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EDITORIAL

Autism spectrum disorders☆

Trastornos del espectro autista

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Autism spectrum disorders (ASDs) are severe neurodevelopmental disorders caused by the abnormal development of the brain before birth and in the early years of life, and they are considered to last a lifetime. Their aetiology is unknown in 80% of patients, and it has only been known in recent years in 20% of them thanks to neuroimaging studies and neurogenetic techniques, which have helped us learn about pathological anomalies and genetic syndromes that cause ASDs. Today, thanks to the development of the criteria proposed in the DSM-V, we will be able to diagnose ASDs with greater sensitivity and specificity.

Recent genome sequencing studies have shown that mutations in 500–1000 different genes may be associated with ASDs. Many of these genes are tied to synaptic activity (pre- and post-synaptic regulatory and signalling activity) needed to maintain an appropriate balance of excitation and inhibition in the neural network. Imbalances in excitation and inhibition in the neural network disturb development and may account for some of the symptoms found in ASDs, such as the high incidence of convulsions and the abnormal responses of these patients to visual and auditory stimuli. These patients have shown alterations in the balance of glutamate and gamma-aminobutyric acid at the synaptic level, which are essential for the correct formation of the neural network. We must bear in mind that the onset of ASD symptoms coincides with the period of maximum synaptogenesis and synaptic plasticity. Some animal models of disorders associated to autism, such as Rett syndrome and fragile X syndrome, have shown alterations in synaptic plasticity. The genes that participate in transcription regulation during brain development, especially those that regulate chromatin, and epigenetic modifications play a fundamental role. Recently, some authors have also been supporting the hypothesis that ASD is produced by a disruption of the neural synchronisation of the cerebral hemispheres, with a particularly strong impact on language.

Environmental risk factors, such as intrauterine infections, low birth weight, and exposure to medications and toxins during pregnancy, are a second set of factors to consider that may exacerbate an underlying condition.

Chromosomal microarray analysis is recommended for aetiological diagnosis in these patients, as well as molecular screening for fragile X in boys and for MECP2 in girls. PTEN testing should be done in patients with macrocephaly, and SHANK3 in patients with severe language and social impairment. Even today, sequencing the entire genome is costly, and the results are very hard to interpret in patients with ASDs, but it has great potential to identify de novo mutations in ASDs. A metabolic screen must be performed when patients also present with regression, lethargy, cyclic vomiting, hypotonia, etc. Some syndromes, such as urea cycle disorder, may occur in patients with ASD features.

Neuroimaging can help visualise structural abnormalities described for some brain regions, especially in the white matter. A subgroup of ASD patients have accelerated brain growth in the early years of life that may be related to accelerated myelination of the brain. Anomalies of the corpus callosum, amygdala–hippocampus, thalamocortical

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radiations, cerebellum, interhemispheric tracts, and brain volume have been described in the literature. At present, it is considered that they have a disorder of the neural network rather than anomalies in specific regions of the brain. The application of spectroscopy to cranial magnetic resonance has shown differences in choline peaks and has led to the diagnosis of brain creatine deficiency.

Today there are different screening instruments for the assessment of ASDs, such as the CHAT for the first 2 years of life and the M-CHAT for children 16 months to 4 years, and for more specific assessment, the ADI-R and ADOS. Scales for social communication (SCQ) and communication and symbolic behaviour (CSBS) are also used.

Early diagnosis is crucial so that behavioural and psychopedagogical treatment can be started. Although there is no cure, it is clear that early intervention after the onset of symptoms leads to better outcomes considering the brain plasticity of children in the early years of life. Different models are used, with some focusing on imitation, social reciprocity, and play (DIR), or on structuring the environment and building skills to attain independence, as is the case of TEACCH, and others like ABA, which teaches behaviours, or ESDM. Medication can help with disruptive behaviours, self-injury, and sleep disorders that may develop in these patients.

This early detection study of pervasive development disorders (PDD) in the Salamanca and Zamora health districts has succeeded in demonstrating, for the first time in Spain, the viability of a population PPD screening programme in the context of the public healthcare system.[1] Diagnosing 22 patients with PPD and 32 with other early childhood disorders in a population of 9524 children at an early age was a success for the professionals who conducted the study.

Knowledge of abnormalities in communication and social development and the diffusion of the red flags among paediatricians, along with the use of the M-CHAT are key for the early detection of these disorders and provision of the treatments available today. This work should serve as a model for health districts so that this method is applied regularly by paediatricians, who should publish their results so that we have accurate knowledge of the prevalence of this pathology in the various autonomous communities of Spain.

Reference

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