

Preface

Data compiled by the Centers for Disease Control and Prevention indicates an alarming and continuing increase in the prevalence of autism. According to the latest survey, among 14 different sites on the Autism and Developmental Disabilities Monitoring (ADDM) Network, the estimated prevalence for autism spectrum disorders (DSM IV-TR) was 11.3 per 1,000 (one in 88) children aged 8 years of age who were living within these communities during 2008. This translates to approximately one in 54 boys and one in 252 girls living in the ADDM Network, a 78 % increase compared to the prevalence reported one decade ago.

More alarming statistics are derived from other countries where the prevalence for autism has been reported as higher than in the USA. In South Korea, for example, the prevalence is 1 in 38 children. The latter study, which screened an overwhelming 55,000 12-year-old children, suggests that when canvassing an entire population, rather than sampling the same, prevalence rates may be higher than expected. Still, it could be argued that higher prevalence rates may be the result of detecting other developmental conditions along with autism.

Along with the rising prevalence rates, there is a new research that estimate autism costs society a staggering \$126 billion per year within the USA alone. The number has more than tripled since 2006. Nonmedical costs such as special education and child day care account for the greatest proportion of expenses with the majority of costs being incurred during adulthood due to residential care and loss of productivity. Cost varies according to the communities the patients live in and the local government agencies that provide education, welfare benefits, and housing. Still, the latest figures do not capture the full impact of the condition for which other financial burdens have still to be considered. The primary caregiver (typically the mother) who has to serve as case manager and advocate for her children usually is negatively impacted in her earning potential. Mothers of children with autism spectrum disorders are thus more likely to work fewer hours and earn less than mothers of neurotypicals or those with other health limitations.

Despite intensive research during the last few decades, autism remains a behavioral-defined syndrome wherein diagnostic criteria lack in construct validity. In essence, contrary to other conditions like diabetes and hypertension, there are no

biomarkers for autism. Diagnosis by behavioral assessments usually occurs around the age of 2 or 3. New imaging methods are changing the way we think about autism, bringing us closer to a falsifiable definition for the condition, identifying affected individuals earlier in life, and recognizing different subtypes of autism.

Early recognition of signs of autism is important as it can lead to early intervention. Controlled studies show that early behavioral-based interventions change the outcome of affected children by significantly improving IQ, cognitive and language abilities, as well as adaptive behaviors. The American Academy of Pediatrics now recommends that children get screened for autism during regular checkups at ages 18 and 24 months. Unfortunately, developmental and behavioral screening tools lack sensitivity to screen specifically for autism and usually require follow-up with an autism screening tool when developmental concerns arise. Even then, autism screening tools have not been widely validated under 18 months of age. In this regard it is useful to consider these instruments as useful guides to inform individuals as to the potential risk for autism rather than regard them as diagnostic tests.

Autism is a challenging condition that has intrigued both clinicians and researchers alike because of its association with significant cognitive disturbances in the absence of gross brain abnormalities. Initial findings suggest that the pathology of autism is at a higher level of resolution, one that may escape gross visual inspection. Unfortunately, few neuropathological studies have been reported in autism, in part, due to the limited availability of postmortem tissue. Early studies suggested the presence of cerebellar pathology in autism. More recently studies have elaborated on abnormalities related to cortical thickness, lamination, and migrational disturbances.

The use of and focus on the cerebral cortex provides a paradigm shift in our approach to this condition. Early studies suggested that the cerebellum was the only site by both imaging and postmortem data wherein cell loss was reported by multiple independent laboratories. More recent imaging studies have shown that MR images of the cerebellum in a substantial number of patients are indistinguishable from those of control subjects. Furthermore, the presence of reactive gliosis to Purkinje cell loss suggests an acquired process. A recent immunocytochemical study comparing cell counts between Nissl-stained sections and calbindin indicates that possible agonal circumstances and even postmortem handling could have accounted for lower Purkinje cell counts in earlier studies. It may be that in many cases, Purkinje cell loss may be related to seizures, medications, and agonal events rather than to a core pathology of the condition.

It is unsurprising that neurologists consider autism a disease of the cortex rather than the cerebellum. The presence of seizures in a significant proportion of cases along with the absence of spasticity or vision loss supports this tentative localization. Furthermore, dysfunction of multiple higher cognitive functions indicates a widely distributed defect involving the cerebral cortex.

The brain's capacity to perform cognitive tasks is made possible by the proper association in function of different brain areas arranged as networks. Research on brain connectivity not only has important implications into the pathophysiology of autism but also presents opportunities/targets for intervention. These promising

findings can provide the first steps towards developing a biomarker that could complement or add construct validity to our present diagnostic criteria. Ultimately imaging techniques may distinguish autism from other developmental conditions, even those that share common symptoms such as speech delay or attention deficits.

Structural brain imaging in conjunction with machine learning methods based on criteria such as cortical thickness is able to classify individuals in the autism spectrum with as much as 90 % accuracy. Other studies using diffusion tensor imaging (DTI) have shown asymmetries between the hemispheres that bear on so-called hot spots associated with motor skills, attention, facial recognition, and social-functioning behaviors that are abnormal in autism. In essence the two hemispheres must work together when performing many brain functions and research is capable of identifying the strength of these connections in autistic patients.

Imaging of structural changes has found striking differences starting at 6 months of age in high-risk infants who later develop autism. The findings are in keeping with autism being a neurodevelopmental condition, one that does not appear suddenly but has its roots in brain development. Furthermore, findings implicate multiple fiber tracts suggesting that autism is a whole brain phenomenon.

It is our hope that in the future some of these structural modalities will be correlated to electrophysiological methods. The blueprint of connectivity for the brain in autism may relate to how we create conscious perception. Gamma frequencies in particular seemingly bring together a distributed matrix of cognitive processes into a coherent cognitive act. A common trait among autistic individuals is that they can see the trees but not the forest. They become wrapped up in details but miss the larger picture. This translates to socialization deficits, which are dependent on integrative concepts as opposed to isolated ideas or sensory inputs.

All of the imaging modalities that we have discussed are important pieces within the autism puzzle. They emphasize the power of new technology to uncover important clues about the condition and give hope for developing effective interventions. This book was created to examine autism from this unique perspective: one that would emphasize results from different imaging technologies. These techniques do show brain abnormalities in a significant percentage of patients, abnormalities that translate into aberrant functioning and significant clinical symptomatology. It is our hope that this newly found understanding will make the field work collaboratively and to provide a road that minimizes technical impediments.

Louisville, KY, USA
Louisville, KY, USA
Roseville, CA, USA

Manuel F. Casanova
Ayman S. El-Baz
Jasjit S. Suri

Imaging the Brain in Autism

Casanova, M.F.; El-Baz, A.S.; Suri, J. (Eds.)

2013, XIV, 387 p., Hardcover

ISBN: 978-1-4614-6842-4