Strong Genetic Influences on the Stability of Autistic Traits in Childhood

Karla Holmboe, PhD, Fruhling V. Rijsdijk, PhD, Victoria Hallett, PhD, Francesca Happé, PhD, Robert Plomin, PhD, Angelica Ronald, PhD

Objective: Disorders on the autism spectrum, as well as autistic traits in the general population, have been found to be both highly stable across age and highly heritable at individual ages. However, little is known about the overlap in genetic and environmental influences on autistic traits across age and the contribution of such influences to trait stability itself. The present study investigated these questions in a general population sample of twins. **Method:** More than 6,000 twin pairs were rated on an established scale of autistic traits by their parents at 8, 9, and 12 years of age and by their teachers at 9 and 12 years of age. Data were analyzed using structural equation modeling. **Results:** The results indicated that, consistently across raters, not only were autistic traits stable, and moderately to highly heritable at individual ages, but there was also a high degree of overlap in genetic influences across age. Furthermore, autistic trait stability could largely be accounted for by genetic factors, with the environment unique to each twin playing a minor role. The environment shared by twins had virtually no effect on the longitudinal stability in autistic traits. **Conclusions:** Autistic traits are highly stable across middle childhood. and this stability is caused primarily by genetic factors. J. Am. Acad. Child Adolesc. Psychiatry, 2014;53(2):221–230. **Key Words:** autism spectrum disorder, autistic traits, behavior genetics, longitudinal

Autism spectrum disorder (ASD) is a neurodevelopmental disorder characterized by impairments in social interaction (SIs) and communication (CIs), as well as restricted and repetitive behaviors and interests (RRBIs). The spectrum ranges from severe (typically accompanied by intellectual impairment and lack of language) to relatively high functioning. With the introduction of *DSM-5*, several disorders previously labeled as pervasive developmental disorders have been merged into a single ASD diagnosis. Furthermore, the 2 symptom domains of SIs and CIs have been combined to form a single social communication impairment domain.[1] Autistic traits show quantitative variation in the general population.[2-7]

ASD is both highly heritable and highly stable over time. Longitudinal studies have found that individuals diagnosed with ASD rarely move off the spectrum (but see Fein *et al.*[8]), although improvement in symptoms is often observed between childhood and adolescence/adulthood (for review, see Matson and Horovitz[9]). Similarly, high stability has been found when autistic traits are measured in the general population.[10-12]

The heritability of ASD has been established in family and twin studies (the twin method is detailed fully in Supplement 1[13]). Twin studies in the United Kingdom, United States, Sweden, and Japan have established that the concordance rate for ASD in monozygotic (MZ) twins is much higher (36–96%) than in dizygotic (DZ) twins (0–36%), suggesting substantial genetic influences (73–93%).[14] Likewise, twin studies of autistic traits in community and population-based samples in middle childhood and adolescence have found evidence for moderate to strong genetic effects (generally ranging between 50% and 90%), with the remaining variance primarily explained by non-shared environmental factors.[14-16] There is now evidence that the 3 symptom domains of SIs, CIs, and RRBIs, although all highly heritable, are influenced by only partially overlapping genetic factors.[7,17-20] The specific genetic mechanisms underlying ASD have also been investigated extensively in recent molecular genetic research (for review, see Abrahams and Geschwind[21]).

Despite extensive research into the causal influences on autistic traits at individual ages and the finding of high stability in these traits, very few studies have investigated the causal influences on autistic trait stability itself. Likewise, little is known about whether causal influences overlap across age. Knowing this is important for understanding the developmental course of autistic traits. Constantino *et al.* followed up a small sample of 95 male twin pairs (aged 3–18 years) from the general population for 5 years and found that change in parent-reported autistic traits across the period could be accounted for largely by genetic factors (73%).[10] These authors also found some limited evidence that genetic influences in childhood overlapped only partially with those in adolescence.

In the present study, our aim was to establish the causal influences on the longitudinal development of autistic traits across middle childhood. We were also interested in investigating sex differences in these influences, given evidence that more boys than girls are diagnosed with ASD,[22,23] and the finding of sex differences in large cross-sectional twin studies of autistic traits.[5,7,17] Furthermore, different raters provide information on a child's autistic-like behaviors in different contexts,[24] and it is therefore important to test whether the causal model of stability in autistic traits is the same across raters. Finally, little is known about the longitudinal development of the three domains of autistic symptoms. The partial independence of SIs, CIs, and RRBIs has been established previously.[7,17,18,20] However, it remains unresolved whether similar causal effects operate on these 3 dimensions across development.

To address these questions, a population-based sample of more than 6,000 twin pairs was assessed. Autistic traits were investigated primarily as an overall trait, but the 3 dimensions of SIs, CIs, and RRBIs were also explored. Male and female twins were assessed on the same measure of autistic traits by teachers at ages 9 and 12 years and by parents at ages 8, 9, and 12 years, allowing investigation of sex differences and rater differences in causal effects.

METHOD

Participants

Participants came from the Twins Early Development Study (TEDS), a population-based longitudinal study of all twins born in England and Wales from 1994 to 1996. The present paper is based on data collected from parents when the twins were approximately 8 (mean ± SD = 7.89 ± 0.53), 9 (9.01 ± 0.29), and 12 (11.28 ± 0.70) years old, and from teachers when the twins were approximately 9 (9.04 ± 0.29) and 12 (11.54 ± 0.66) years old. Zygosity in same-sex twins was established using a parent-rated twin similarity questionnaire[25] (60.5% of twins) and DNA genotyping (39.5% of twins). Twin pairs were excluded from the analyses if severe pre- or postnatal complications were reported or if either twin had a severe medical condition. To retain the full range of variability in autistic traits, children who had suspected or confirmed ASD (n = 238) based on the Development and Well-Being Assessment (DAWBA)[26] were included in the analyses when data were available. After exclusions, parent-reported data on both twins were available from 6,280 families at age 8 years, 3,126 families at age 9 years (the 9-year sample was a subsample of families with twins born between January 1994 and August 1995), and 5,339 families at age 12 years. Teacher data were available from 2,663 families at age 9 and 4,405 families at age 12. The sample at each of these ages was representative of the U.K. population.[20,24,27] Further details on the recruitment and study protocol are reported elsewhere.[28,29]

Measures

Autistic traits were assessed using the Childhood Autism Spectrum Test (CAST, formerly the Childhood Asperger Syndrome Test).[30] The CAST was developed as a screening questionnaire for use in non-clinical settings. The published measure consists of 37 items, 31 of which relate to autistic traits (raters are asked to rate the child on specific behaviors associated with autistic traits), the remaining 6 being control questions on general development. At age 12 years, 1 item (regarding pretend play) was removed for not being age appropriate. Each question was rated "Yes" (1)/"No" (0) at ages 8 and 12, and as "Not true" (0), "Somewhat true" (1), or "Certainly true" (2) at age 9. Questionnaires with half or more of the items rated were included in the analyses. Only between 0.19% and 2.38% of questionnaires were excluded based on this criterion at any individual age. CAST subscale scores were calculated using the method described by Ronald *et al.*[7,31]

The CAST has good internal consistency: in the present study Cronbach's α ranged from 0.71 to 0.81, depending on age and rater. It has high sensitivity and specificity for ASD (both > 95%) using a cut-point of $\geq$ 15,[32] as well as high test–retest reliability.[33] Recently, the CAST has been used successfully in epidemiological research to screen for previously undetected cases of ASD.[23]

At ages 8 and 12 years, the full CAST was used. At age 9, the 20-item abbreviated version of the CAST was used.[24] Between ages 8 and 9, the full and