This Part of the thesis is based on (or adapted from) the following publications:

Focus on fatty acids in the neurometabolic pathophysiology of psychiatric disorders. Mocking RJ, Assies J, Ruhé HG, Schene AH. J Inherit Metab Dis. Under Review.


Part V: Clinical implications
INTRODUCTION

The existing evidence summarized in Part II, III, and IV for a role of fatty acid alterations in MDD pathophysiology resulted in several intervention trials aiming at correcting these alterations. Naturally, the most logical way to increase omega-3 fatty acid concentrations would be to eat more omega-3 fatty acids (e.g. fatty fish) and less omega-6 fatty acids. Several dietary trials are still underway in persons with psychiatric disorders, others already show potential of dietary modification, including increasing omega-3 fatty acid intake, e.g. from nuts and fish.\textsuperscript{1-3} For example, in depression, a well-conducted 12-week, single blind, randomized controlled trial of an adjunctive dietary intervention versus a social support protocol showed a promising number needed to treat of 4.1 for remission of depression in favor of the dietary intervention.\textsuperscript{4} Moreover, additive effects resulting from combination with other dietary and lifestyle factors, e.g. physical exercise, seems particularly promising.\textsuperscript{1,5-8} For example, an intervention composed of exercise and dietary management (versus standard health classes) in obese persons with serious mental illnesses as schizophrenia, bipolar disorder or MDD, led to more weight loss than comparable lifestyle-intervention trials in the general population.\textsuperscript{7}

Despite the above promising findings for lifestyle modification, it generally seems hard to implement, follow and maintain dietary guidelines. Many people do not yet manage to increase their dietary omega-3 fatty acid intake.\textsuperscript{3} Therefore, several trials attempted to correct fatty acid alterations using supplements. Most trials supplemented omega-3 fatty acids, mainly in the form of eicosapentaneoic acid (EPA) and/or docosahexaenoic acid (DHA). Some studies also supplemented arachidonic acid or other fatty acids. Most trials have been performed for mood disorders, some studies included patients with psychotic, anxiety or other disorders, including attention deficit hyperactivity disorder, autism spectrum disorder, or aggression.\textsuperscript{9-12}

In this part, we present two meta-analyses on the effects of omega-3 fatty acid supplementation for MDD and peripartum depression. In addition, we describe potential concerns regarding the supplementation of omega-3 PUFAs, particularly during pregnancy. By testing the effects of omega-3 fatty acids on oxidative stress in a third meta-analysis, we aim at providing more insight for which specific subgroups omega-3 fatty acid supplementation may help and for which subgroups it may have adverse effects.