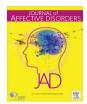


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Review article

# Tea, cocoa, coffee, and affective disorders: vicious or virtuous cycle?



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## ABSTRACT

Background: The prevalence of psychiatric disorders is increasing worldwide, which underscores the importance of increasing research in this field, in terms of better detection, prevention based on improvement of lifestyle and diet, and effectiveness of treatment. Increasing evidence suggest that diet and exercise can affect proper neuronal development and physiology and protect the brain from neurological illnesses or injuries. Of note, cocoa, tea, and coffee are being actively investigated because they are rich in (poly)phenolic compounds that can modulate mental health, namely brain plasticity, behavior, mood, depression, and cognition.

*Methods:* We here systematically review human studies conducted on tea, cocoa, and coffee as related to affective disorders such as depression and anxiety. We carried out a systematic literature search in April 2016, using MEDLINE, on data from the last 10 years. After screening 955 articles, we selected 17 articles that met the criteria of being human studies and that used whole foods or their components.

Results: The results of our systematic review indicate that consumption of tea, cocoa, or coffee might have protective effects against depression.

Conclusions: Even though this is encouraging, it should be underscored that the near totality of the current evidence comes from observational studies. Ad-hoc human trials and mechanistic, basic science studies are needed before we can provide sound advice to the public.

## 1. Introduction

The prevalence of psychiatric disorders is increasing worldwide (Vigo et al., 2016). In the EU (with a population of 466 million), at least 21 million people are affected by depression, out of which almost 80% are men. Treatment of psychiatric disorders is very expensive: the total annual cost of depression in Europe was estimated to be 118 billion  $\mathfrak E$  in 2004, which corresponds to a cost of 253  $\mathfrak E$  per inhabitant. The cost of depression alone accounts for 1% of the total EU economy (Trebaticka and Durackova, 2015). These figures underscore the importance of increasing research in this field, in terms of better detection, prevention based on improvement of lifestyle and diet, and effectiveness of treatment.

The main types of affective disorders are depression, bipolar disorder, and anxiety disorder, all of which can be mild or severe (Global Burden of Disease Study, 2015). Some basic science studies suggest that neurotransmitter imbalances, increased neuronal inflammation, defects in neurogenesis and synaptic plasticity, mitochondrial dysfunction, and redox impairments play etiological roles (Visioli and Burgos-Ramos, 2016).

Increasing evidence suggest that diet and exercise can affect proper

neuronal development and physiology and protect the brain from neurological illnesses or injuries (Chin et al., 2015; Jackson et al., 2016; Visioli and Burgos-Ramos, 2016). Of note, cocoa, tea, and coffee are being actively investigated because they are rich in (poly)phenolic compounds that can modulate mental health, namely brain plasticity, behavior, mood, depression, and cognition (Visioli and Burgos-Ramos, 2016). Specifically, polyphenolic compounds might play important roles because of their manifold biological activities such as metal ion (Fe, Cu, and others) chelation, modulation of antioxidant enzyme activities antioxidant ability, and anti-inflammation (Giordano et al., 2014; Nicod et al., 2014).

We here systematically review human studies conducted on tea, cocoa, and coffee as related to affective disorders such as depression and anxiety.

#### 2. Methods

#### 2.1. Literature selection

We carried out a systematic literature search in April 2016, using MEDLINE. Our search strategy combined the following keywords: tea,

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cocoa, coffee, depression, anxiety, and affective disorder. We limited our search to the last ten years and to papers published in English. In addition, we performed a manual search of references from review articles, to identify additional relevant trials.

The first PubMed search identified 955 articles: 427 articles using the keyword coffee combined with depression, anxiety, and affective disorder, 99 articles resulting of the combination of cocoa and the same keywords, and 429 in the case of tea. In the first step, we eliminated duplicate citations and we then refined the search to: (a) studies in humans; (b) studies in English; (c) studies in the last 10 years; and (d) text available through direct or indirect links. After this screening, we obtained a total of 294 articles: 146 for coffee, 41 for cocoa, and 107 for tea. In the next step, we excluded reviews and select the articles which the title and abstract were directly related with the topic of our paper and also the whole food or its components were used. In the end, we selected 17 articles that met our criteria and prepared three Tables, i. e. one for each food item (tea, cocoa, and coffee) and its association with affective disorders. The most important aspects we delineated were: first author, publication year, sex and age, exposure, study design, results, adjusts, and the conclusion (positive, negative, or null associations).

#### 3. Results

Table 1 shows the nine articles that reported associations between the intake of tea and the incidence of affective disorders, specifically depression. The total amount of subjects studied in the nine selected trials were 276666, although one of them (Guo et al., 2014) contributed the largest population. Two of these articles show null associations between tea intake and risk of depression. While Ruusunen and colleagues shown a RR of 1.19 (95% CI, 0.54-2.23) between tea drinkers and non-drinkers (Ruusunen et al., 2010), Guo et al. observed ORs of 1.03 for iced-tea and 1.14 for hot tea (95% CI) comparing ≥4 cans/cups per day with none (Guo et al., 2014). In the latter study, an association was found between tea sweetened with sugar or honey and lower risk of depression (0.95, 95% CI, 0.83-1.04). The rest of the studies show that daily tea use is associated with a reduced risk of becoming depressed, with OR values between 0.47 and 0.96 (95% CI). Pham and colleagues observed - in a cross-sectional study - that participants consuming ≤1 cup/d and those consuming ≥4 cups green tea/d had a 51% significantly lower prevalence of depressive symptoms (Pham et al., 2014). In the study of Yoto et al., the authors attributed the protective effect of tea to its content in the amino acid L-theanine (Yoto et al., 2012). In addition, Chen and colleagues showed that regular tea consumption (>100 g dried tea leaves/m) is inversely associated with overall depression (OR, 0.39; 95% CI, 0.19-0.84) in breast cancer survivors (Chen et al., 2010). Therefore, tea consumption might be useful to prevent depression in this type of patients.

Table 2 outlines the papers that associated the intake of cocoa with affective disorders, specifically with depression. The total amount of subject studied in the six selected trials was 8779. One of those, which studied a large (~4.500 subjects) prospective cohort aimed at evaluating the association of regular chocolate consumption with physical and mental components of health-related quality of life. After ~3.5 years of follow-up, no association became apparent between chocolate intake and incidence of mental illness (Balboa-Castillo et al., 2015). The other paper is a cross-sectional analysis that evaluated the mood of 1.018 adults (694 men and 324 women) using the Center for Epidemiologic Studies Depression Scale (CES-D). Interestingly, the authors found that higher CES-D scores were associated with greater chocolate consumption (Rose et al., 2010). However, four studies indicate a positive association between cocoa intake and affective disorders. Ibero-Baribar et al. studied the effects on affective disorders of a supplementation with 645 mg of cocoa polyphenols/day and a restricted diet compared with a control group, during one year of follow up. They observed that depressive symptoms decreased in both groups after the intervention

(control: -9.4%, P < 0.001; cocoa: -6.3%, P=0.008) and they concluded that cocoa extract intake is associated with depressive symptoms, but not with anxiety symptoms (Ibero-Baraibar et al., 2016). A study published by Pase and colleagues employed similar administrations of 500 gr, 250 gr, or 0 gr/d, for one month. Cocoa polyphenols did ameliorate symptoms associated with clinical anxiety or depression (Pase et al., 2013). Martin et al. studied two groups with high or low anxiety, which were assigned to a) milk chocolate snack (n =16 high anxiety trait, 14 low anxiety trait), b) dark chocolate (n =13, n=17), or c) cheese and crackers (n =15, n=15). The authors measured mood changes immediately and up to one hour after consumption and observed an association between milk chocolate ingestion and lower anxiety levels. These results were not seen with dark chocolate which conversely - increased anxiety levels (Martin et al., 2012). Finally, Parker et al. observed - in a cross-sectional analysis - that the intake of chocolate is beneficial for depression, anxiety, and irritability and that it is specifically associated with personality traits (Parker and Crawford, 2007).

Table 3 reports the available studies on the associations between coffee intake and affective disorders, namely depression. The total amount of subject studied in the only two trials reviewed in this study was 50828, with the Nurses' Health Study contributing the largest population (Lucas et al., 2011). Omagari et al. studied, in a crosssectional study, this association in patients with diabetes, by comparing the intake of coffee with symptoms of depression measured with the Japanese version of the Hospital Anxiety and Depression scale. The authors concluded that there were more (36.5%) patients in the nondepressed group (who drank three or more cups of coffee per day) than in the depressed group (7.1%), with a p value of 0.032 (Omagari et al., 2014). The investigation of Lucas and colleagues is relevant because it employs a larger sample size, totaling 50,739 U.S. women free from depressive symptoms (Lucas et al., 2011). That study also reported a positive association between coffee consumption and less frequent use of antidepressants. Of note, this was a longitudinal study with 10 years of follow up. After adjusting for confounders, compared with women consuming ≤1 caffeinated coffee/week, relative risk of depression was 0.85 (95% C.I., 0.75-0.95) for those who consumed 2-3 cups/day and 0.80 (0.64–0.99; P = < 0.001) for those who consumed  $\ge 4$  cups/day. Relative risk of depression was 0.80 (95% C.I., 0.68-0.95; P=0.02) for women in the highest (≥550 mg/d) vs. those in lowest (<100 mg/d) of the five caffeine consumption categories (Lucas et al., 2011).

#### 4. Discussion

According to the global burden of disease report of 2015, major depressive disorders are among the world's top 12 health problems when ranked by years lived with disability (Global Burden of Disease Study, 2015). Most of the risk factors that cause the greatest "loss of health" are environmental in nature such diet, physical inactivity, and pollution (Cohen, 2012). Therefore, the use of dietary interventions to co-treat or prevent behavioral disorders might be a feasible approach to prevent many affective disorders. In this paper, we only evaluated human studies conducted on tea, coffee, and cocoa and their associations with mood disorders. Out of 17 studies, seven on tea, three on cocoa, and two on coffee reported a positive association with lower depression levels, whereas three from cacao and two from tea described null associations, and one an increase of depression risk associated with cocoa consumption. Although a large amount of subjects (≈276 K) were analyzed for tea, data on most of them (≈266 K) showed no association with depression (Guo et al., 2014; Ruusunen et al., 2010). In the case of cacao, a considerable amount of subjects showed either positive or null association (≈7 K), while the other ones showed negative effects (≈1 K) (Rose et al., 2010). By contrast, both coffee studies showed a clear association (≈50 K) between coffee consumption and reduced levels of depression (Lucas et al., 2011; Omagari et al., 2014). Overall, these data suggest that, although intake of these food

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