Fatty acids in context
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INTRODUCTION

In the first Part of this thesis we introduced MDD as a main health problem, and identified strategies to relieve MDD’s burden of disease. In the second Part, we introduced fatty acids and their roles in the pathophysiology of MDD, which suggested ways in which they could be applied to attenuate MDD’s health impact. In the third Part, we introduced two other main aspects of MDD’s pathophysiology: neuroendocrinological stress and emotional processing. Besides being two important aspects of MDD’s pathophysiology on their own, evidence suggests interesting cross-links of fatty acid metabolism with neuroendocrinological stress and emotional processing. In this fourth Part of the present thesis, we will describe our research on the cross-links of fatty acids with neuroendocrinological stress and emotional processing.

Considering the relationship of fatty acid metabolism with neuroendocrinological stress, preclinical evidence suggests that fatty acids can influence hypothalamic-pituitary-adrenal (HPA)-axis activity and feedback as described in more detail in the subsequent chapters of this part. The other way around, cortisol has been shown to affect fatty acid synthesis and breakdown. Nevertheless, the clinical associations between neuroendocrinological stress and fatty acid metabolism remained largely uninvestigated. In chapters 7, 8 and 9 we will describe studies in three independent samples investigating the association between fatty acid metabolism and HPA-axis activity.

Considering the relationship of fatty acid metabolism with emotional processing, several lines of evidence suggest interesting cross-links. Several studies observed a direct association between fatty acid concentrations (mainly omega-3 and omega-3/omega-6 ratio) and emotional processing. In addition, supplementation of omega-3 fatty acids proved to influence emotional processing in recovered depressed individuals. Some studies investigated associations with brain circuits that could underlie these effects. For example, fatty acid status has been associated with structure and function of limbic and controlling brain regions in healthy, neurologic and attention deficit hyperactivity disorder (ADHD) subjects. Also integrity of white matter connections between these regions was associated with fatty acid status. Nevertheless, the associations between fatty acids and brain activity of emotional processing regions in MDD remained uninvestigated. In chapter 10 we will describe the association between fatty acid metabolism and reactivity to emotional faces of a main limbic emotional processing brain structure: the amygdala.

In sum, in this fourth Part we will describe our studies on the relationships between fatty acids and the two other main pathophysiological aspects introduced in Part III: neuroendocrinological stress (chapter 7, 8 and 9) and emotional processing (chapter 10). We will finish this Part with a short overall discussion.