Clinical and neurobiological relevance of current animal models of autism spectrum disorders: therapeutic approaches based on excitation/inhibition (E/I) imbalance

The exact etiology and pathophysiological mechanisms that could explain the core symptoms of ASD are still poorly understood. This task is greatly overwhelmed by the clinical heterogeneity of ASD and its overlap with other neurodevelopmental syndromes. Over the last few decades, diverse risk factors for ASD have been identified and their role in the manifestation of autistic symptoms has been investigated through the use of animal models. Research in this area has elucidated how different sets of symptoms are paralleled by alterations in specific neurophysiological and biological pathways. This in turn has led to gradual segregation and stratification of ASD subgroups. Yet, the translational relevance of animal models of ASD has yet to be proven useful, as it has not been sufficiently justified and apprehended by the clinical field, and even among disagreeing researchers. It is henceforth paramount that we unify the current knowledge in the field and find a common ground for convergence in preclinical research for ASD.

In this review, we cluster the ASD animal models into lesion and genetic models based on common risk factors such as environmental, epigenetic and genetics. We then summarize and compare the symptoms and neuropathology of each animal model in relation to their clinical and neurobiological relevance. As a conclusion, we present a schematic representation of the E/I imbalance theory of ASD, based on the convergent evidence of current knowledge and research.