Chapter 6
Recent Advances and Neural Connectivity in Autism

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ABSTRACT
The current chapter has reviewed the functional and structural brain connectivity in children with autism spectrum disorders (ASD). Neuropathological studies of the cerebral cortex in autism indicate abnormalities of synaptic and columnar structure and of neuronal migration. The MRI morphometry in young children with autism reveals excessive volume of cerebrum or cerebral white matter or increased total brain volume. The absence of such a volume difference in adults suggests that early hyperplasia in autism is followed by a plateau during which brain growth in normal subjects catches up. The developmental course of brain connectivity and the categorization potential of different connectivity processes are important topics that are investigated by different studies. Finally, several studies contribute to a better understanding of the links between cellular abnormalities in the autistic cortex (both cerebral and cerebellar) and disturbances in network connectivity.

INTRODUCTION
Autism spectrum disorders (ASDs) are a family of neurodevelopmental syndromes with the prevalence of roughly 0.5–1.5% (Brugha, McManus, Bankart, Scott, Purdon, Smith, & Meltzer, 2011). ASDs are very common in males than in females, with a gender ratio of around 4:1 (Maenner & Durkin, 2010). ASD is a contemporary term which takes into account older concept of ‘autism’ or ‘childhood autism’, but in addition covers cases which, while sharing many of the symptoms of autism, do not cover the strict criteria for this disorder (Geschwind, 2009). ASDs are diagnosed on the basis of impairments in mainly three domains of behavior: social contact and relationships, verbal communication and repetitive, limited interests and behaviors (Robinson, Koenen, McCormick, Munir, Hallett, Happé, & Ronald, 2012). These symptoms are in attendance from early life (before 36 months of age). ASDs are clinically
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diverse, with the severity of the variety of symptoms, and the impairment they cause, varying extensively (Geschwind, 2009). Some community with an ASD also have an intellectual disability (low intelligence quotient; IQ), but at least 25% of those with ‘classic’ autism, and advanced proportion of those with milder ASDs, show normal or superior intellectual function (Rutter, 1983).

Autism Spectrum Disorder featuring both average range IQ and a history of ordinary language acquisition is called Asperger’s syndrome (Sharma, Woolfson, & Hunter, 2010). Nonetheless, it is debated whether Asperger’s is strictly a syndrome separate from autism (Wing, Gould, & Gillberg, 2011) and future DSM-5 diagnostic criteria would eliminate it as a separate diagnosis as well as be introducing additional changes to ASD diagnosis. ASDs are acknowledged to be highly genetic, with estimates of heritability ranging from roughly 0.5 to 0.9 (Ronald & Hoekstra, 2011). However, environmental factors, including perinatal and obstetric problems, also play a role (Gardener, Spiegelman, & Buka, 2011). First-degree relatives of affected persons are at augmented risk of an ASD, and also of milder social and communication impairments dubbed the ‘broader autism phenotype’ (Whitehouse, Coon, Miller, Salisbury, & Bishop, 2010). These studies provided a diverse picture. Clear cut abnormalities were identified in some individual cases of ASD, however, there was immense inconsistency in these researches outcome, with a range of diverse focal and generalized pathologies being reported in a wide range of studies.

The majority of persons with an ASD showed no qualitative abnormalities noticeable with such methods, although some quantitative differences were found, for example, reduced size of the corpus callosum and cerebellum, and amplified volume of the caudate nucleus in ASD, on standard, compared with controls, although with small or average effect sizes for a review and meta-analysis (Stanfield, McIntosh, Spencer, Philip, Gaur, & Lawrie, 2008). For example, near the beginning case reports recognized cerebellar hypoplasia and ventricular bulge in ASD cases (Courchesne, Hesselink, Jernigan, & Yeung-Courchesne, 1987) but other investigators reported no magnetic resonance imaging (MRI) malformation in nearly all cases, and normal cerebellar development (Garber, Ritvo, Chiu, Griswold, & Kashanian, 1989). In Asperger’s syndrome, many case reports of left temporal (Jones & Kerwin, 1990) left frontal and bilateral opercular cortical abnormalities (Berthier, Starkstein, & Leiguarda, 1990) were reported, with little consistency. MRI findings did not present a single pattern. Autism is a mixed disease entity containing various clinical subgroups, which do not demonstrate similar radiologic pictures (Nowell, Hackney, Muraki, & Coleman 1990).

Early positron emission tomography (PET) review likewise produced contradictory findings. Early findings reported widespread increases in glucose metabolism crossways in the brain of some autistic adults (Rumsey, Duara, Grady, Rapoport, Margolin, Rapoport, & Cutler, 1985) but another study found no dissimilarity (Herold, Frackowiak, Le Couteur, Rutter, & Howlin, 1988). These studies inferred that, while some cases of ASD are connected with qualitative neurological abnormalities, there is no clear localization of exact areas of the brain, with a variety of cortical, subcortical and cerebellar regions all having been involved in different cases. In addition, abnormalities in the mean volume of diverse areas have been found, these are of modest magnitude, with considerable overlap between ASD and control groups. Hence, in order to understand the neurobiology of autism, an understanding of the whole brain, rather than individual areas of interest, is required.