Dietary patterns and depressive symptoms across different countries and ethnicities living in Europe

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CHAPTER 1

General introduction
Chapter 1

Depression

Depression is a common mental disorder that is characterized by persistent sadness, loss of interest and an inability to carry out daily activities for at least two weeks. Furthermore, this disease is associated with reduced quality of life and increased morbidity and mortality (1) and, at its worst, it can lead to suicide (2). Depression is estimated to affect more than 350 million people worldwide and due to its highly recurrent nature, it is a major contributor to the global burden of disease (2). Consequently, depression is ranked as the second highest cause of life lost due to disability (3) and it is expected to be ranked number one by 2020. Therefore, prevention of depression is a high priority in public health globally.

Depression has a multi-causal pathogenesis and shares several underlying mechanisms with cardiovascular disease (CVD) (4-6), with elevated inflammation markers and obesity being mostly investigated. More specifically, epidemiological evidence from meta-analyses demonstrate that higher levels of inflammatory biomarkers, such as C-reactive protein and necrosis factor α modulate the synthesis, release and re-uptake of mood-related neurotransmitters (e.g. serotonin and dopamine) (7), which in turn is related to higher depressive symptoms (8-10). Furthermore, there is an increasing amount of evidence for obesity to be linked to higher depressive symptoms (11-13) with one of the most important underlying mechanisms being chronic inflammation (13).

In general, two definitions are applied for depression. The first definition is depression and is based on a clinical diagnosis. The second definition is based on a questionnaire and is often defined as depressive symptoms when using continuous scores or depressed mood when using a cut-off point, which is indicative for depression.

Diet and depressive symptoms

Nutrition plays an important role in preventing CVD and is closely linked to obesity. Moreover, due to the shared underlying mechanisms of CVD, obesity and depression, nutrition is being increasingly investigated in relation to depression as well (14). Evidence from systematic reviews indicate that dietary nutrients, like omega-3 fatty acids, B vitamins and several minerals may indirectly influence the underlying mechanisms of depressive symptoms (15, 16), such as inflammation, oxidative stress and maintenance of normal brain function. This may be through their anti-inflammatory, anti-oxidant and neurotransmitter signalling properties. In particular, there are several nutrients that have been commonly studied in relation to depressive symptoms. Recent meta-analyses of randomized controlled trials indicate that supplementation of eicosapentaenoic acid and docosahexaenoic
acid may be inversely associated with prevalent depressive symptoms (17, 18), possibly by influencing neurotransmitter signalling, which in turn contributes to the maintenance of normal brain function. Furthermore, a systematic review of prospective studies indicates an inverse association of magnesium supplementation in relation to depressive symptoms (19). This inverse association is supported by a recent randomized controlled trial that found a protective effect of magnesium supplementation for depressive symptoms (20). Possible underlying mechanisms for this association are that magnesium plays a role in several pathways such as inflammation, hormones and neurotransmitters involved in mood regulation (21). There are also indications that folate is associated with lower depressive symptoms from a systematic review (22) and a cross-sectional meta-analysis (23) that investigated several B vitamins, although the evidence is not consistent. The potential biological pathway for the folate-depressive symptoms relationship is that low levels of folate are related to low serotonin levels, which in turn is related to low mood. The strongest evidence is found for zinc, as a meta-analysis of randomized controlled trials found a protective effect (24) and a meta-analysis of observational studies an inverse association (25) for supplementation of this mineral and depressive symptoms. In contrast to the possible protective effect of the abovementioned nutrients on depressive symptoms, there are indications from prospective cohort studies that saturated fatty acids (26) and mono-disaccharides (sugar) (27-29) are positively related to depressive symptoms. Potential biological mechanisms for these macronutrients to be related to depressive symptoms are endothelial dysfunction, pro-inflammatory changes, insulin resistance (30) and obesity (28).

Overall, evidence for separate nutrients to be related to depressive symptoms is still scarce and somewhat conflicting. This may be explained by the fact that most chronic diseases, specifically depression with its multi-factorial nature, are most likely associated with several nutrients or foods (31). Furthermore, people do not consume isolated nutrients, but they eat meals consisting of multiple foods with complex combinations of nutrients that are likely to be synergistic and highly correlated, making it difficult to examine their separate effects (32). Hence, a shift has been observed from studying separate nutrients and foods to examining dietary patterns, or combinations of nutrients and foods, which are often represented as total diet or as the key factors of diet (33). More specific, two recent randomized controlled trials performed in Australia observed a protective effect for a ‘healthy Mediterranean’ dietary pattern to lower depression in patients (34, 35). Moreover, systematic reviews and meta-analyses indicated that higher consumption of ‘healthy’ dietary patterns (characterized by high intakes of vegetables, fruit, olive oil, fish, whole grains, nuts and legumes and low intakes of meat and processed foods) are associated with lower depressive symptoms (36, 37).
However, the trials and the majority of the observational studies have not included ethnically diverse populations or older adults for whom the diet-depressive symptoms relationship may differ. Moreover, in contrast to the evidence for ‘healthy’ dietary patterns to reduce depressive symptoms and the risk of depression, evidence is less consistent concerning the relationship between ‘unhealthy’ dietary patterns (characterized by high intakes of sugary and fatty foods) and higher depressive symptoms (36). Only three prospective studies observed that consumption of ‘unhealthy’ dietary patterns were associated with higher depressive symptoms (38-40) whereas four prospective studies failed to find an association (41-44). Due to this contradictory evidence and because the research field of nutrition and mental health is fairly new, more studies are needed in diverse populations to get more insight into the ‘unhealthy’ dietary patterns-depressive symptoms relationship. Indeed, the scientific report of the 2015 Dietary Guidelines for Americans advisory committee concluded that current evidence is still limited for the diet-depressive symptoms relationship (45).

Studies of the link between dietary patterns and depression use a priori (hypothesis-driven quality scores) or a posteriori (driven by the underlying dietary data) methods to derive dietary patterns. These methods have several shortcomings. A priori methods only include specific foods that are hypothesized to have an effect on health and hereby may miss other relevant foods, while a posteriori methods may not optimally represent dietary patterns most relevant to the outcome under study due to sole reliance on inter-correlations among dietary variables. Reduced rank regression (RRR) shows complementary value in identifying dietary patterns by combining both methods. Dietary patterns are derived in an exploratory way using the whole diet (similar to Principal Component analysis) while also using a priori knowledge of nutrients/biomarkers that are thought to link diet to disease; these are used as response variables in deriving dietary patterns. RRR-derived dietary patterns are therefore more reflective of food groups that are strongly related to depressive symptoms and due to the data-driven approach, more likely to identify and incorporate ethnic-specific dietary patterns, which may provide new insights in the relationship between diet and depression (46, 47).

Diversity in depression and diet across countries and ethnicities

There is great variation in dietary patterns and the prevalence of depression across and within European countries. In particular, South-European countries such as Italy are known for their ‘healthy’ Mediterranean style dietary pattern, whereas countries like the Netherlands and the UK generally consume a less healthy, ‘Western style’ dietary pattern. Moreover, a relatively lower number of prevalent depression cases is observed in Southern European countries compared to
Northern European countries, perhaps due to diet. Besides differences in eating habits and depression prevalence across countries, heterogeneity in dietary patterns and depression prevalence is observed within countries as well, due to the multi-ethnic society we are currently living in. For example, ethnic minority groups living in Europe consume different dietary patterns as ethnic-specific foods are an important part of their diet and the prevalence of depressive symptoms is higher in these groups than for the host population (48, 49). Despite the known health inequalities across ethnic groups and the fact that European populations are becoming increasingly ethnically diverse, the majority of studies that investigated the relationship between dietary patterns and depressive symptoms included populations with limited ethnic diversity.

The multi-factorial nature of depression makes it challenging to understand what potential mechanisms are related to this disease. Due to the broad variation in culture, age and ethnic background in and between studies, we are able to examine the diet-depressive symptoms relationship from different angles in this thesis. By comparing different countries and populations, we may get more insight into if this relationship is explained by biological mechanisms or whether it is more a reflection of lifestyle characteristics and environmental factors. When biological mechanisms play an important role in the relationship between diet and depression, we expect to find consistent relationships across studies. When the diet-depressive symptoms relationship is more a reflection of lifestyle characteristics and environmental factors, we expect to find less consistent results as there are major differences in the above-mentioned characteristics across studies.

**Aim of the thesis and research questions**

The overall aim of this thesis is to identify dietary patterns that may be related to depressive symptoms and test these associations in different populations, including ethnic minorities, living in Europe. Furthermore, this thesis explores some potential underlying mechanisms of depressive symptoms that may be influenced by diet. These aims will be addressed in three objectives:

1. To investigate the relationship of ‘healthy’ dietary patterns with depressive symptoms. Is this association consistent in different populations and ethnic groups?

2. To study the relationship of ‘unhealthy’ dietary patterns with depressive symptoms. Is this association consistent in different populations and ethnic groups?

3. To explore the underlying mechanisms for the relationship between dietary patterns and depressive symptoms.
Chapter 1

Study designs

The studies described in this thesis were based on three sources of data that were part of the MooDFOOD ‘Multi-country cOllaborative project on the rOle of Diet, FOod-related behaviour, and Obesity in the prevention of Depression’ project.

The HELIUS study
The HELIUS (Healthy Life in an Urban Setting) study is a large, multi-ethnic cohort study which aims to unravel the causes of the unequal burden of disease and included Surinamese, Turkish, Moroccan and Dutch ethnic groups living in Amsterdam, the Netherlands. Ethnicity was defined according to the country of birth of the participant as well as that of his/her parents. Participants, aged 18-70 years, were recruited randomly, but stratified by ethnicity, through the municipality registry of Amsterdam. Baseline data collection took place from 2011 until 2015 among nearly 25,000 participants. The current study is a sub-sample of the HELIUS study and included 5,188 participants that completed an additional ethnic-specific food frequency questionnaire (FFQ).

The InCHIANTI study
The InCHIANTI (Invecchiare in Chianti, aging in the Chianti area) study is an ongoing Italian population-based cohort study performed in two sites in Tuscany, Italy (Greve in Chianti and Bagno a Ripoli). Baseline data collection took place from 1998 until 2000 and follow-up data were collected after 3, 6 and 9 years (from 2001-2003, 2004-2006 and 2007-2009, respectively). At baseline, 1,453 people were randomly recruited for the study using a multistage sampling method and included participants were aged 20-102 years.

The Whitehall II study
The Whitehall II study is an ongoing cohort study performed in London, the United Kingdom (UK) among 10,308 British civil servants aged 35-55 years. Baseline data collection (phase 1) took place in 1985-1988 and follow-up data on diet was collected in intervals of 5 years from 1991-1993 (phase 3) until 2016 (phase 12) and depressive symptoms from 2003-2004 (phase 7) onwards. Analyses were restricted to participants with complete data on diet at phase 7 and depressive symptoms at phases 7 and 9. Therefore, we were able to include 5,044 participants at phase 7 and 4,515 participants at phase 9.
Outline of the thesis

Part I: Healthy dietary patterns and depressive symptoms

Chapter 2  The association between dietary patterns derived by reduced rank regression and depressive symptoms over time: the InCHIANTI study

Chapter 3  Dietary pattern derived by reduced rank regression and depressive symptoms in a multi-ethnic population: The HELIUS Study

Part II: Unhealthy dietary patterns and depressive symptoms

Chapter 4  A combined high-sugar and high-saturated fat dietary pattern is associated with more depressive symptoms in a multi-ethnic population: the HELIUS study

Chapter 5  High-sugar, high-saturated fat dietary patterns do not associate with depressive symptoms in mid-life men and women: prospective study

Part III: Underlying mechanisms for the relationship between dietary patterns and depressive symptoms

Chapter 6  Inflammatory dietary patterns and depressive symptoms in Italian older adults

Chapter 7  The mediating role of BMI on the association between dietary patterns and depressive symptoms
Table 1. Overview of chapters presented in this thesis

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References


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