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**Living and Coping with Stress: Neuroimaging Findings in the
Framework of an ongoing Longitudinal Study**

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The present thesis addresses the complex interplay of environmental adversities, psychopathology, neural development, and coping mechanisms in a longitudinal at-risk cohort study following its participants since birth.

Specifically, in study 1, we investigated the long-term impact of life stress at different developmental stages, namely infancy, childhood, and adolescence, on prefrontal brain alterations. Therefore, life stress was recorded in regular intervals starting at the age of 3 months until the age of 25 years by reporting chronic and adverse life events occurring not more than one year prior to the assessment time point. Structural brain imaging was conducted at the age of 25 years. Moreover, depressive symptoms were assessed in young adulthood via self-report. In a sample of 190 healthy adults, increased exposure to life stress in infancy predicted cortical thickness reductions in the orbitofrontal cortex, a key region for affective processing. Neither life stress in childhood nor in adolescence was further related to abnormal brain development. Moreover, increased depressive symptoms in young adulthood were found in those previously exposed to life stress in infancy, and predicted cortical thickness reductions in later life. Finally, a mediation model revealed that depressive symptoms partially mediated the impact of life stress in infancy on abnormal brain maturation in the orbitofrontal cortex at the age of 25 years.

Study 2 investigated the predictive value of coping strategies in response to a natural stressor. In more detail, emotion regulation and inhibitory control were assessed in 104 participants during functional neuroimaging prior to the COVID-19 crisis, an unprecedented global stressor affecting physical and mental health. Stress burden due to the pandemic was recorded at three time points during the course of the crisis, that is four weeks after the initial lockdown during the first wave of the pandemic, then during the summertime when restrictions loosened and infection rates went down, and finally at the beginning of the second wave of the pandemic in late 2020 when case numbers exponentially increased. Higher neural activity in the inferior frontal gyrus during emotion regulation predicted less stress burden in consequence of the crisis at the first and second wave of the pandemic, whereas enhanced neural activity of the medial frontal gyrus during inhibitory control predicted diminished stress levels during the summer. These findings hold true after controlling for several important confounders, which were previously linked to stress reactivity. Therefore, adequate emotion regulation is particularly needed in the face of first-level threats, such as emotional distress and acute socio-affective challenges, which were caused by the immediate changes in everyday life at the beginning of the crisis when social contact restrictions were initially installed. In contrast, we propose that effective usage of inhibitory control is required in response to second-level threats, such as dealing with ongoing socio-economic challenges, which were present during the summer.

Taken together, our findings highlight the long-term impact of early life stress during infancy on brain structure in adults and point to a critical involvement of internalizing psychopathology. Given the high rates of early life adversities in clinical samples, future prevention strategies are particularly needed to overcome those long-term consequences. In addition, our findings emphasize the importance of effective coping mechanisms, such as adequate emotion regulation and inhibitory control, in response to a natural stressor. Therefore, we suggest early, easy to reach and affordable interventions delivered via smartphone or tablet to foster coping strategies in everyday life.