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Genetic and environmental influences on symptom domains in twins and siblings with autism

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Abstract

Clarifying the sources of variation among autism symptom domains is important to the identification of homogenous subgroups for molecular genetic studies. This study explored the genetic and environmental bases of nonverbal communication and social interaction, two symptom domains that have also been related to treatment response, in 1294 child and adolescent twins and siblings with pervasive developmental disorders (PDDs) from the Autism Genetic Resource Exchange under the age of 18. Twin/sibling resemblance was assessed through correlations and behavior genetic modeling of autism diagnostic interview (ADI) nonverbal communication and social scores. Variation in these phenotypes was explained by additive genetic, dominant genetic, and unique environmental factors with no evidence for shared environmental factors. Broad heritability estimates were higher for nonverbal communication (45%) than

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social interaction (28%). Nonverbal communication and social scores were partially accounted for by the same underlying genetic and environmental factors. Gender differences were not supported. These results add to information on familial resemblance of these symptom domains based on correlational methods, and this study is one of the first to apply behavioral genetic modeling to a PDD population. The results have implications for molecular genetics as well as treatment.

Keywords: Autism; Autism diagnostic interview; Behavioral genetics; Twins; Social interaction; Nonverbal communication

1. Introduction

Pervasive developmental disorders (PDDs) such as autism involve impairment in social interaction, delayed and/or stereotyped communication, and restricted or repetitive behaviors and interests (American Psychiatric Association, 2000). Risk for autism is 60–100 times higher for siblings of affected individuals than the general population (see Rutter, Silberg, O'Connor, & Simonoff, 1999 for review). In addition, concordance rates for monozygotic (MZ) twins range from 60% to 90% as compared to 2–10% for dizygotic (DZ) twins and siblings; it has been concluded that the heritability of autism is over 90% (Rutter et al., 1999). However, despite this strong genetic influence, research suggests significant genetic heterogeneity as well as the influence of environmental factors (Andres, 2002). Studies of possible candidate genes for autism thus far have been remarkably inconsistent (Bacchelli & Maestrini, 2006).

Several different strategies have been utilized in an attempt to select homogenous groups for molecular genetic studies, including choosing participants based on characteristics such as the presence of language delay (e.g., Spence et al., 2006) or a clear history of developmental regression (e.g., Molloy et al., 2005). However, it is unclear whether characteristics that have been used for sample selection are influenced more by genetic or environmental factors. Power would be strengthened if subgroups were chosen empirically—based on behavioral genetic analyses suggesting that variation in a particular characteristic has a strong genetic basis. One potential strategy that, to our knowledge, has not been employed, is selecting participants based on treatment response. It is clear that some children respond well to intensive behavioral treatment and that this intervention impacts the core features of autism (e.g., Birnbrauer & Leach, 1993; Eikeseth, Smith, Jahr, & Eldevik, 2002; Sallows & Graupner, 2005; Sheinkopf & Siegel, 1998); however, it is equally clear that the success of behavioral treatment in altering the developmental trajectory of children with autism is *not* universal (e.g., Goin-Kochel, Mazefsky, Riley, & The Autism Genetic Resource Exchange, under review; Goin-Kochel, Myers, Hendricks, Carr, & Wiley, 2007; Rogers, 1998; Lovaas, 1987). A possible explanation is that responders and non-responders have different autism etiologies—a premise that assumes that the factors contributing to the development of autism are the same as those regulating responsiveness to treatment. Clarifying whether symptom characteristics found to predict treatment response are largely genetic would begin to answer this question and possibly suggest a more fruitful strategy for molecular genetic subject selection. Two core symptom characteristics have recently been found to predict treatment response (Sallows & Graupner, 2005). Specifically, fewer pretreatment nonverbal communication deficits, as measured by the *Autism Diagnostic Interview—Revised* (ADI; Lord, Rutter, & Couteur, 1994), were positively related to improvement in both IQ and social skills following treatment, and higher pretreatment levels