Brain, Behavior, and Immunity xxx (2017) xxx–xxx

Contents lists available at ScienceDirect

Brain, Behavior, and Immunity

journal homepage: www.elsevier.com/locate/ybrbi

Full-length Article

# Inflammatory dietary patterns and depressive symptoms in Italian older adults

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ARTICLE INFO

*Article history:*
Received 25 April 2017
Received in revised form 6 September 2017
Accepted 9 September 2017
Available online xxxx

*Keywords:*
Inflammatory dietary patterns
Inflammation
Reduced rank regression
Depressive symptoms
Older adults

ABSTRACT

*Background:* Older adults are more susceptible to higher inflammatory levels and depression. Moreover, diet may influence inflammation as well as depression but no previous study examined whether inflammatory dietary patterns are related to depression in an older population.
To investigate the longitudinal association between inflammatory dietary patterns (using reduced rank regression (RRR)) and depressive symptoms in a population sample of Italian older adults.
*Methods:* We included 827 participants (aged ≥ 65 years) at baseline in 1998. Follow-up measurements were collected after 3, 6 and 9 years. We used RRR to identify inflammatory dietary patterns at baseline. The Centre for Epidemiologic Studies Depression (CES-D) scale was used to assess depressive symptoms by using continuous scores and depression by using a cut-off point (CES-D ≥ 20).
*Results:* We identified two inflammatory dietary patterns using different sets of response variables. Dietary pattern I was related to inflammatory markers C-reactive protein (CRP), interleukin (IL)-6, tumor necrosis factor α and was characterized by high intakes of refined grains, sweet snacks, pasta and rice. After full adjustment for confounders, no longitudinal association was found when comparing extreme quartiles of this dietary pattern and depressive symptoms (Q1 vs Q4, model 4: B = 0.04, 95% CI: −0.06, 0.13) or depression (Q1 vs Q4, model 4: OR = 0.90, 95% CI: 0.55, 1.45). Dietary pattern II was related to inflammatory markers CRP, IL-18, IL-1β, IL-1 receptor antagonist and was characterized by high intakes of pasta, sugar-sweetened beverages, processed meat and chocolate and sweets. When comparing extreme quartiles, this dietary pattern was not longitudinally associated with depressive symptoms (Q1 vs Q4, model 4: B = −0.04, 95% CI: −0.13, 0.05) but an inverse association was found for depression (Q1 vs Q4, model 4: OR = 0.56, 95% CI: 0.40, 0.94).
*Conclusion:* Our study does not support the hypothesis that dietary patterns linked to inflammatory markers are associated with higher depressive symptoms and higher depression incidence. However, dietary intake in our population of older adults was quite homogeneous which makes it difficult to show clear associations.



## 1. Introduction

Depression is a mental health disorder that is highly prevalent in older adults and is associated with reduced quality of life and increased morbidity and mortality rates (Charney et al., 2003; Blazer, 2003). An important predictor for depression in this specific age group is the number of chronic diseases, with inflammatory processes as a common link (Vink et al., 2008; Howren et al., 2009). Furthermore, there is a growing body of evidence that higher levels of the inflammatory biomarkers C-reactive protein (CRP), interleukin (IL)-6, tumor necrosis factor α (TNF-α) and IL-1 are related to higher depressive symptoms (Howren et al., 2009; Goldsmith et al., 2016; Haapakoski et al., 2015; Hiles et al., 2012;

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http://dx.doi.org/10.1016/j.bbi.2017.09.005
0889-1591/

Milaneschi et al., 2009). A suggested underlying mechanism for this link is that pro-inflammatory markers modulate the synthesis, release and re-uptake of mood-related neurotransmitters (e.g. serotonin and dopamine) (Sanchez-Villegas and Martinez-Gonzalez, 2013; Miller and Raison, 2016).

The origin of the mild pro-inflammatory state, that is typical in older persons, is still not clear but there is some evidence that inflammation is sustained in part by modifiable lifestyle factors, such as physical activity and diet (Luciano et al., 2012; Collard et al., 2015). Moreover, consuming an unhealthy dietary pattern, with high intakes of high-sugar and high-fat snacks, sugar-sweetened beverages, processed meat and fast foods, might increase the risk of depression (Akbaraly et al., 2009; Le Port et al., 2012; Jacka et al., 2017). Therefore, investigating the role of diet and depression and the influence of inflammation in older adults is needed. There is an increasing amount of evidence that inflammation is influenced by diet (Barbaresko et al., 2013; Minihane et al., 2015; Esmaillzadeh et al., 2007; Lopez-Garcia et al., 2004) but until now, few studies investigated the relationship between dietary patterns, inflammation and depressive symptoms in older adults, with contrasting results (Luciano et al., 2012; Milaneschi et al., 2011). Milaneschi et al. found that a Mediterranean diet can buffer the effect of depression on IL-6 inflammation levels in older Italian adults (Milaneschi et al., 2011), while a Scottish study did not find a moderating effect of a Mediterranean diet in the depressive symptoms-inflammation relationship (Luciano et al., 2012). Another study, performed in the same sample, investigated dietary patterns in relation to inflammation and observed that a Mediterranean diet was associated with lower fibrinogen levels, but not with lower CRP levels. In contrast, a "health aware" (low-fat) diet was associated with lower CRP levels (Corley et al., 2015). These previous studies support the hypothesis that a Mediterranean dietary pattern may prevent or downregulate inflammation. However, more recent studies suggest that inflammation is more likely to be influenced by 'unhealthy' Western-type dietary patterns (Barbaresko et al., 2013; Esmaillzadeh et al., 2007). Additionally, strong evidence for the link between unhealthy dietary patterns and inflammation has been offered by recent studies that have explored the inflammatory potential of dietary patterns in relation to depression by using the dietary inflammatory index (DII). These studies have consistently observed that a more pro-inflammatory dietary pattern was related to higher depressive symptoms (Shivappa et al., 2016; Sanchez-Villegas et al., 2015; Akbaraly et al., 2016; Lucas et al., 2014). All these recent studies on unhealthy dietary patterns were performed in middle-aged populations, while there are some suggestions in the literature that unhealthy Western-type dietary patterns are related to higher depressive symptoms in middle-aged adults (Akbaraly et al., 2009; Le Port et al., 2012; Jacka et al., 2017) but not in older adults (Chan et al., 2014; Gougeon et al., 2015).

In summary, older adults are more susceptible to higher inflammatory levels as well as depression (Organization, 2016; Panda et al., 2009; Krabbe et al., 2004). Diet may influence inflammation as well as depression, to our knowledge, no previous studies examined the influence of inflammatory dietary patterns on depression in an older population. Therefore, the objective of this study is to investigate the longitudinal association between inflammatory dietary patterns (using reduced rank regression (RRR)) and depressive symptoms in a population sample of older Italian adults. RRR allows us to empirically identify inflammatory dietary patterns by incorporating disease-specific inflammatory biomarkers as intermediate response variables in deriving these dietary patterns. We hypothesize to identify unhealthy dietary patterns that are highly associated to the included inflammatory biomarkers. Consequently, it is expected that higher consumption of these unhealthy dietary patterns are related to higher depressive symptoms and depression.

## 2. Methods

### 2.1. Subjects and study design

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) among 1155 older adults (≥65 years). Baseline data collection took place from 1998 until 2000 and follow-up data were collected after 3, 6 and 9 years (from 2001 to 2003, 2004 to 2006 and 2007 to 2009, respectively). Participants conducted a home interview where data on lifestyle, diet and depression was collected. Consequently, a clinical examination was performed at the study location within 21 days after the home interview. More information about the study protocol can be found elsewhere (Ferrucci et al., 2000). The ethics committee of the Italian National Institute of Research and Care on Aging approved the study protocol and informed consent was obtained from all individual participants included.

### 2.2. Depressive symptoms assessment

Depressive symptoms were measured by using the Centre for Epidemiologic Studies Depression (CES-D) scale at baseline and after 3, 6 and 9 years and was completed by the participants during the home interview (Radloff, 1997). The CES-D is a 20-item self-report questionnaire with scores ranging from 0 to 60 points. In this study, we used continuous CES-D scores, hereafter referred to as "depressive symptoms" and CES-D scores as dichotomous outcome (CES-D ≥20), hereafter referred to as "depression". The cut-off point of CES-D scores ≥20 has been previously validated for identifying depression in older adults (Beekman et al., 1997) and an Italian population (Fava, 1983).

### 2.3. Laboratory procedures of inflammatory markers

During the clinical examination at baseline, blood samples were drawn in the morning after an overnight fast of almost 12 hours and after participants had been sedentary for at least 15 minutes. A 60-ml blood sample was drawn and delivered within two hours to the central laboratory that performed several tests of hematology and clinical chemistry and prepared the samples for the biological bank and were stored at −80 °C. The samples had never been previously thawed until 2003, when they were used to measure circulating levels of cytokines. Serum CRP was measured in duplicate with the Dade Behring (now Seimens) BNII nephelometer (Dade Behring Inc., Deerfield, IL, USA). Serum levels of Soluble IL-6, IL-1β, IL-1ra, TNF-α receptor II (kits from BIOSOURCE International, Camarillo, California) and IL-18 (kits from Quantikine HS, R&D Systems, Minneapolis, Minnesota) were measured by ELISA kits. The inter-assay coefficients of variation were as follows: 4.5% for IL-1ra, 5% for CRP and 7% for IL-6, TNF-α, IL-1β and IL-18.

### 2.4. Dietary pattern assessment at baseline

A country-specific validated food frequency questionnaire (FFQ) from the European Prospective Investigation into Cancer study was used to collect dietary data at baseline and contained 248 questions with 188 different food items (Riboli et al., 2002; Pala et al., 2003). The validation procedure for the FFQ has been described in more detail elsewhere (Pisani et al., 1997).

Please cite this article in press as: Vermeulen, E., et al. Inflammatory dietary patterns and depressive symptoms in Italian older adults. Brain Behav. Immun. (2017), http://dx.doi.org/10.1016/j.bbi.2017.09.005