An understanding of how the brain produces cognition ultimately depends on knowledge of its large-scale organization and wiring. The human brain undergoes protracted structural and functional changes during which it constructs dedicated large-scale brain networks comprised of discrete, interconnected, brain regions. Aberrations in brain connectivity have been widely reported in autism, but their relation to its three core symptoms—social communication, language and repetitive-restricted behaviors—are unknown. In this talk I will describe recent progress in our understanding of large-scale brain networks in autism and demonstrate that its core deficits can be linked to distinct features of atypical brain connectivity in affected individuals. I will also describe progress in development of connectivity based biomarkers of the disorder and predictors of symptom severity. Although under-connectivity has been posited to be a hallmark of atypical brain organization in autism, emerging findings in children with autism are painting a decidedly more complex picture, one that has thrown into sharp relief the challenges facing our understanding of brain connectivity over the lifespan in autism. At the same time, they open new possibilities for a deeper understanding of the neurobiological origins of the disorder. In this vein, I will describe preliminary findings from a computational “virtual brain” model which demonstrates that regional imbalance in excitation and inhibition can lead to altered global brain connectivity similar to those observed in individuals with autism. Our model provides novel mechanistic insights into the neurophysiology of the disorder. Implications of our findings for early detection and treatment of autism will be discussed.