson, Edmonds, & Asztalos, 1991; Saigal, Hoult, Streiner, Stoskopf, & Rosenbaum, 2000; Stevenson, Roach, Leavitt, Miller, & Chapman, 1988; Taylor, Hack, Klein, & Schatschneider, 1995; H. G. Taylor, N. Klein, N. M. Minich, & M. Hack, 2000a; H. G. Taylor, N. M. Klein, N. M. Minich, & M. Hack, 2000b; Teplin, Burchinal, Johnson-Martin, & et al., 1991; Vohr & Msall, 1997; Whitfield, Grunau, & Holsti, 1997; Wolke & Meyer, 1999). These studies reveal that the more premature the child, the greater the risk of language impairment or delay, but even children born between 32 and 36 weeks gestation do more poorly than children born full term (Hediger, Overpeck, Ruan, & Troendle, 2002; Huddy, Johnson, & Hope, 2001). The fact that MZ twins tend to be born at lower gestational ages than DZ twins means that the linguistic risks associated with premature birth are likely to affect MZ twins than DZ twins.

3.6 Hyperbilirubinemia

While in utero, the maternal liver can clear toxins from a fetus's blood. Once a baby is born, however, the baby's liver must take over this function. Of particular concern is excess unconjugated bilirubin, which causes neonatal jaundice and, in severe cases, can lead to bilirubin encephalopathy (kernicterus) in which cerebral grey matter is destroyed. In the acute phase, symptoms include stupor (excessive sleepiness) and hypotonia, which is followed a few days later by hypertonia (rigidity and spasticity), and seizures (Volpe, 1995). Neonates who survive usually have major neurological impairments including mental retardation, athetoid cerebral palsy, and sensorineural hearing loss (for a review, see Dennery, Seidman, & Stevenson, 2001). Even transiently high levels are neurotoxic, and low levels (10 mg) of unconjugated bilirubin can be neurotoxic in certain situations. The neurotoxicity of bilirubin depends on factors such as prematurity (the blood brain barrier is more permeable in premature infants), albumin levels which are often lower in premature infants (albumin binds or conjugates bilirubin), anoxia which increases blood/brain barrier permeability, and infection (which leads to an acidotic state which impairs bilirubin conjugation, Watchko & Claasen, 1994).

As reviewed above, twins are more likely than singletons to be born prematurely, low birth weight, anoxic and polycythemic and, for each of these factors, MZ twins are at greater risk than DZ twins. Not only are MZ more likely to be hyperbilirubinemic than DZ twins, but MZ cotwins are more likely than DZ cotwins to be discrepant for the billirubin levels. Among the reasons for this are 1) MZ cotwins birth weights are more likely to be different; 2) it is more likely that only one MZ twin will experience chronic or transient ischemic injuries; and 3) it is more likely that only one MZ twin will be polycythemic,

3.7 Excess perinatal glucocorticosteroids

Glucocorticosteroids (GCs) affect neural migration, differentiation, myelination, and axon and dendritic growth and pruning (Gould, 1994; Gould, Woolley, & McEwen, 1991). The developing nervous system is particularly vulnerable to the effects of excess GCs, and these effects are dose- and time-dependent (Adams, Ment, & Vohr, 2001; Matthews, 2000). Many studies have investigated the

effects of excess GCS and the consensus is that the effects of excess GCs depend on size of dose (higher or repeated doses are worse), the age of the animal at the time of administration (earlier exposure is generally worse), the species tested (animals that give birth to immature young are typically more affected), and whether the GC was natural or synthetic (synthetic GCs are worse, Baud et al., 1999; Rayburn, Christensen, & Gonzalez, 1997; Whitelaw & Thoresen, 2000). Excess GC exposure also adversely affects the developing nervous system's ability to recover from neuronal insults (Prodanov et al., 1998; Tsubota et al., 1999). Animal studies have revealed that the developing hippocampus is particularly sensitive to GC-exposure (DeKloet, Vreugdenhil, Oitzl, & Joels, 1998; Takahashi, 1998; Uno et al., 1994; Weinstock, 1997). In addition to having obvious structural effects on animals' brains, excess perinatal GCs adversely affect animals' behavior (Golub, 1982; Gramsbergen & Mulder, 1998; Kamphuis, Croiset, Bakker, Wiegant, & van Bel, 2000; Lupien & McEwen, 1997; Neal & al, 2000).

Women who seem likely to deliver prematurely are often given one or more courses of GCs because prenatal GCs hasten fetal lung maturation and lessen the risk of neonatal respiratory distress syndrome (Liggins & Howie, 1972). Some recent studies have found that multiple courses of prenatal GCs are associated with greater maternal and infant morbidity and mortality than a single course of prenatal GCs (Abbasi et al., 2000; Agustines et al., 2000; Banks et al., 1999; Bernstein, Horbar, Badger, Ohlsson, & Golan, 2000; Bhandari & Brodsky, 1999; Bos et al., 1998; Crowley, 2000; del Moral & et al., 2000; Doyle et al., 2000; French & et al., 1998; French, Hagan, Evans, Godfrey, & Newnham, 1999; Hack & et al., 1998; Kay, Bird, Coe, & Dudley, 2000; Klinger & Koren, 2000; Leung, Kenney, O'Riordan, & Miller, 2000 May May May; Smith, Qureshi, & Chao, 2000; Vermillion, Soper, & Newman, 2000; Vohr et al., 2000). For example, in the only randomized controlled study of multiple versus single GCs, babies exposed to weekly prenatal GCs were 4 times more likely to have severe intraventricular hemorrhages than babies exposed to 1 course of GCs (p = .06, Guinn et al., 2001). Compared to preterm infants who did not receive GCs in the neonatal intensive care unit (NICU), preterm infants who did receive GCs have significantly smaller head circumferences and brain volume (Murphy et al., 2001; Stark et al., 2001), and are three times as likely to have cerebral palsy and twice as likely to have a major neurodevelopmental impairment (Barrington, 2001a, 2001b).

Twins are more likely than singletons to be exposed to perinatal GCs for several reasons. First, mothers carrying twins are more likely to threaten to deliver prematurely, and therefore, they are more likely to be given exogenous GCs to hasten fetal lung maturation. Second, twins are more likely to be born prematurely and/or small and, hence, they are more likely to receive GCs in the NICU to improve respiration. Third, twins are more likely to suffer intrauterine growth restriction (IUGR), and cortisol levels are higher in growth restricted fetuses (Goland, Conwell I.M, & Jozak, 1995; Goland et al., 1993). Because MZ twins tend to be born smaller and more premature than DZ twins, perinatal GCs may have a greater impact on MZ than DZ twins. Compare to DZ twin pairs, MZ twin pairs are more likely to be discordant for fetal growth restriction and, hence, discordant for perinatal GC-exposure.

4. Perinatal Risk Factors and Language Development

The special genetic and perinatal environmental factors associated with twinning result in 1) perinatal mortality rates in monochoronic twins being twice as high as in dichorionic twins (Machin, Bramforth, Innes, & Minichul, 1995) and 4 times as high as in singletons (Malinowski, 1997); 2) congenital malformations being more common in twins (particularly MZ twins) than singletons (Little & Bryan, 1988; Luke & Keith, 1990); 3) discordance for congenital malformations being more common in MZ twins than DZ twins (Luke & Keith, 1990); and 4) long-term neurodevelopmental disabilities being more common in twins than singletons, with certain neurodevelopmental disabilities (e.g., cerebral palsy) being more common in MZ twins than DZ twins (Bryan, 1993). There are at least two reasons why children who experience perinatal hardships are more likely to exhibit language delays than children who don't experience these hardships. The first reason is that, because language is one of the most complicated tasks that children must master, children with subtle (but non-specific) neurodevelopmental dysfunction are likely to exhibit language delays. The second reason is that language may be particularly

vulnerable to the effects of these perinatal hardships. Because normal language function involves many different regions of the brain, damage to any of these regions could result in language disorders. This section reviews why these regions may be particularly vulnerable to the perinatal hardships described in section 3.

4.1 Hypoxic/ischemic injuries of prematurity and intrauterine growth restriction.

Even preterm children with normal cognitive function and no major neurodevelopmental disability are at least 2 to 3 times more likely to suffer from written and spoken language disorders than full-term children (e.g., Barlow & Lewandowski, 2000; Davis et al., 2001; Fawer et al., 1995; Halsey et al., 1996; Hediger et al., 2002; Huddy et al., 2001; Klein, Hack, & Breslau, 1989; Kopp & Kaler, 1989; Luoma et al., 1998; Nobel-Jamieson, Lukeman, Silverman, & Davies, 1982; Saigal et al., 2000; Taylor et al., 2000b; Whitfield et al., 1997). Similarly, even low-birth weight full term children who are apparently neurologically intact do worse on language tasks than normal birth weight children (Breslau et al., 1996; Breslau et al., 2000; Low et al., 1992; Walther, 1988). These findings suggest that the neural structures involved in language may be particularly vulnerable to factors associated with being born premature or low birth weight.

Periventricular leukomalacia (PVL) refers to necrosis of the white matter adjacent to the ventricles. PVL is the major form of brain injury that preterm infants suffer from, and is believed to be the underlying cause of most frank neurological disorders associated with prematurity (Perlman, 1998; Volpe, 2001b). PVL is associated with hypoxic/ischemic events, and the immaturity of the vascular system in premature infants is thought to be a major factor in the incidence of PVL. Penetrating branches of major cerebral vessels (such as the middle cerebral artery that feeds the auditory cortex and underlying white matter) have long branches that terminate in the deep periventricular white matter and short branches that terminate in the subcortical white matter. Until about 30 weeks gestation, the long penetrating vessels have few side branches and intraparenchymal anastomoses with short branches, which means that border zones in white matter extend beyond the periventricular regions. Because disruptions of cerebral white matter have profound affects on migration of neurons in the cortical plate, PVL in the white matter underlying the auditory cortex will result in abnormalities in gray matter in the auditory cortex.

Hypoxia/ischemia disrupts the reuptake of glutamate, and excess glutamate is associated with neuronal death (Perlman, 2001). Because glutamate receptors are more widely distributed in the fetal brain than the mature brain, transient hypoxia/ischemia may cause more widespread damage to the fetal and neonatal brain than the mature brain. Unlike in the mature brain, fetal basal ganglia, subthalamic nuclei and hippocampus have large numbers of glutamate receptors and thus are vulnerable to glutamate accumulation. The subthalamic nuclei are part of the auditory system, and the hippocampus has been has implicated in processing and memory of language (Brockway, 1999; Mackay, Stewart, & Burke, 1998). (For a general review of the neurobiological insults associated with prematurity, see Dammann & Leviton, 1999, 2000; Perlman, 1998; Perlman, 2001; Volpe, 2001a.; 2001b)

MRI studies of prematurely born children have revealed that unmyelinated white matter is the predominant brain tissue prior to 36 weeks gestation, and the rate of myelination increases dramatically between 35 and 41 weeks gestation (Huppi, Maier et al., 1998; Huppi, Warfield et al., 1998; Inder & Huppi, 2000). Myelination precedes in an orderly fashion beginning in the brain stem at 29 weeks and proceeding anteriorly and reaching the centrum semiovale by 42 weeks gestation. Myelination of the cerebral hemisphere white matter begins at the central sulcus and proceeds toward the poles with mature myelin appearing in the temporal poles by postnatal month 24 (Inder & Huppi, 2000). Oligodendroglia that are in the process of myelination are most vulnerable to injury (Perlman, 1998; Volpe, 2001b), and the relative late myelination of the temporal poles means that the brain regions that subserve language are in a vulnerable state for an extended period.

A recent volumetric MRI study of 8 year olds showed that children born before 34 weeks gestation (mean gestational age = 29 weeks, mean birth weight = 997 grams) had significantly larger ventricular volumes and significantly smaller cortical volumes (particularly in the sensorimotor, premotor

and midtemporal cortices) and smaller basal ganglia, amygdala, hippocampus, and cerebellar volumes than full-term children (Peterson et al., 2000). Sensorimotor and midtemporal cortical volumes (i.e., cortical regions that include auditory cortex) were positively associated with full scale, performance, and verbal IQs in the preterm children (Peterson et al., 2000).

4.2 Intrapartum complications

With the types of intrapartum complications discussed in section 3.5, the main worry is that the neonate will become hypoxic during labor and delivery. Thus, these intrapartum complications may selectively put babies at risk for language delays for the same reasons that intrauterine hypoxia during the third trimester may increase the risk of language problems (see section 4.1). Fetal hypoxia around the time of delivery is believed to play a role in some cases of otherwise unexplained hearing loss. Hypoxia or anoxia has been shown in experimental animals to produce lesions of the auditory pathways of the central nervous system and may also produce cochlear damage.

4.3 Hyperbilirubinemia

Although hyperbilirubinemia can affect any part of the central nervous system, the auditory pathways are particularly sensitive to the effects of bilirubin (Shapiro, 2002; Spencer, Shaia, Gleason, Sismanis, & Shapiro, 2002), and sensorineural hearing loss and auditory dysfunction are the most comman major sequelae of neonatal hyperbilirubinemia (Amin et al., 2001; Hack et al., 2000). Recent studies suggest that children with even minimal hearing losses (hearing thresholds of between 16 and 25 dBs) are more likely to suffer from language delays and impairment as compared to children with normal hearing (Bess, 1999; Finitzo-Hiever, 1981; Gravel, Wallace, & Ruben, 1996; Loutonen, Uhari, & Aitola, 1996; Yoshinaga-Itano, Sedey, Coulter, & Mehl, 1998).

4.4 Excess glucocorticosteroids

Endogenous and exogenous GCs preferentially affect several brain regions involved in language. As discussed in section 3.7, the hippocampus is particularly vulnerable to the effects of endogenous and exogenous GCs. Although not traditionally considered language areas, the hippocampus has been implicated in higher cognitive function and memory in animals, normal human language processing (Brockway, 1999) and injuries to the hippocampus (Brockway, 1999; DeLong, 1992; Mackay et al., 1998) and are associated with language disorders (Beggs et al., 1999; DeKloet et al., 1998). Results of animal studies indicate that perinatal GCs also preferentially affect the developing cerebellum (Ferguson & Holson, 1999; Gramsbergen & Mulder, 1998; Howard, 1968). Again, although the cerebellum is not a language area per se, the cerebellum has been implicated in language and language disorders (Courchesne, 1991; Leiner, Leiner, & Dow, 1993; Levinson, 1988; Wang, Hesselink, Jernigan, Doherty, & Bellugi, 1992), and preterm children have smaller cerebellums than full-term children (Allin et al., 2001). Although follow-up studies have generally found few, if any, significant difference in the linguistic abilities and development of children who were exposed to one versus no courses of prenatal GCs ((Collaborative Group on Antenatal Steroid Therapy, 1984; Dessens, Haas, & Koppe, 2000; MacArthur, Howie, Dezoete, & Elkins, 1981, 1982)), Stromswold and colleagues (2003) recently reported that babies exposed to multiple courses of prenatal GCs have worse language outcomes than babies exposed to only a single course of prenatal GCs, and that the deleterious effect of multiple courses of GCs affects language development more than other aspects of development (e.g., gross motor, fine motor, social or cognitive development).

4.5 Third trimester acoustical environments

By 23 to 25 weeks gestation, the cochlea is connected to the brainstem and is sufficiently mature for loud noise to produce physiological responses such as changes in human fetal heart rate, blood pressure, oxygenation and movement (Lecanuet, 1998). Thus, from 24 to 40 weeks gestation, full-term babies receive auditory stimulation but not visual stimulation. Because their mother's body selectively absorbs and attenuates frequencies above 250 Hz (Lecanuet, 1998), while in the womb, fetuses are

preferentially exposed to low frequencies that correspond to prosodic aspects of language, and only after birth are they exposed to high frequencies used to convey phonemic, lexical and syntactic information. Preterm twins don't have as much opportunity for this type of phased learning.

Many studies have shown that environmental deprivation during critical postnatal periods adversely affects auditory structure and function in animals and humans, and human language does not develop normally without adequate linguistic input during sensitive periods. For example, Chang and Merzenich (2003) recently demonstrated that rats exposed to 70 dB white noise from postnatal day 7 have less well-organized primary auditory cortex than rats reared in normal auditory environments. Some studies have demonstrated *negative* effects of early sensory enrichment. For example, quails that receive visual stimulation prior to hatching fail to respond appropriately to maternal visual cues, continue to respond to maternal auditory cues into later stages of postnatal development and fail to learn prenatally their mother's unique call (Lickliter, 1990; Sleigh & Lickliter, 1995). Sleigh and Lickliter (1995) conclude that "stimulation beyond the range of the species norm can result in intersensory interference." Although no animal or human studies have shown detrimental effects of enrichment within a sensory domain, work in computational neuroscience suggests that artificial neural systems develop in a more organized and efficient manner if learning is done in phases with each phase devoted to a different aspect of the learning task. For example, Christiansen and Dale (2001) have found that training simple recurrent networks on input filtered in such as way as to simulate the auditory experience of fetuses in the womb enhances the networks' later ability to perform syntactic tasks.

In addition to the possible detrimental effects of hearing high frequency speech sounds prematurely**,** preterm twins often spend many weeks in neonatal intensive care units (NICUs), where they are exposed to loud, unpredictable, high frequency sounds such as NICU alarms and predictable (rhythmic) high and low frequency sounds (e.g., the click of IV pumps, whosh of ventilators) that are *not* language. Background noise levels in modern NICUs range from 60 to 90 dB(A) with maximal sound levels of up to 120 dB(A) (American Academy of Pediatrics Committee on Environmental Health, 1997; Benini, Magnavita, Lago, Arslan, & Pisan, 1996; Chang, Lin, & Lin, 2001; Chen & Chang, 2001; Graven, 1997, 2000; Guimaraes et al., 1996; Magnavita, Arslan, & Benini, 1994; Nzama, Nolte, & Dorfling, 1995; Philbin, 2000; Philbin, Ballweg, & Gray, 1994; Philbin, Robertson, & Hall 3rd, 1999). In his review of NICU environments, Graven (2000) recommends that nurseries maintain an hourly Leq of 50 dB(A), an hourly L10 of 55 dB(A) and a 1-second Lmax of 70 dB(A), levels that are regularly exceeded within NICU incubators (American Academy of Pediatrics Committee on Environmental Health, 1997; Chang et al., 2001). There is growing concern about the possible adverse effects of NICU noise. The American Academy of Pediatrics Committee on Environmental Health (1997) concluded that exposure to excessive noise in the womb and the NICU could result in hearing loss and poor growth, and the Study Group on NICU Sound (Graven, 2000) has recommended that chronic and transient sound levels in the NICU be reduced and that infants not be given supplementary auditory stimulation in the womb or the NICU. (For further discussion of the effects of NICU noise on language, see Stromswold & Sheffield, 2004.)

5. Postnatal Environmental Differences and Language Development

5.1 Linguistic input of twins

Postnatally, because twins have a sibling of the same age, twins usually receive less adult linguistic input than singletons (Reznick, 1997; Stafford, 1987; Tomasello, Mannle, & Kruger, 1986), and mothers of twins engage their twins in fewer verbal exchanges than mothers of singletons (Conway et al., 1980; Lytton, Conway, & Suave, 1977). Studying typically-developing twins, Conway et al. (1980) found that differences in complexity and frequency of maternal speech accounted for more of the variance in twins' language development than differences in Apgar scores, gestational age, or weight at birth.

5.2 Linguistic input and zygosity

If MZ twin pairs have more similar linguistic environments than DZ twin pairs (e.g. because people

treat twins who look alike more similarly than twins who do not look alike, etc.), then heritability estimates of language will be inflated. Heritability estimates will be further accentuated if people treat MZ twins more similarly than DZ twins and there are gene-environment interactions. It does not appear, however, that, from a linguistic standpoint, people treat MZ twins more similarly than DZ twins. For example, the linguistic performance of MZ twin pairs whose parents incorrectly thought they were DZ is no less similar than correctly-classified MZ twins, and the linguistic performance of DZ twin pairs whose parents thought they were MZ is no more similar than correctly-classified DZ twins (Munsinger & Douglass 2nd, 1976). For twins that are reared apart, MZ-DZ differences cannot be the result of MZ twins being treated more similarly than DZ twins. Thus, one can investigate the role of postnatal factors on language by comparing heritability estimates obtained for twins reared together and twins reared apart. The one study that has compared the linguistic abilities of twins reared together and twins reared apart (Pedersen, Plomin, & McClearn, 1994) obtained very similar results for vocabulary as studies of twins reared together (Stromswold, 2001), suggesting that postnatal factors do not play a major role in normal twins' linguistic abilities.

Because the rate of DZ twinning increases with maternal age and the rate of MZ twinning does not, DZ twins will have older mothers than MZ twins. This difference will also mean that, on average, DZ twins are also likely to have more, older siblings than MZ twins. Most studies have shown that first-born children acquire language somewhat more rapidly than later born children, presumably because they are receive more attention and linguistic input from their parents. To the extent that results from non-twin siblings can be generalized to twins, this may mean that MZ twins, on average, will receive more linguistic input than DZ twins. However, it would not lead one to expect within twin pair differences in linguistic input.

5.3 Intra-twin pair variability in linguistic input

If mothers prefer one twin to another, they may provide more or better linguistic input to the preferred twin. Minde and colleagues (1990) reported that the majority of the mothers in their study of premature twins admitted to preferring one twin within 2 weeks after birth. In general, mothers preferred the healthier, heavier infant, and this preference was stable for at least 4 years (Minde et al., 1990). However, maternal preference for the healthier child was not found in a recent longitudinal study that investigated the relationship between maternal expressed emotions and antisocial behaviors in monozygotic twins (Caspi et al., 2004). As part of this study, researchers asked mothers of over 550 MZ twin pairs to describe their twins. Although twin's illness affected mothers' feelings for their twins, some mothers were more positive and some were less positive about the sicker twin (Caspi et al., 2004).

Due to the perinatal factors reviewed in section 3, not only are MZ twins be born somewhat sicker and smaller than DZ twins, there is more likely to be intra-twin pair discrepancies in the neonatal health and size of MZ twins than DZ twins. The greater discrepancies for MZ twin pairs could result in mothers of MZ twins treating their twins more differently from one another than mothers of DZ twins treat their twins. Unfortunately, if there is no systematic relationship between a twin's health and the mother's feeling for that twin, it will not be simple to predict or investigate how postnatal maternal treatment affects language development. However, we can say that differences in how mothers feel about their each of their twins could result in discordance in MZ twins.

6. Interactions Among Genetic and Environmental Factors

In discussing the role of gene-environment interactions, it is crucial that we distinguish between environmental factors that are predominantly psychosocial (e.g., quality and quantity of social or linguistic interactions with adults) and those that are more likely to have direct effects on neural structures (e.g., prenatal or postnatal malnutrition, brain injuries, or exposure to neurotoxins such as billirubin or lead). It is also important to distinguish between early and late environmental factors because early environmental factors are likely to have larger effects on brain structures, and prenatal environmental

factors are much more to be predominantly biological, whereas postnatal environmental factors may be either psychosocial or biological.

6.1 Genetic-prenatal interactions

Perinatal factors could either accentuate or obscure the effects of heritable factors. In an intriguing study, Koeppen-Schomerus et al. (2000) found that, whereas genetic factors played a significant role in the verbal and nonverbal development of moderately preterm and full-term twins, for twins born very preterm, shared environmental factors completely overshadowed the effects of genetics. Koeppen-Schomerus et al.'s (2000) findings are fairly consistent with results obtained from 400 set of twins who had participated in our Perinatal Risk Factor Study as of December 2003. Preliminary analyses of these data indicate that heritable factors play a greater role in the linguistic and non-linguistic development of twins born full-term than twins born pre-term, and that heritable factors account for more of the variance for normal birth weight twins than low birth weight twins {Stromswold, 2003 #4011}. When we divide the twin pairs into two groups based on whether or not at least one twin suffered a perinatal brain injury, for most of our developmental outcome measures, heritable factors account for a significant amount of the variance in developmental outcome for the non-brain injured twin pairs, but not for the brain-injured twin pairs {Stromswold, 2003 #4011}. (For a description of the Perinatal Risk Factor Study, see http://ruccs.rutgers.edu/~karin/PERINATAL/language_perinatal.htm.)

Prenatal factors might affect twins differentially according to their genetic make up. A relatively minor ischemic injury to brain areas involved in language or a mild sensorineural hearing loss might have devastating effects on a twin genetically at risk for language impairments, yet have no discernible adverse affect on a twin who is not genetically at risk. Consider possible effects of the Factor V Leiden (FVL) mutation. FVL is an autosomal (co)dominant thrombophilic (clot-promoting) disorder that results from a point mutation in the factor V gene leading to a replacement of Arg506 with Gln. Epidemiological studies reveal that 5-10% of people of European descent have one copy of the FVL allele, and such people have a 7 to 10 fold increased risk of having an adverse venous clotting event (Agorastos et al., 2002; Alonso et al., 2002; Arias, Romero, Joist, & Kraus, 1998; Arkel & Ku, 2001; Blumenfeld & Brenner, 1999; Brenner & Kupferminc, 2003; De Stefano, Rossi, Paciaroni, & Leone, 2002; Gibson, MacLennan, Goldwater, & Dekker, 2003; Grandone, Margaglione, Colaizzo, Pavone, & Paladini, 2002; Hallak et al., 1997; Hankey et al., 2001; Lynch, Nelson, Curry, & Grether, 2001; Madonna et al., 2002; Many et al., 2002; Martinelli et al., 2001; Mercuri et al., 2001; Verspyck et al., 2002). Between 1 in a thousand and 1 in five thousand people have two copies of the FVL gene, and this is associated with a 70 to 100 fold increased risk of an adverse clotting event. Because FVL is a dominant disorder, a child can have the clotting disorder (inherited from her father), even if her mother is unaffected. Such a child is at increased risk for perinatal stroke (Barreirinho et al., 2003; Lynch et al., 2001), and that risk is elevated even further in perinatal environmental factors that are associated with in anoxic or thrombotic brain injuries (Barreirinho et al., 2003). Not only is such as child more likely to suffer a perinatal stroke in situations where a non-FVL child would not, her functional outcome is likely to be worse (Mercuri et al., 2001).

Although MZ twins have the same FVL allelic status, to the extent that the perinatal environments of MZ twins are different (due to twin-twin transfusion, differences in cord insertion etc.), one could have a stroke and the other one not. In addition, even if both MZ twins suffered strokes, the locations of the infarcts are likely to be different for the two twins, resulting in different phenotypes. If a mother has FVL, her children are biologically at risk even if they do not carry the mutation themselves. The reason is that women who have clotting disorders are more likely to suffer pregnancy complications such as placental infarctions, placental insufficiency, placental abruptions, preeclampsia (pregnancy-induced hypertension), the HELLP syndrome (hemolysis, elevated liver function and low platelets), premature delivery, and intrauterine growth restriction. MZ twins could be affected asymmetrically if only one of the placentas (or only part of a shared placenta) was infarcted or abrupted. Serious maternal/fetal interactions are possible if both mother and child have the FVL allele.

6.2 Genetic-postnatal interactions

Postnatal environmental factors may have different effects on different people depending on their genetic makeup. Although within a fairly wide range, linguistic environment appears to have relatively minor effects on normal children's language acquisition (e.g. Heath, 1983), children who are genetically at risk for developing language disorders may be particularly sensitive to subtly impoverished linguistic environments. Because genetically at-risk children are likely to have relatives who are language impaired, they are likely to be reared in linguistically impoverished environments. Children who are linguistically less adept (for genetic and/or environment reasons) may respond less to linguistic input. Their parents may unconsciously respond by providing less (or less complex) linguistic input, which could negatively impact children's rate of language acquisition. Less linguistically-adept children might unconsciously avoid linguistically challenging situations, preferentially choosing activities and friends that make less linguistic demands of them, thereby further impeding their linguistic development.

As discussed in section 5.1, twins receive less adult linguistic input than singletons. Therefore, if there are synergistic interactions between genetic and postnatal environmental factors, we would predict that twins would be more likely to be language-impaired than singletons with the same genetic makeup. Consistent with this prediction, the rate of positive family history for language impairment is somewhat lower for twin SLI probands than for singleton SLI probands (22% versus 32%, respectively, see Bishop, 1992). At the other end of the scale, if there are synergistic interactions between genetic and postnatal environmental factors, people who have the genetic propensity to succeed at language might benefit more from enriched environments (and better tolerate impoverished environments). Because genetically well-endowed children are more likely to have relatives who are linguistically able, they are likely to be reared in linguistically enriched environments. In addition, genetically well-endowed children might seek out environments that are linguistically challenging.

Genetic-postnatal environmental interactions do not necessarily have to involve psycho-social environmental factors. Children who are genetically at risk for language impairments may be more susceptible to the ill effects of malnutrition, environmental toxin, or postnatal head injury, whereas children who are not genetically at risk may be more resilient to the effects of such insults. Returning to the example of genetic thrombophilic disorders, we can see how genetic factors could interact with postnatal factors. Recent studies have suggested that children with genetic thrombophilic disorders are more likely to suffer a stroke after a minor head injury (Kieslich, Fiedler, Heller, Kreuz, & Jacobi, 2002) and recover less well from strokes (Mercuri et al., 2001) than children who are not thrombophilic. Given this, even a relatively minor head injury or stroke in one thrombophilic MZ twin could result in phenotypic discordance in MZ twin pairs.

6.3 Prenatal-postnatal environmental interactions

Prenatal and postnatal environmental factors may be correlated (e.g., prenatal and postnatal malnutrition in poor families) or interact with one other. For example, children with mild hearing losses (which can be the result of perinatal hardships) may be more susceptible to the effects of slightly impoverished linguistic input. Nelson & Soli (2000) have argued that the language delays seen in children with mild hearing losses are the result of reduced opportunities to communicate in noisy environments, and that if the signal-to-noise ratio could be improved in such settings, the children's language would develop at a normal rate. Studies that have followed preterm children longitudinally generally find that the discrepancy in performance between full-term and preterm children becomes more apparent as children get older (e.g., Botting, Powls, Cooke, & Marlow, 1998; Saigal et al., 2000; Taylor et al., 2000a). One interpretation of this finding is that prenatal and postnatal environmental factors interact.

7. Future Directions: Teasing Apart the Role of Genetic and Environmental Factors

7.1 Molecular genetic studies

One way to study the role of genetic and epigenetic factors on language development is to perform fine-grained molecular genetic analyses to determine whether linguistically discordant MZ twins differ more genetically (e.g., in terms of frequency of spontaneous mutations) or epigenetically (e.g., in terms of methylation patterns) than linguistically concordant MZ twin pairs. This type of molecular genetic study of MZ twins is beginning to bear fruit in the study of other diseases that are believed to have multi-factorial polygenic origins (e.g., schizophrenia, Petronis et al., 2003).

One could also perform linkage analyses of linguistically-concordant and discordant DZ twins (and their first degree relatives). Although DZ twins are no more genetically similar than full siblings, there are clear advantages of performing linkage analyses on twins as opposed to non-twin siblings. First, the environments of DZ twins are almost certainly more similar than the environments of nontwin siblings. Thus, phenotypic differences between DZ twins are less likely to reflect environmental factors than are phenotypic differences between non-twin siblings. Second, because DZ twins are the same age, one can use the same tests and measures to evaluate their linguistic function, thus eliminating a huge source of noise in linkage studies. Third, because MZ twins are the same age, one does not have to worry about the possibility that the language-disordered genotype may be expressed phenotypically in different ways at different ages (e.g., that a toddler might not speak at all, that a preschooler might selectively leave out grammatical markers, that a school age child might have difficulty learning to read, and that an adult while not clinically impaired, nonetheless avoids linguistically-taxing social or professional settings). Eliminating this phenotypic problem greatly reduces a source of noise and uncertainty in linkage analyses.

7.2 Genetic load in concordant and discordant MZ twins

Perhaps for multifactorial disorders such as language impairments, MZ twins that are concordant for a disorder have a higher genetic load than MZ twins that are not discordant. This possibility can be explored empirically by comparing the family histories of MZ twins where both twins are impaired, one twin is impaired, and where neither twin is impaired. If the genetic load hypothesis is correct, concordant language-impaired MZ twins should have higher rates of family history of language impairment and a higher percentage of impaired relatives than discordant MZ twins who, in turn, should have higher rates than MZ twins where neither twin is impaired. However, as is the case with family aggregation studies, it is possible that what appears to be the result of having a higher genetic load for language impairment is actually the result of having a higher environmental load for language impairment (the Deviant Linguistic Environment Hypothesis, DLEH). Put another way, it could be that the reason both MZ twins are language impaired is because they have received more impoverished or deviant linguistic input from their language impaired relatives, not because they received more of the wrong genes from these relatives. (For a discussion of the DLEH, see Stromswold, 1998.)

7.3 Language disorders in offspring of concordant and nonconcordant MZ pairs

Recall that heritability is the proportion of the variance that is due to genetic factors. We can distinguish between broad-sense heritability and narrow-sense heritability. Broad-sense heritability refers to the variance accounted for by all genetic factors, whereas narrow-sense heritability is the variance accounted for by additive genetic factors. Broad-sense heritability includes the influence of gene dominance, epistasis (interactions between genes) and interactions between genes and environment, whereas narrow-sense heritability estimates the amount of genetic influence that is likely to be passed on to offspring. One way of distinguishing between broad- and narrow-sense heritability is to study the offspring of discordant MZ twins. If an impaired MZ twin's disorder is purely due to environmental factors (either pre- or post-natal), then the offspring of the non-impaired cotwin should not have an increased risk of being language impaired (unless of course, the offspring spends considerable time with his language-impaired aunt or uncle). If the language-impaired and non-impaired MZ cotwins share a genetic predisposition for being language-impaired, but the non-impaired twin has not experienced the environmental insults that precipitate or contribute to being language disordered, then the non-impaired cotwin will transmit this genetic predisposition to his or her offspring, and these offspring will have

higher-than-normal rates of language impairment. Returning once again to the case of thrombophilic disorders, consider the case of a mother who has the FVL gene but does not transmit this gene to her MZ twins. As discussed in section 6.1, the pregnancy complications associated with FVL could affect one MZ twin but not the other. If we looked at the offspring of the affected and unaffected MZ twins, we would expect similar rates of impairment in both twins' offspring.

The strategy of looking at the affectedness rate among non-impaired MZ twins was first used to contrast broad-sense and narrow-sense heritability of schizophrenia (Fischer, 1971; Gottesman & Bertelsen, 1989). In these studies, Fischer (1971) and Gottesman and Bertelsen (1989) discovered that schizophrenic MZ cotwins' offspring and well cotwins' offspring were equally at risk for schizophrenia, suggesting that the discordance between MZ cotwins was largely due to differences in the cotwins' environments. Although offspring of discordant MZ twin studies do provide insights about whether a phenotype is the result of genetic or environmental factors, this type of study does not allow one to distinguish between the effects of differential prenatal and postnatal environments, nor does it allow one to distinguish between the effects of biological environmental factors (e.g., perinatal brain injuries) and social environmental factors (e.g., amount of linguistic input).

7.4 Birth weight discrepancies and linguistic development

Traditional methods of analyzing behavioral twin data do not distinguish between the effects of prenatal and postnatal environment. Because DZ twins share only 50% of their DNA, birth weight differences in DZ twin pairs reflect differences in the genetic endowment of twin pairs (one twin might be genetically predisposed to be bigger than his cotwin) and differences in the prenatal environment. In contrast, because MZ twins share 100% of their DNA, differences in MZ twin pairs' birth weights solely reflect differences in the cotwins' prenatal environments. By comparing MZ cotwins that have very similar birth weights with MZ cotwins that have very dissimilar birth weights,[6] we can obtain an estimate of the effect of intrauterine environment on later development. To the extent that, in childhood, MZ cotwins with very similar birth weights are linguistically more similar to one another than MZ cotwins with very different birth weights, this is a measure of the effect of intrauterine environment on language development. Estimates of the effect of intrauterine environment can be calculated using slight variants of methods traditionally used to calculated heritability estimates. However, instead of contrasting the linguistic similarity of MZ and DZ cotwins, we compare the linguistic similarity of MZ cotwins with similar and dissimilar birth weights. The effect of interactions between genetics and intrauterine environmental factors can be estimated by comparing how great an effect having very different birth weights has for MZ and DZ twins (in essence calculating a difference of a difference score).

Some birth weight discrepant MZ twin pairs remain discrepant postnatally, whereas others become more similar in size as they get older. One theory is that MZ twins who catch-up to their cotwin in weight were only malnourished in the latter part of the pregnancy after they had already acquired their full cellular complement, whereas MZ twins who remain smaller than their cotwins were malnourished throughout pregnancy (Bryan, 1993). If this is true, then one can investigate how early versus late fetal growth restriction affects linguistic development by comparing the linguistic similarity of MZ twins whose weights remain discrepant with the linguistic similarity of MZ twins whose weights equalize over time.

Factors that inhibit intrauterine growth early in pregnancy (e.g., viral infection that affects mitosis) cause symmetric growth-retardation, whereas factors that inhibit later intrauterine growth (e.g., uteroplacental insufficiency) cause asymmetrical growth retardation. A symmetrically growth-restricted neonate has a normal ponderal index[7] but is below the 10th percentile for gestational age in length,

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[6] It is an open question what degree of birth weight discrepancy should be used as the threshold for "similar" vs. "dissimilar" birth weights. Overall, 80% of twins have birth weights that differ by less than 15%. Subsequently, some researchers take birth weight differences of 15% or more as the threshold for intrauterine growth restriction, whereas other researchers prefer to use 20% as the threshold (Charlemaine et al., 2000).

[7] Ponderal index is weight/length^3.

weight, head and abdominal circumferences. In an asymmetrically growth retarded neonate, length and head circumference are relatively preserved, but weight is reduced (Hack, Breslau, Rivers, & Fanaroff, 1989; Hack et al., 1991). Hence, another way to compare the effects of early versus late prenatal growth restriction would be to compare height discrepant MZ twins (who presumably have different early prenatal experiences) versus weight discrepant MZ twins (whose prenatal experiences began to deviate later).

7.5 Perinatal brain injuries and linguistic disordance in MZ twins

The most consistent biologic predictors of poor later mental development and behavior in prematurely-born and intrauterine growth restricted children are hypoxic-ischemic brain injuries and subnormal brain growth (Berg, 1989; Harvey, Prince, Burton, Parkinson, & Campbell, 1982; Ounsted, Moar, & Scott, 1988; Parkinson, Wallis, & Harvey, 1981; Westwood, Kramer, Munz, Lovett, & Watters, 1983). Brain growth is typically spared in intrauterine growth restriction, and when this protective mechanism fails, neurodevelopmental outcome is adversely affected (Kramer, McLean, Olivier, Willis, & Usher, 1989). This is especially true when brain growth (head size) fails to catch up during infancy and childhood (Hack et al., 1989; Hack et al., 1991). Neonatologists and pediatricians routinely measure and record infants' head circumferences, and it is trivial to obtain this measurement on older children and adults. One could easily see if discrepancy in head circumference in MZ twins is associated with linguistic discordance. Because there are well-normed growth curves for head circumference, one could also use MZ twins to investigate whether MZ twins whose head circumferences are persistently discrepant are more likely to be linguistically discordant than twins whose head circumferences become more similar with time.

Neonatal neural ultrasounds are routinely obtained on neonates admitted to NICUs. Neural ultrasounds are used primarily to detect and determine the severity (on a 4 point scale) of intraventricular hemorrhages (IVHs). Although these scans do not allow for precise localization of injuries, they can be used to determine whether an IVH is on the left, right or bilateral sides the brain. One way of determining whether perinatal brain injuries account for linguistic (and nonlinguistic) discordance in MZ twins is the result of perinatal brain injuries is to determine whether MZ twin pairs whose neural ultrasounds are more discrepant are more likely to be linguistically discordant.

7.6 Intrapartum complications and linguistic discordance

Mothers seem to be very good at remembering whether or not they experienced complications during labor and delivery. For example, over 90% of the mothers of twins in our Perinatal Risk Factor Study were able to report whether each of their twins was breech, how long they were in labor, what drugs they received during labor, how much time passed between the delivery of the first twin and the second twin, whether forceps or vacuum extraction was used for each twin, and whether there were any cord complications {Stromswold, 2003 #4011}. These data could easily be used to test whether linguistically discordant MZ twins experience more obstetrical complications than linguistically concordant MZ twins, as has been done for MZ twins who are concordant and discordant for schizophrenia (McNeil et al., 1994).

7.7 Dermatoglyphic features and linguistic disordance

At first blush, suggesting that one study dermatolglyphic patters (fingerprints) to investigate anything as complex as language sounds akin to palm-reading and phrenology. However, given that researchers have a had fair degree of success using dermatoglyphic analyses to investigate the role of prenatal factors in the development of fetal alcohol syndrome (Wilber, Newell-Morris, & Streissguth, 1993) and sexual orientation (Hall & Kimura, 1994; Hall, 2000), it might not be as crazy as it sounds.

Dermatoglyphic patterns have polygenic inheritance, with individual genes contributing an additive genetic component (Babler, 1991a, 1991b; Chakraborty, 1991; Plato, Garruto, & Schaumann, 1991; Schaumann & Alter, 1976). Normally, dermatoglyphic patterns are extremely similar for MZ twin pairs (Bouchard, Lykken, McGue, Segal, & Tellegan, 1990; Nylander, 1971). For example, in one study, the

intra-pair MZ correlation coefficient for total finger ridge count was 0.96 (Bouchard et al., 1990). Although dermatoglyphic traits are largely the result of genetic factors (Babler, 1991a, 1991b), MZ twins may have very different fingerprints if MZ cotwins are exposed to different prenatal environments (Babler, 1991a; Bracha, Torrey, Gottesman, Bigelow, & Cunniff, 1992; Chakraborty, 1991). For example, intrauterine growth retardation tends to decrease ridge count, whereas fetal edema tends to increase ridge count (Babler, 1991a; Bracha et al., 1992; Chakraborty, 1991).

Because dermatoglyphic characteristics do not change after the second trimester, dermatoglyphic discordance among MZ twins is a marker for prenatal environmental differences. Dermatoglyphic traits develop between the 12th and 19th gestational weeks and, specifically, a-b ridges develop between the 15th and 17th gestational week (Babler, 1991a, 1991b), Hence, dermatoglyphic discordance in MZ twins can be used to pinpoint fairly precisely when MZ twins experienced different perinatal environments. If dermatoglyphic discordance in MZ twin pairs is associated with linguistic discordance in MZ twin pairs', this would suggest that second trimester prenatal environmental factors are (in part) responsible for the twins' discordance. One might even argue that the degree of correlation between dermatoglyphic and linguistic similarity in MZ cotwins could be taken as a rough measure of the extent to which second trimester *in utero* factors affect language development. By studying MZ dermatoglyphic discrepancies, coupled with MZ birth weight, ponderal index, and head circumference discrepancies, we may gain fresh insights into how intrauterine hardships at different points in gestation affect the development of the neural substrates of language and how the developing brain recovers from these insults.

7.8 Neuroimaging data from concordant and discordant MZ twins

Functional and volumetric neuroimaging studies of normal MZ twins may help elucidate the neural bases of language. It is well established that people who are right-handed are more likely to have language lateralized in the left hemisphere than people who are left handed. It is also well established that 10-25% of MZ twins are discordant for handedness. (For a discussion of how environmental and genetic factors affect handedness, see Medland, Wright, Geffen, Hay, & Levy, 2003.) In a recent fMRI study, MZ twins, who were either concordant for handedness (with both twins being right handed) or discordant for handedness, performed verb generation and semantic decision tasks (Sommer et al., 2002). All of the twins were at least 35 weeks gestation and 2000 grams at birth, and all had normal language. There was a significant intra-twin pair correlation for language lateralization scores in the handedness-concordant twins ($r = .74$, $p < .01$), but not in the handedness-discordant twins. Sommer and colleagues (2002) argue that the significant correlation for the handedness-concordant MZ twins suggests that genetic factors play a role in language lateralization, and that discordant language lateralization and hand dominance results when MZ splitting occurs after the establishment of the embryo's left-right axis has already been established. If they are correct, then we might predict greater linguistic similarity for MZ twins that are the result of early splitting (i.e., dichorionic twins) than late splitting (i.e., monochorionic twins), independent of additional perinatal risks associated with sharing a placenta.[8]

Neuroimaging studies of MZ twins who are discordant for developmental language disorders can be used to study the neural bases of these disorders, as is being done with other neurological disorders such as attention deficit hyperactivity disorder (Castellanos et al., 2003), Alzheimer's disease (Jarvenpaa et al., 2004; Jarvenpaa, Raiha, Kaprio, Koskenvuo, Laine, Kurki, Vahlberg et al., 2003; Jarvenpaa, Raiha, Kaprio, Koskenvuo, Laine, Kurki, Viljanen et al., 2003; Lipton et al., 2003), schizophrenia (Reveley, Reveley, & Baldy, 1987; Sommer, Ramsey, Mandl, Van Oel, & Kahn, 2004; Spaniel et al., 2003; Suddath, Christison, Torrey, Casanova, & Weinberger, 1990; Weinberger, Berman, Suddath, & Torrey,

[8] Left-handedness is more prevalent in people with perinatal risk factors such as premature birth, low birth weight, perinatal brain injuriesm RH incompatibility, breech delivery and prolonged labor (Medland et al., 2003). It is possible that lateralization findings for handed-discordant MZ reflect intra-twin pair differences in the perinatal environments of twins who are discordant for handedness. Unfortunately, because Sommer et al. (2002) do not report birth weights or gestational ages for handedness-concordant and -discordant MZ twins, we cannot rule out this possibility.

1992) and epilepsy (Briellmann, Jackson, Torn-Broers, & Berkovic, 2001). We can use neuroimaging data from linguistically-concordant and -discordant MZ twins to help elucidate how prenatal and postnatal environmental factors affect the neural substrates of language. Examples of how this work might proceed can be seen in recent studies of other neurodevelopmental disorders. For example, Kunugi and colleagues (2003) recently described a case of MZ twins who were discordant for schizophrenia. The schizophrenic twin weighed 30% less than the normal twin at birth, and whereas the unaffected twin had an unremarkable MRI, the schizophrenic twin's MRI revealed high intensity signal in the white matter and enlarged ventricles consistent with a prenatal hypoxic injury. Kunugi et al (2003) argue that the affected twin's schizophrenia is (at least partially) the result of this prenatal injury. Exploring how postnatal factors may play a protective role in the development of neurological disorders, Jarvenpaa and colleagues (2003) have studied a pair of 90 year old MZ twins in which one twin has long-standing Alzheimer's dementia and the other is still normal (even though half of all 90 year olds suffer from Alzheimer's disease). Jarvenpaa and colleagues (2003) suggest that non-steroidal anti-inflammatory drugs (NSAIDs) may protect against Alzheimer's disease because the only factor that distinguishes the two sisters is that the unaffected twin frequently took NSAIDs, whereas the twin with Alzheimer's dementia did not.

7.9 Summary

We have learned much about how environmental and genetic factors shape language development by comparing the similarity of MZ twins and DZ twins. We can learn even more by carefully studying what makes members of twin pairs linguistically different from one another. By studying differences in the perinatal environments of linguistically discordant and concordant MZ twins, we can learn how intrauterine environment affects neural development, and how the resulting differences in neural structures can affect language development. We can also use linguistically concordant and discordant MZ twins to explore whether and how postnatal psychosocial and biological insults affect language development. We can simplify the task of identifying loci and genes that affect language by analyzing the DNA of MZ and DZ twins. By applying recently developed techniques and advances from molecular and behavioral genetics, neuroimaging, perinatalogy, and typical and atypical language development to the study of twins, we can gain new insights into the genetic and environmental forces that enable people to acquire and use language.

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