Editorial

Autism: Fitting the Pieces Together

The United Nation declared April 2 as World Autism Awareness Day in 2007, to highlight the need to help improve the lives of children and adults with autism. The Autism Society of America marks April as National Autism Awareness Month, while in the UK, from March 27 to April 2, 2015, the National Autism Society also holds World Autism Awareness Week with the campaign “Stand Out for Autism”. These events are to raise public awareness of this lifelong developmental condition that can affect the way a person communicates with and relates to others, as well as how they make sense of the world. Not only might autism negatively impact the quality of life of affected individuals and their caregivers, but providing the healthcare, social care and education that individuals need and deserve is also costly.

Autism prevalence has increased substantially from 1 in 2500 in the 1980s when autism was first included in DSM-III to 1 in 100 at present. This increase can in part be attributed to a number of factors, including early detection, increased awareness, and broadening of the definition from the original entity first described by Kanner in 1943 to include so-called autistic spectrum disorders. Autism can be diagnosed at 2–3 years of age, and affected individuals usually have a normal lifespan. This puts autism on the same magnitude in terms of patient years with one of the most prevalent neurological disorders—Alzheimer’s disease.

There is no known cure for autism; however, there are many approaches and forms of support that can help people with autism to manage their condition and fulfill their potential. Successful management can depend on early diagnosis and behavioral and educational therapies. While medication (e.g., antipsychotics) does not address the core neurological issues associated with autism, it can help with mental health problems such as anxiety and depression and treat other behaviors such as aggression. There is a clear unmet need in autism management due to a lack in basic understanding of definitive causative factors, how they lead to autism, and whether any of them may be amenable to interventions.

Dating back nearly 40 years to the work of Folstein and Rutter, family and twin studies have demonstrated a highly heritable component to autism, evident by high concordance rate in mono- and dizygotic twins. Given this genetic predisposition, significant efforts have been made in identifying autism risk genes. Geneticists have levered genome-wide and candidate gene approaches and have linked dozens of gene variants to autism; however, no single locus accounts for more than 1% of cases. Some of these genes have a role in neuronal synaptic activities. These genes also affect other neurological and psychiatric disorders and not just autism. Nevertheless, the fact that autism can sometimes run in families suggests strong genetic risk factor(s) yet to be pinpointed. Exposure to environmental factors (e.g., certain drugs and toxins during early pregnancy) has also been implicated to increase the risk of developing autism in the newborn. However, research in this area is difficult due to a large number of variables that need to be controlled for; hence the results to date are not conclusive.

With the aid of advanced imaging techniques, neurobiologists have made important breakthroughs in understanding brain structures and functions in autism. Neuroimaging studies have shown excessive brain growth during the first 2 years of life in 20–30% of autistic children. There are also structural abnormalities in the autistic brain; however many of them are of unknown clinical significance. Is autism therefore associated more with brain function than brain morphology? Functional MRI reveals that, compared with normal controls, people with autism use different brain areas for object and human face recognition. In adults with autism, there appears to be a long-distance under-connectivity and short-range over-connectivity in the brain, although this observation is less clear in children. This ‘miswiring’ could result in a lack of integration between brain regions and ineffective information processing. As the brain is highly plastic and capable of making new synaptic connections and changing the strength of such connections, especially in early life, this ‘miswiring’ may in theory be ameliorated with behavioral therapy, brain stimulation and practice, and the treatment success is highly dependent on early and accurate diagnosis of autism.

Studies from other science disciplines have also shown that biochemically, children with autism can have reduced antioxidant capacity thus may have chronic oxidative stress, which could lead to neuron dysfunction and affect synaptic plasticity, learning and memory. Immunologically, autism individuals may overexpress pro-inflammatory cytokines. Other proposed biomarkers include low levels of oxytocin, increased levels of platelet serotonin, and reduced levels of plasma growth factors. Can all of these seemingly unconnected findings be the result of the interplay between genetic and environmental factors?

The possible interconnections among different factors in autism pathogenesis highlight the importance of a multidisciplinary approach, where psychologists, psychiatrists, neurobiologists, geneticists, immunologists, biochemists as well as bioinformaticians should come together, pool their resources and analyze the available data. A clear priority should be to define molecular signaling pathways in the developing brain for normal cognitive and motor development, language ability and social interaction. The next hurdle is to delineate the molecular, cellular and neurobiological factors, or combinations of those factors, that may be responsible for the pathogenesis of autism, then to identify factors that may be amendable to interventions. Transforming big data into new insights requires parallel computational studies, preclinical in vivo testing, and clinical and validation trials—all of which when done in concert should strengthen one another and hopefully lead us to a solution for our autism puzzle. Beyond this and perhaps even more importantly, these new insights can help us understand and appreciate the differences in social cognition, language and behavior from the perspective of individuals with autism, and find effective ways to empower them to have a role in the society.