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Early clinical intervention in psychosis has recently become a major objective of mental health services, and the development of specialist early intervention services has greatly facilitated research on the early phases of the disorder. Research at this stage is potentially a way of investigating the mechanisms underlying psychosis, as the same individuals can be studied before and after the onset of illness, often with minimal confounding effects of previous treatment. The identification of a clinical syndrome (an “at risk mental state”) that reflects an “ultra high risk” predisposition to psychosis is fundamental to both clinical and research work in this area.

Endorsing the genetic high-risk approach, putative endophenotypes can be evaluated for association with genetic risk for schizophrenia by comparing the unaffected co-twins or the unaffected relatives of patients with normal controls. Alternatively, “close in”, i.e., clinical high-risk, approaches are able to identify a group at high risk of psychosis with higher transition rates than those observed in studies purely based on genetic inclusion criteria. The latter approach, focusing on individuals who are considered to be at increased risk for psychotic disorders, is based primarily on the presence of clinical symptoms. This clinical strategy aims at identifying neural changes occurring prior to the onset of psychosis and may improve our ability to predict schizophrenia outcomes based on the combined perspectives of both neural and clinical characteristics observed at the baseline assessment.

The presence of individuals who are at high risk but not psychotic is consistent with evidence that schizophrenia results from the interaction of environmental with genetic and neurodevelopmental factors, with the latter associated with clinical, neurobiological and neuropsychological features before the onset of psychosis. Over the past years, neuroscience techniques such as: structural brain imaging—magnetic resonance imaging (MRI) and diffusion tensor imaging (DTI); functional brain imaging—positron emission tomography (PET), single-photon emission computed tomography (SPECT), functional magnetic resonance imaging (fMRI); neurochemical imaging—magnetic resonance spectroscopy (MRS); and computerized models (Virtual Reality), have rapidly developed as powerful tools to explore the neurophysiological basis of vulnerability to psychosis.

This monograph is indented to provide a state-of-the-art review of neurobiological research in people at high risk of psychosis, with a particular
focus on the processes that may underlie the transition from a high-risk state to a first episode of frank psychosis. These neurobiological findings will be presented in the context of what is now known about the psychopathology and cognitive impairments that are evident in people at high risk of psychosis, and environmental factors that may influence the risk of the onset of illness. The monograph thus aims to bring together a diversity of new information from a range of different research modalities, which are sometimes studied separately.