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Original Research

Inflammation mediates the association between fatty acid intake and depression in older men and women

Jun S. Lai[a], *Christopher Oldmeadow*[b], *Alexis J. Hure*[a,b], *Mark McEvoy*[a,b,*], *Sarah A. Hiles*[c], *Michael Boyle*[d], *John Attia*[a,b,d]

[a] *School of Medicine and Public Health, University of Newcastle, Callaghan, NSW 2308, Australia*
[b] *Hunter Medical Research Institute, New Lambton Heights, NSW 2305, Australia*
[c] *Department of Psychiatry, VU University Medical Center, Amsterdam 1070BB, The Netherlands*
[d] *Division of Medicine, John Hunter Hospital, New Lambton Heights, NSW 2305, Australia*

ARTICLE INFO

Article history:
Received 8 September 2015
Revised 24 November 2015
Accepted 26 November 2015

Keywords:
Carotenoid
Fatty acid
C-reactive protein
Interleukin-6
Depression

ABSTRACT

Antioxidants and fatty acids are associated with depression and inflammation, and inflammation appears to predict depression risk; hence, the associations between these nutrients and depression may be mediated by inflammation. We hypothesized that inflammatory markers interleukin (IL)-6 and C-reactive protein (CRP) mediate the associations between antioxidant and fatty acid intakes, and depression. Participants were from the Hunter Community Study, a longitudinal cohort of adults aged 55-85 years. Dietary intake was assessed using the Older Australian's Food Frequency Questionnaire. Fasting blood samples were drawn for analysis of nutrient and inflammatory biomarkers. Depressive symptoms were assessed using the 20-item Center for Epidemiologic Studies—Depression scale at baseline and at 5-year follow-up. Linear mixed models were used to investigate longitudinal associations between dietary intakes and depression, and mediation analyses were carried out to determine if IL-6 and/or CRP were the mediators. Analyses were conducted on men and women separately and adjusted for potential confounders. Fruit and monounsaturated fat intakes were negatively associated with depression, whereas total fat and saturated fat intakes were positively associated with depression in both sexes. Omega-3 polyunsaturated fat was inversely associated with depression in men only. IL-6 was a significant mediator of the association between fruits with low carotenoid content and depression in women. CRP significantly mediated the relationship between total fat, saturated fat, and monounsaturated fat intakes and depression in women, and saturated fat intake and depression in men. Our findings raise the possibility that the association between fatty acid intake and depression is partially mediated by inflammatory markers.

Abbreviations: BMES, Blue Mountain Eye Study; BMI, body mass index; CES-D, Center for Epidemiologic Studies—Depression scale; CRP, C-reactive protein; FFQ, Food Frequency Questionnaire; HCS, Hunter Community Study; IL-6, interleukin-6; MUFA, monounsaturated fat; n-3 PUFA, omega-3 polyunsaturated fat; SFA, saturated fat.

* *Corresponding author*. Tel.: +61 2 40420518.
E-mail addresses: jun.lai@uon.edu.au (J.S. Lai), christopher.oldmeadow@hmri.com.au (C. Oldmeadow), alexis.hure@newcastle.edu.au (A.J. Hure), mark.mcevoy@newcastle.edu.au (M. McEvoy), s.hiles@vumc.nl (S.A. Hiles), michael.boyle@hnehealth.nsw.gov.au (M. Boyle), john.attia@newcastle.edu.au (J. Attia).

http://dx.doi.org/10.1016/j.nutres.2015.11.017
0271-5317/

1. Introduction

Depression is a highly prevalent mental health disorder that results in substantial disability [1]. Much work has been devoted to understanding the cause of depression to allow for development of prevention and treatment strategies. The pathophysiology of depression is understood to be influenced by endocrine, immunological, and metabolic mediators, and cellular, molecular, and epigenetic forms of plasticity [2]. In particular, several lines of research have implied that systemic, low-grade inflammation may have a causative role in the onset of depression [2,3]. Inflammatory markers such as interleukin (IL)-6, tumor necrosis factor–α, interferon-α, and C-reactive protein (CRP) may modulate the synthesis, release, and reuptake of neurotransmitters which are involved in mood regulation [2]. Inflammatory cytokines may also exert effects on the hypothalamic-pituitary-adrenal axis hormones where high levels of corticotrophin-releasing-hormone and cortisol are suggested to contribute to the signs and symptoms of depression [2]. Administration of low doses of proinflammatory cytokines to rodents resulted in depression-like behavior including social withdrawal, and decreased exploratory and sexual behavior [4]. High concentrations of inflammatory markers have also been found in depressed patients [3,5]. Thus, the causal connection between inflammation and depression is plausible.

Emerging evidence from epidemiological studies has shown how various dietary components are associated with inflammation and depression. Studies have found higher intake of omega-3 polyunsaturated fat (n-3 PUFA) to be associated with lower inflammatory cytokine production [6]. Likewise, consumption of fish or n-3 PUFA supplements may be associated with lower depression risk [7]. Antioxidants and phytochemicals (usually found in fruits and vegetables) may be beneficial in reducing levels of inflammation [8], and a diet high in fruit and vegetables has been demonstrated to be associated with reduced odds of depression [9]. Conversely, diets characterized by high glycemic index [10] and high saturated fat (SFA) [11] may be associated with elevated levels of inflammatory markers. This nutrient profile is typical of a Western diet that includes high amounts of refined grains, red and processed meat, and fast food, which is potentially associated with an increased risk of depression [9]. In other words, diets rich in anti-inflammatory components may reduce the risk of depression, whereas proinflammatory diets could fuel depressive symptoms.

Current large-scale epidemiological evidence suggests consumption of a diet high in fish, fruit and vegetables, and whole grains may reduce depression risk [9]. However, these results have been somewhat inconsistent. This may be due to the fact that many studies examining diet and depression do not incorporate existing knowledge of nutrient-disease associations or possible mechanisms linking the diet-depression relationship, and may not capture the aspect of diet most relevant to depression.

A number of studies have examined the association between dietary intake and inflammation [6,8,11] or the association between inflammation and depression [3]. Others have examined the association of dietary intake with depression [7]. However, it is not known whether inflammatory markers mediate the relationship between diet and depression. Based on available evidence, we hypothesized that nutrients with anti- or proinflammatory properties such as antioxidants and fatty acids would be associated with depressive symptoms and that inflammatory markers IL-6 and CRP would mediate these associations. Therefore, we aimed to (1) explore the prospective associations between carotenoids, vitamin E, fatty acids, fruit and vegetables, and depressive symptoms among a group of older Australian adults and (2) test the potential mediating effects of inflammatory markers using mediation analyses.

2. Methods and materials

2.1. Study sample

Data for this study were drawn from the Hunter Community Study (HCS), which is a population-based cohort study of adults aged 55-85 years at recruitment residing in Newcastle, New South Wales, Australia [12]. Study participants were randomly selected from the New South Wales State Electoral Roll and recruited between December 2004 and December 2007. A total of 3254 individuals participated in the study. The HCS participants were similar in sex and marital status to the national profile but were slightly younger [12]. At baseline, all participants were required to attend a face-to-face clinical assessment at the HCS clinic with trained study assessors, provide a fasting blood sample, and complete a series of self-report questionnaires which included assessment of dietary intake and depressive symptoms (for details on measures, see McEvoy et al, 2010) [12]. In 2010, participants were invited to complete follow-up questionnaires, and 2250 participants completed the follow-up. Full methodological details have been published previously [12]. The present study was restricted to participants who had complete dietary data, provided a blood sample, and completed the assessment for depressive symptoms (n = 2035). The HCS has received ethics approval from the University of Newcastle Research Ethics Committee (H-820-0504). Written informed consent was obtained before participants were enrolled in the study.

2.2. Assessment of dietary intake

Dietary intake was assessed at baseline using the self-administered Older Australian's Food Frequency Questionnaire (FFQ). This 145-item semiquantitative FFQ was developed by the Blue Mountain Eye Study (BMES) specifically for use with older Australians [13]. Participants were required to indicate their usual frequency of foods consumed in the past year, with 9 categorical frequency options: "never" to "four or more times per day." Open-ended questions were included on the types of fruit juices, breakfast cereal, and other frequently consumed foods that were not included in the list. The FFQ also assessed dietary supplements use. The FFQ has been validated twice, against 4-day weighed food records in the BMES [13] and against plasma biomarkers in the HCS [14]. This FFQ demonstrated reasonable validity against both self-reported and objective biochemical measures. The correlation coefficient for