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## Review

## Nutritional Psychiatry: Where to next?

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## ABSTRACT

The nascent field of 'Nutritional Psychiatry' offers much promise for addressing the large disease burden associated with mental disorders. A consistent evidence base from the observational literature confirms that the quality of individuals' diets is related to their risk for common mental disorders, such as depression. This is the case across countries and age groups. Moreover, new intervention studies implementing dietary changes suggest promise for the prevention and treatment of depression. Concurrently, data point to the utility of selected nutraceuticals as adjunctive treatments for mental disorders and as monotherapies for conditions such as ADHD. Finally, new studies focused on understanding the biological pathways that mediate the observed relationships between diet, nutrition and mental health are pointing to the immune system, oxidative biology, brain plasticity and the microbiome-gut-brain axis as key targets for nutritional interventions. On the other hand, the field is currently limited by a lack of data and methodological issues such as heterogeneity, residual confounding, measurement error, and challenges in measuring and ensuring dietary adherence in intervention studies. Key challenges for the field are to now: replicate, refine and scale up promising clinical and population level dietary strategies; identify a clear set of biological pathways and targets that mediate the identified associations; conduct scientifically rigorous nutraceutical and 'psychobiotic' interventions that also examine predictors of treatment response; conduct observational and experimental studies in psychosis focused on dietary and related risk factors and treatments; and continue to advocate for policy change to improve the food environment at the population level.

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## 1. Introduction

The field of 'Nutritional Psychiatry' is relatively new. While there had been a focus on the possible utility of omega-3 fatty acid and folate

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supplementation in mood disorders during previous decades (e.g. [Su et al., 2003](#); [Stoll et al., 1999](#); [Taylor et al., 2004](#)), as well as a number of observational studies focusing on the intake of single nutrients or foods (e.g. [Morris et al., 2003](#); [Hibbeln, 1998](#)), the first studies to examine and establish a link between overall diet quality and the common mental disorders, depression and anxiety, were not published until the last decade ([Jacka et al., 2010a](#); [Akbaraly et al., 2009](#); [Sanchez Villegas et al., 2009](#)). Given that nutritional research has, justifiably, moved away from a focus on single foods or nutrients, cognisant of the fact that humans do not consume these in isolation ([Hu, 2002](#)) and that what we eat in excess is as important as what we do not eat enough of, these initial studies were influential and prompted a wider and more nuanced interest in this topic. We coined the term 'Nutritional Psychiatry' in order to promote a new field of research focused on developing a comprehensive, cohesive and scientifically rigorous evidence base to support a shift in thinking around the role of diet and nutrition in mental health ([Sarris et al., 2015a,b](#)). This narrative review and commentary provides an update on the field as it stands to date. It incorporates a discussion of the methodological issues and challenges, and identifies and discusses significant gaps in the literature with a view to informing the developing research agenda.

## 2. Observational Data in Humans

Since the initial studies the field has grown rapidly, with published observational studies originating in many different countries. In 2013–14, the evidence base was advanced enough for systematic reviews, and there were several published examining the evidence for a relationship between measures of diet quality and mental disorders, particularly depression. Two of these incorporated a meta-analysis. In one of these studies, 20 observational studies out of a possible 45 were considered methodologically rigorous to be included in the systematic review ([Lai et al., 2013](#)). Of these, 13 studies (four cohort and nine cross-sectional) had dietary exposures of sufficient similarity to be included in a meta-analysis. The results suggested that higher intakes of a 'healthy' diet (i.e. fruit, vegetables, fish, and whole grains) were associated with a reduced likelihood of depression (OR: 0.84; 95% CI: 0.76, 0.92). There was little evidence of publication bias. The trend for an association between consuming a 'western' (unhealthy) dietary pattern and depression (OR: 1.17; 95% CI: 0.97, 1.41) was not statistically significant in the meta-analysis, likely due to insufficient power as a result of the small number of included studies ([Lai et al., 2013](#)). The second meta-analysis, which included eight cohort studies and one case-control study, identified a dose-response association between high adherence (pooled effect estimate = 0.68, 95% CI: 0.54–0.86) and moderate adherence (pooled effect estimate 0.77, 95% CI: 0.62–0.95) to a Mediterranean diet and the risk for depression ([Psaltopoulou et al., 2013](#)). In common with the [Lai et al.](#) study ([Lai et al., 2013](#)), the study failed to find evidence of publication bias.

Concordant with these meta-analyses arising from adult data, there are now many cross-sectional and prospective observational studies reporting inverse associations between adherence to healthy dietary patterns and reduced risk for or likelihood of mental health disturbances in children and adolescents, while unhealthy dietary habits are positively associated with mental health problems. These relationships are, also in common with the adult data, usually observed to be independent of other key health behaviours, including physical activity and smoking, but are also independent of key environmental factors such as socioeconomic circumstances, family conflict, poor family functioning and social support, and adolescent dieting behaviours ([Jacka et al., 2011, 2010b, 2013a](#)). They are even documented in very young children, suggesting important opportunities for preventive interventions focused on prenatal and early life nutritional exposures ([Jacka et al., 2013b](#); [Pina-Camacho et al., 2015](#)). A systematic review in 2014 confirmed an association between higher unhealthy diets and poor mental

health in children and adolescents ([O'Neil et al., 2014a](#)), although this review now requires updating.

The findings of the studies included in these systematic reviews and meta-analyses are notable for their consistency across countries, cultures and age groups. At their core, the many and varied versions of a 'healthy' diet comprise higher intakes of nutrient-dense plant based foods and quality sources of protein. Thus, healthy diets in Spain, Norway, Japan, Australia, China, the UK, and the many other countries from which the published data are derived, are unified in being characterized by these dietary components, despite differing on culturally specific foods. On the other hand, 'western' diets are more homogeneous in their composition due to their common source (i.e. industry). What is also notable is that the relationship between both healthy and unhealthy diets and mental health are consistently independent of each other, indicating that each (i.e. low intakes of healthy, nutrient and fibre-dense foods and higher intakes of processed, sugary and fat-laden foods) are associated with poor mental health via potentially different, although overlapping, pathways. Finally, the extant evidence largely supports a causal relationship between diet quality and depression on the basis of the Bradford Hill criteria: that of consistency, with concordant findings and effect sizes across cultures, genders and age groups, with multiple methods used to assess diet quality and mental health; biological gradient; temporality; biological plausibility; and coherence of the findings with what we already know about the impact of habitual diet on noncommunicable disorders ([Jacka et al., 2012a](#)).

However, while many results from more recent population-based studies support the systematic reviews, there are negative findings. In particular, one prospective study from the very large Nurses Health Study failed to find strong evidence for the hypothesized relationship between diet quality and depression in women after adjustments ([Chocano-Bedoya et al., 2013](#)). Moreover, while a large repeated cross-sectional study ( $n = 296,121$ ) reported consistent inverse relationships between fruit and vegetable intake and major depressive disorder ([McMartin et al., 2013](#)), a more recent longitudinal study in the same population, utilizing data from more than eight thousands Canadians, found that the inverse relationship between fruit and vegetable intake and depression observed in univariate analyses was attenuated by the addition of other measures of health behaviours to the model ([Kingsbury et al., 2015](#)). Another large Australian cohort study also reported that the weak relationships arising from univariate analyses were attenuated by adjustment for other health behaviours or by measures of socioeconomic position in younger and middle-aged groups. However, associations between dietary patterns and depression over time remained significant in the older cohort ([Jacka et al., 2014a](#)). On the other hand, when the dietary data from the Nurses Health Study were re-analysed according to the 'inflammatory potential' of the diet, by use of a Dietary Inflammatory Index (DII), the DII did predict depression over twelve years of follow up ([Lucas et al., 2013](#)). These studies point to the need to identify and address critical methodological issues, including those relating to the measurement and quantification of diet, and issues relating to the shared variance between lifestyle factors, such as diet, smoking and exercise.

## 3. Methodological Issues

Methods for accurately measuring people's dietary intakes remain problematic. Extensive research in nutritional epidemiology points to high levels of measurement error with the use of the various methods for capturing dietary intakes (e.g. [Freedman et al., 2014](#)). Given that there is also error associated with the measurement of mental health, the relationships between diet and health outcomes may be obscured and attenuated by measurement error. However, an equally important issue relates to the methods chosen to examine associations between 'diet quality' and health outcomes. In many studies, diet quality is measured using a priori dietary quality indexes derived from recommended dietary guidelines, or by other composite measures of dietary intake.

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