Summary
In this thesis we set out to investigate potential mechanisms and processes underlying the development of psychosis. In chapter two, we investigated whether the determinants of reactivity to stress in a general population twin sample are genetic or environmental factors, or a combination of both. Using a novel task, we exposed adolescent and young adult twins to peer evaluation – one possible source of social stress – comparable to what they may experience daily in online social interactions. The proportion of variance in reactivity to peer evaluation due to genetic and environmental factors, as well as the association with specific a priori environmental risk factors (e.g., childhood trauma, bullying experiences), was then estimated. We found evidence that more severe experiences of bullying and a lower subjective social status were associated with increased reactivity to an experimentally induced social stressor.

In chapter three, we examined stress-reactivity by studying micro-level dynamics in daily life in three samples varying on the continuum of psychosis – healthy control subjects, relatives of individuals with a psychotic disorder with a certain genetic liability for developing the disorder as well, and patients with a psychotic disorder. We applied a network approach to psychopathology to the experience sampling method (ESM) data to gain insights into the mechanisms at the level of micro-dynamic moment-to-moment effects between stress, other daily experiences and psychotic experiences. In particular, with an increased risk for developing a psychosis, elevated levels of stress were directly associated with increases in affective and psychotic experiences at the next moment. Furthermore, we found evidence that the number of significant micro-level associations increased with a higher risk for developing a psychosis. The findings of this study point towards stress-reactivity being a putative mechanism underlying the development of psychotic experiences.

In recent years, various models of psychosis have suggested that experiences of stress contribute to the development of psychotic experiences via pathways of negative affect, cognitive biases, and anomalous experiences. In chapter four, we systematically tested comprehensive models of these pathways in three samples that varied on the continuum of psychosis – healthy control subjects, individuals with an at-risk mental state for psychosis, and individuals with a first-episode psychosis. We fitted multilevel moderated mediation models to ESM data to investigate how stress, enhanced threat anticipation, and experiences of aberrant salience combine to increase psychotic experiences in daily life. There was consistent evidence that stress increases the intensity of psychotic experiences via pathways through
affective disturbance – in FEP individuals, ARMS individuals, and controls – with some evidence of greater indirect effects in FEP and ARMS individuals than controls.

In **chapter five**, we investigated whether findings of the previous chapter replicate in a different sample. Additionally, we investigated longitudinal associations of momentary stress, negative affect and psychotic experiences across two measurement occasions. This sample again consisted of three groups varying in risk for psychosis – healthy control subjects, relatives of individuals with a psychotic disorder, and patients with a psychotic disorder. Again, we found consistent evidence that stress increases the intensity of psychotic experiences via pathways through affective disturbance. Additionally, we found evidence for an indirect effect from psychotic experiences on momentary stress via affective disturbance. Interestingly, the magnitude of this indirect effect was considerably larger than that of the reverse pathway (from stress to psychotic experiences via affective disturbance). Tentatively, taken together, these findings suggest that there may be rapid vicious cycles of stress impacting psychotic experiences, and vice versa, via emotional reactivity. Only in controls, there was evidence of a longitudinal indirect effect of stress on psychotic experiences via negative affect.

There is accumulating evidence for micro-level dynamics of momentary experiences, affect and symptomatology. Real-world delivery of treatment, therefore, seems a promising prospect for patients and individuals with an increased risk for developing a disorder. In **chapter six**, we conducted a concise review on the feasibility, content and efficacy of currently available ecological momentary interventions in psychiatry. Findings of this review suggest that mobile health may be an important asset to mental health care, while at the same time it underscores that it is still in its early stages. Based on our findings, we discuss ways to improve ecological momentary interventions (EMIs) for severe mental illness to ultimately implement them in routine mental health services.

In sum, this thesis provides new evidence on the dynamic interplay between psychological processes and stress in the origin of psychosis and, thereby, contributes to improving our understanding of the complex etiology of psychosis. Our findings underscore the important role of emotional reactivity as putative mechanism through which stress impacts on the formation of psychotic experiences. Understanding these processes involved in the development and persistence of psychotic experiences provides us with further insights concerning prevention and treatment.