Nutritional Psychiatry: recent advances in evidence for diet and nutrition for mental and brain health

Prof Felice N Jacka
Food & Mood Centre, Deakin University
Murdoch Childrens Research Institute
The Black Dog Institute

f.jacka@deakin.edu.au
Global Burden of Disease study


GBD 2016 Risk Factors Collaborators*

Lancet 2017; 390: 1345–422
Poor diet?

• Diets low in:
  – Fruits
  – Vegetables
  – Wholegrains
  – Nuts and seeds
  – Fibre
  – Healthy fats
Poor diet?

• Diets high in:
  – Red meat
  – Processed meat
  – Added sugars
  – Sugar Sweetened Beverages
  – Trans fats
  – Sodium
Mental and Substance Use Disorders

Leading cause of global disability
Overview of Nutritional Psychiatry: what do we know so far?
Association of Western and Traditional Diets With Depression and Anxiety in Women

Felice N. Jacka, Ph.D.
Julie A. Pasco, Ph.D.
Arnstein Mykletun, Ph.D.
Lana J. Williams, Ph.D.
Allison M. Hodge, Ph.D.
Sharleen L. O’Reilly, Ph.D.
Geoffrey C. Nicholson, M.D., Ph.D.
Mark A. Kotowicz, M.D.
Michael Berk, M.D., Ph.D.

Objective: Key biological factors that influence the development of depression are modified by diet. This study examined the extent to which the high-prevalence mental disorders are related to habitual diet in a 1,046 women ages 20-93 years randomly selected from the population.

Method: A diet quality score was derived from answers to a food frequency questionnaire, and a factor analysis identified habitual dietary patterns. The 12-item General Health Questionnaire (GHQ-12) was used to measure psychological symptoms, and a structured clinical interview was used to assess current depressive and anxiety disorders.

Results: After adjustments for age, socioeconomic status, education, and health behaviors, a “traditional” dietary pattern characterized by vegetables, fruit, meat, fish, and whole grains was associated with lower odds for major depression or both anxiety and for anxiety disorders. A “western” diet of processed or fried foods, refined grains, sugar products, and beer was associated with a higher GHQ-12 score. There was also an inverse association between diet quality score and GHQ-12 score that was not confounded by age, socioeconomic status, education, or other health behaviors.

Conclusions: These results demonstrate an association between habitual diet quality and the high-prevalence mental disorders, although inverse causality and confounding cannot be ruled out as explanations. Further prospective studies are warranted.

(Am J Psychiatry Jacka et al., 11:3-7)
Healthy dietary indices and risk of depressive outcomes: a systematic review and meta-analysis of observational studies

Camille Lassale1,2, G. David Batty3,4, Amanie Baghdadi3,4, Felice Jacka5,6, Almudena Sánchez-Villegas7,8, Mika Kivimäki7,9, and Tasnime Akbaraly1,3,9

Decreased incidence of depression:
Adherence to a Mediterranean diet: 0.67 (95% CI 0.55–0.82)
Lower Dietary Inflammatory Index: 0.76 (95% CI 0.63–0.92).

Diet and Mood in Adolescents

Associations between diet quality and depressed mood in adolescents: results from the Australian Healthy Neighbourhoods Study

Felice N. Jacka, Peter J. Kremer, Eva R. Leslie, Michael Berk, George C. Patton, John W. Toumbourou, Joanne W. Williams

Healthy Neighbourhoods Study
n = 7114
Age 10 - 14 years

Impact of early life nutritional exposures extends from physical to mental health
Consistent observational data across countries, cultures and age groups

- fulfill Bradford Hill criteria for causality
- largely independent of SES, education, body weight, other health behaviours
- Not apparently explained by reverse causality

Very extensive data from animal studies

NEED for RCTs
Dietary improvement as a treatment strategy in major depression: the SMILES trial

O'Neil A...Jacka F. A randomised, controlled trial of a dietary intervention for adults with major depression (the SMILES trial): study protocol. *BMC Psychiatry* 2013 13:114
Study aim

To investigate the efficacy and cost-effectiveness of dietary improvement in the treatment of major depression
Participants randomly assigned to receive either........

Dietary support (clinical dietitian) or Social support (RA)
<table>
<thead>
<tr>
<th>Protein</th>
<th>Cereals and Starchy Vegetables</th>
<th>Vegetables</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tinned sardines</td>
<td>with wholegrain biscuits</td>
<td>plus avocado, tomato and cucumber</td>
</tr>
<tr>
<td>Tinned salmon</td>
<td>with tinned chickpeas</td>
<td>and salad</td>
</tr>
<tr>
<td>Tinned tuna</td>
<td>plus instant brown or basmati</td>
<td>with tinned corn, peas and beetroot</td>
</tr>
<tr>
<td>Egg</td>
<td>on wholemeal toast</td>
<td>with avocado, tomato and mushrooms</td>
</tr>
<tr>
<td>Supermarket rotisserie chicken</td>
<td>with couscous</td>
<td>and frozen vegetables</td>
</tr>
</tbody>
</table>
Effect size:
Cohen’s d = -1.16
(95% CI -1.73, -0.59)

NNT= 4.1

N=67

Jacka et.al. 2017 BMC Medicine
Change in MADRS over 3 months across quartiles of adherence to ModiMedDiet

Jacka et al. 2017 BMC Medicine
Is it cheaper to eat an unhealthy vs a healthy diet?

• Trial participants spent an estimated mean of $138 per week on food and beverages for personal consumption at the start of the trial.

• Total food and beverage costs per person per week for the recommended modified Mediterranean diet was estimated at $112.

• The modified Mediterranean diet at $1.54 per mega-joules (MJ) was cheaper per energy unit than the cost of the current dietary intake of the SMILES participants at a mean of $2.35 per MJ.

$138 vs $112 per week
Economic Evaluation

• We measured time lost (absenteeism) from paid and unpaid work (volunteering, study, house-keeping)
• We measured visits to health care professionals
• We measured the costs of delivering the interventions and the diet itself
• Compared with the social support condition, average total health sector costs were $856 lower and average societal costs were $2591 lower for those receiving dietary support.
• These differences were driven by lower costs arising from fewer allied and other health professional visits and lower costs of unpaid productivity (Chatterton et al. 2018 BMC public health)
A Mediterranean-style dietary intervention supplemented with fish oil improves diet quality and mental health in people with depression: A randomized controlled trial (HELFIMED)

Natalie Parletta, Dorota Zarnowiecki, Jihyun Cho, Amy Wilson, Svetlana Bogomolova, Anthony Villani, Catherine Itsiopoulos, Theo Niyonsenga, Sarah Blunden, Barbara Meyer, Leonie Segal, Bernhard T. Baune & Kerin O’Dea

To cite this article: Natalie Parletta, Dorota Zarnowiecki, Jihyun Cho, Amy Wilson, Svetlana Bogomolova, Anthony Villani, Catherine Itsiopoulos, Theo Niyonsenga, Sarah Blunden, Barbara Meyer, Leonie Segal, Bernhard T. Baune & Kerin O’Dea (2017): A Mediterranean-style dietary intervention supplemented with fish oil improves diet quality and mental health in people with depression: A randomized controlled trial (HELFIMED), Nutritional Neuroscience, DOI: 10.1080/1028415X.2017.1411320

To link to this article: https://doi.org/10.1080/1028415X.2017.1411320
HELFIMED study: effect of Mediterranean diet on mental health in people with depression

DASS Depression Score ($P=0.027$ for treatment interaction, $N=152$)
The Effects of Dietary Improvement on Symptoms of Depression and Anxiety: A Meta-Analysis of Randomized Controlled Trials

Joseph Firth, PhD, Wolfgang Marx, PhD, Sarah Dash, PhD, Rebekah Carney, PhD, Scott B. Teasdale, PhD, Marco Solmi, MD, Brendan Stubbe, PhD, Felipe B. Schuch, PhD, André F. Carvalho, MD, Felice Jacka, PhD, and Jerome Sarris, PhD

Psychosomatic Medicine (2019)

• N=16 RCTs with 45,826 participants
• Dietary interventions significantly reduced depressive symptoms
• No effect was observed for anxiety (but few studies)
• Greater benefits in females for both depression and anxiety
Take-home message

Diet matters to mental and brain health

DIET IS MODIFIABLE – TARGET FOR PREVENTION AND TREATMENT
Current Clinical Practice Guidelines

Royal Australian and New Zealand College of Psychiatrists clinical practice guidelines for mood disorders

Gin S Malhi¹,², Darryl Bassett³,⁴, Philip Boyce⁵, Richard Bryant⁶, Paul B Fitzgerald⁷, Kristina Fritz⁸, Malcolm Hopwood⁹, Bill Lyndon¹⁰,¹¹,¹², Roger Mulder¹³, Greg Murray¹⁴, Richard Porter¹³ and Ajeet B Singh¹⁵
Current Clinical Practice Guidelines

Figure 6. Management of major depressive disorder.

**GOAL**
The main objective of treatment is the complete remission of depression with full functional recovery and the development of resilience.

- Taper and cease any agents that can potentially lower mood
- Institute sleep hygiene
- Implement appropriate lifestyle changes e.g. smoking cessation, adopt regular exercise and achieve a healthy diet
- Address substance misuse if relevant

**STEP 0**

<table>
<thead>
<tr>
<th>GENERIC PSYCHOSOCIAL INTERVENTIONS</th>
<th>FORMULATION-BASED INTERVENTION</th>
<th>PHARMACOTHERAPY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Psychoeducation (family, friends, caregivers)</td>
<td>Cognitive Behavioural Therapy (CBT)</td>
<td>First line - SSRIs, NaSSAs, NDRIs, SNRIs, NARIs, melatonin agonist, serotonin modulator</td>
</tr>
<tr>
<td>Low intensity interventions (e.g. internet based education)</td>
<td>Interpersonal therapy</td>
<td>Second line - Tricyclic antidepressants, MAOIs</td>
</tr>
<tr>
<td>Formal support groups, community groups</td>
<td>Acceptance and Commitment therapy</td>
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<td>Employment, housing</td>
<td>Mindfulness-Based Cognitive Therapy</td>
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**STEP 1**

<table>
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<tr>
<th>IF STEP 1 INSUFFICIENT</th>
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<tbody>
<tr>
<td>- Combine pharmacotherapy and psychological therapy</td>
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<tr>
<td>- Increase dose of antidepressant medication</td>
</tr>
<tr>
<td>- Augment antidepressant medication with lithium and/or antipsychotic medication</td>
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<td>- Combine antidepressants</td>
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<td>- rTMS (if available)</td>
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**STEP 2**

<table>
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<th>IF STEP 2 INSUFFICIENT</th>
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<td>- ECT</td>
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FOOD & MOOD CENTRE

A DEAKIN IDEA
The Lancet Psychiatry Commission: a blueprint for protecting physical health in people with mental illness


Lancet Psychiatry 2019; 6: 675–712
Where to next?
Food & Mood Centre Program

Early Life

Health Behaviours & Determinants

Mental & Brain Health

Physical Health

Healthy Ageing

Population health | Novel interventions | Mechanisms | Implementation science | Education and training

Pregnancy
Birth
Infancy
Neurodevelopment

Diet
Stress
Physical Activity
Sleep

Depression
Anxiety
Psychosis
Eating disorders
PTSD
Cognition
Neurobiology

Gut health
Cardio health
Metabolic health
Vascular health

Cognitive decline
Neurodegeneration
Mechanistic pathways

INFLAMMATION AND OXIDATIVE STRESS
BDNF AND BRAIN PLASTICITY
GUT MICROBIOTA
Personality and Total Health Through Life study: n = 255; aged 60 – 64 years; 4 years follow-up

Jacka et al. 2015 BMJ Med
Better diet quality relates to larger brain tissue volumes

The Rotterdam Study

Pauline H. Croll, MSc, Trudy Voortman, PhD, M. Arfan Ikram, MD, PhD, Oscar H. Franco, MD, PhD, Josje D. Schouten, PhD, Daniel Bos, MD, PhD, and Meike V. Vermeij, MD, PhD

Correspondence: Dr. Vermeij
m.v.vermeij@erasmusmc.nl

Diet Quality and Brain Plasticity

n = 4,213
Aged 46 – 98 years
10 years follow-up

Results: “...better overall diet quality is related to larger total brain volume, gray matter, white matter, and hippocampal volume.”
The Microbiota-Gut-Brain Axis
• 100 trillion microorganisms
• 99.5% of our genetic material
  • 23,000 human genes vs
  4.4 million microbial genes
Biological Dysregulation in Depression

- Inflammatory and oxidative stress (cytokines, CRP, ROS)
- Metabolic (insulin resistance, metabolic syndrome)
- HPA axis (cortisol)
- Neurotransmitter/neuropeptide (dopamine, serotonin, GABA, BDNF)

Each modified by gut microbiota

‘GERM FREE MICE’

- Altered stress response
- Altered brain plasticity
- Altered levels of neurotransmitters
- Altered behaviours
- Altered immune system
- Altered BBB
FMT from patients with MDD induced depressive-like behaviours in contrast to FMT from patients without MDD
The gut microbiome from patients with schizophrenia modulates the glutamate-glutamine-GABA cycle and schizophrenia-relevant behaviors in mice


- Observed profound gut microbiota alterations in patients with SCZ relative to HC subjects (incl lower alpha-diversity)
- Identified unique bacterial taxa that were strongly associated with SCZ severity
- GF mice colonization with human SCZ microbiota resulted in SCZ-relevant behavioral changes similar to those observed in glutamatergic mouse models of SCZ
- Mice receiving gut microbiome transfers from patients with SCZ displayed disturbances of microbial genes and host metabolites involved in amino acid and lipid metabolism, including glutamate, which has been strongly implicated in SCZ pathology
Main factors influencing microbiota

• Age
• Geography
• Stress
• Infection
• Medication use
  • Diet
The Healthy Parents, Healthy Kids Study

Samantha Dawson\textsuperscript{1,2}, Jeff Craig\textsuperscript{1,2}, Gerard Clarke\textsuperscript{3}, Mimi Tang\textsuperscript{4,5}, Felice Jacka\textsuperscript{1,2}

1. Deakin University
2. Murdoch Childrens Research Institute
3. University College Cork, Ireland
4. Melbourne University
5. Royal Children’s Hospital
MOVING MOODS
Human microbial transfer as an adjunctive treatment for MDD

<table>
<thead>
<tr>
<th>Primary outcome measure</th>
<th>Aim</th>
<th>Target population</th>
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<tr>
<td>Feasibility</td>
<td>n = 60</td>
<td>adults with moderate to severe MDD</td>
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**Primary objective**
Investigate the feasibility of FMT as an adjunctive treatment for depression in adults

**Secondary objectives**
Establish whether FMT changes biological parameters in depressed adults, including the faecal microbiome, Hypothalamic Pituitary Axis activity, Neurogenesis, inflammation, cardiovascular and metabolic risk factors, cognition, Quality of life, gastrointestinal symptoms and tolerability. Depression symptoms (MADRS) will also be assessed.

Dr Jessica Green
Healthy Brain Project - Microbiome

How does the gut microbiome relate to Alzheimer’s disease pathophysiology?

• Healthy Brain Project – Florey Institute (lead by Drs Rachel Buckley & Yen Ying Lim)
  • PI: Dr Amy Loughman, RA: Madi West
  • Ultimate aim: predict relative risk of Alzheimer’s disease in healthy middle-aged adults on the basis of genetic, microbiome & behavioural data.

Funded by: Jack Brockhoff Foundation.

Dr Amy Loughman
Exploring the association between dietary polyphenols and brain health

- Epidemiological studies
  - UKBiobank (N=\textasciitilde 500,000), general population
  - Ausimmune case-control study (N=600), first dx of multiple sclerosis and healthy controls
  - Outcomes: incidence of mental illness, cognitive performance, fatigue, 
    \textit{metabolomic} and \textit{microbiome-related} pathways
THE MOO’D STUDY
DOUBLE BLINDED 16-WEEK RCT

Control
Conventional milk (≥250ml/day), cheese

Intervention
A2 milk (≥250ml/day), cheese

Randomised

Primary outcome
Psychological distress (DASS-21 total)

Secondary outcomes
Sub scores of depression, anxiety and stress (DASS-21)
Severity of depressive symptoms (PHQ-8)
Cognitive function (Cogstate)

Recruitment + Data Collection
2018-2020

n= 160
≥18 y
≥ 250ml milk/day
Low mood

No other dairy
Ketogenic Diet for psychotic symptoms – PsyDiet study

KETOGENIC DIET

- Glucose is restricted → production of ketone bodies
- Used to manage epilepsy in children since the 1920s
- Only few case and animal studies in psychotic disorders/ schizophrenia
- Neuroprotective effects (adenosine and glutamate metabolism, AMPA receptor)?

A 6-week randomized, controlled ketogenic diet pilot intervention study in psychotic inpatients (n=40)

- Carbohydrates limited to max 20 grams/day
- Ketone-body levels, blood glucose levels
- Primary outcome: psychotic symptoms
- Secondary outcomes: depression, anxiety, functioning

Dr Anu Ruusunen
Global Obesity Collaboration

- Based in Centre for Population Health Research
- Community-based systems trial WHO STOPS (n>5000 children, 10 communities)
- Primary outcome of interest = childhood (6-12 years) obesity
  - FAMC (Dr Erin Hoare) will assess the mental and emotional health outcomes of nutritional and physical activity intervention
  - Opportunities to build mental health-related strategies into step-wedge design
• Medicare item numbers for Dietitians and Exercise Physiologists
• Large-scale pragmatic trials
• New models of clinical treatment (e.g. shared appointments)
• Global Burden of Disease Study
Joint WFSBP & ASLM International Taskforce

• *Clinical Therapeutic Guidelines for Lifestyle Medicine in Mental Health Treatment*
Knowledge Translation Recipients

- GPs
- Dietitians
- Psychiatrists
- Psychologists
- Nurses
- Allied Health

- Universities
- Schools
- Kindergartens

- Medical facilities
- Professional associations
- Government Departments

- Medical Professionals
- Educational Organizations

- Community Groups
- Health and Government Bodies

- Youth Organization
- Community Groups
- Charity Organizations
- Sporting Groups
- Retirement Villages

Individuals with mental health issues
Brain Changer

The latest cutting-edge science on how diet can affect your risk of anxiety and depression, and influence the health of your brain

PROFESSOR FELICE JACKA

FOOD & MOOD CENTRE

Pan Macmillan Press
February 2019
# Acknowledgements

**Food & Mood Centre Director Prof Felice Jacka & Deputy Director A/Prof Adrienne O’Neil**

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<thead>
<tr>
<th>Research assistants and honorary members</th>
<th>PhD Students</th>
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<tr>
<td>Helene Nauwelaers</td>
<td>Samantha Dawson</td>
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<td>Genevieve Mosely</td>
<td>Claire Young</td>
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<td>Dr Tiril Borge</td>
<td>Amelia McGuinness</td>
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<td>Dr Rachelle Opie</td>
<td>Hajara Aslam</td>
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<td>Tanya Marie Freijy</td>
<td>Sara Campolonghi</td>
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<td>Prof Bryndís Birgisdóttir</td>
<td>Meg Hockey</td>
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<td>Dr Sarah Dash</td>
<td>Jessica Davis</td>
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<td>Melissa Lane</td>
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<td>Gina Howland</td>
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<td>Madi West</td>
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<td>Samantha Collins</td>
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Postdoctoral

Dr Anu Ruusunen
Dr Tetyana Rocks
Dr Wolfgang Marx
Dr Erin Hoare
Dr Amy Loughman
Dr Heidi Staudacher

PhD Students

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Claire Young
Amelia McGuinness
Hajara Aslam
Sara Campolonghi
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Jessica Green
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