VIEWPOINT

Japanese spectrum

BY **JOHN CONSTANTINO**

9 APRIL 2013

One of the major questions in autism research is whether most occurrences of the disorder represent the extreme in a **continuous distribution** of social-communicative competencies that occur in nature, or whether children with autism form a **subgroup with distinct clinical features**.

Although some cases of autism result from **rare, individual mutations**, scientists suspect that a substantial proportion of children with autism — perhaps the majority with familial autism syndromes — carry multiple mutations that influence autism risk, which would result in continuous distributions of symptoms in the general population.

Research over the past ten years has shown that some **family members** of children diagnosed with autism have impairments themselves, even if not severe enough to warrant a diagnosis. What's more, the extent to which the symptoms of the 'autism triad' travel together as subtle traits in the general population entirely mimics the co-occurrence of the symptoms that define the autism syndrome.

Quantitative traits of autism, such as social awkwardness or over-focus on details, are as heritable as autism itself, and the genetic underpinnings of mild social-communicative deficits (for example, at the highest fifth percentile of the population distribution) turn out to be the same as those that result in more severe deficits (for example, at the highest first percentile of the population distribution).

In a paper published in *Acta Psychiatrica Scandinavica* in November, my collaborator **Yoko Kamio** and I showed that this distribution of autism traits occurs across cultures[1].

Kamio and her colleagues at the National Institute of Mental Health in Tokyo administered a Japanese translation of the Social Responsiveness Scale (SRS), a short parent survey assessing social deficits in autism that **I helped develop**. They gave the survey to parents of a nationally representative sample of 22,529 children, aged 6 to 15 years, in Japan.

Bell curve:

As has been observed in U.S. and European samples, SRS scores correspond well with clinical diagnosis, exhibit a ‘bell curve’ in the Japanese population and have no significant relationship to intelligence scores within the normal range.

The severity of subclinical traits reflecting each of the symptom domains — social reciprocity, communication and rigid and **repetitive behaviors** — is tightly correlated within individuals across the entire population, and there is no evidence of a natural cutoff that would differentiate populations of categorically affected children from unaffected children.

This study therefore provides cross-cultural evidence of the continuous nature of autism symptoms. The findings suggest that paradigms for diagnosis that rest on arbitrarily imposed categorical cutoffs may underestimate the prevalence of affectation in girls in the same manner that has been observed in Western cultures.

What’s more, they suggest that diagnostic methods that do not allow case assignments to be made on the basis of percentile (as is universally done for height, weight and intelligence) would be expected to be unstable or difficult to interpret across disparate populations, particularly for **boys versus girls**.

In addition, these results underscore the utility of so-called ‘**rapid-phenotyping’** measures — symptom measurements that can be completed briefly and inexpensively by untrained raters — for reliably screening and characterizing large populations of children, or for feasibly monitoring the severity of symptoms over time or as a function of response to intervention.

Now that we have a better picture of the population structure of quantitative traits of autism and the transmission of genetic risk factors, my own laboratory is exploring the origins of quantitative variation early in development, including the nature of profound **sex differences** in the traits and symptoms that are expressed among individuals who carry a given set of inherited susceptibilities for autism.

To this end, we are following the early social development of an epidemiologic sample of 400 young twin pairs (beginning at age 12 to 18 months), and are exploring resiliency factors that may **protect a majority of girls** from developing the full spectrum of autism symptoms.

John N. Constantino *is director of the Division of Child Psychiatry and associate director of the Intellectual and Developmental Disabilities Research Center at the Washington University School of Medicine in St. Louis, Missouri.*

References:

1. Kamio Y. *et al. Acta Psychiatr. Scand*. Epub ahead of print (2012) **PubMed**