Flavonoids and brain health: Does consuming flavonoid-rich foods benefit cognitive function?

Dr Daniel J Lamport
Dietary Flavonoids

A wide array of Fruits and vegetables

Green & Black Tea: (Flavanols)

Citrus: (Flavanone)

Red wine: (Flavanol, Flavanols)

Cocoa: (Flavanols and procyanidins)

Berries: (Anthocyanins)
Blueberry Supplements reverse deleterious effects of ageing on memory & motor behaviour

• Williams et al. 2008 Fr Rad Bio Med. 45; 295-305

Radial arm maze

Water maze
Rats are not little humans and humans are not big rats
Improvements in human executive function (attention) following BB intervention

Go-NoGo task: measures Executive function/attention

Subjects: 18-30 yrs

Subjects: 60-75 yrs

Sustained ability to correctly detect target stimuli following flavonoid supplementation compared to the control (*p < 0.05; n=48).

How 2009 PhD thesis
Acute improvements in cognitive function following intervention with ~579mg anthocyanins/flavanols

Blueberry powder, the equivalent of 200g blueberries, with semi-skimmed milk
N = 19 young adults (20-27 years) and 18 older adults (62-73 years)

Dodd 2013 PhD thesis
Citrus fruits = flavonoid rich
Orange & Grapefruit juice, placebo controlled, crossover acute trial (70.5mg flavonoid dose)

24 healthy adults aged 18-30 years

DSST Total Score (max 118)

Lemon Squash Control

Orange and grapefruit juice

*** p<0.001, improvement in processing speed from 0 to 2 hours

Lamport et al. under review
Orange juice & processed whole orange, placebo controlled, crossover acute trial (272mg flavonoid dose)

22 healthy adults aged 30-65 years

![Graph showing change from baseline Z-score and alertness rating over time for placebo and high flavonoid conditions. The graph indicates a significant difference (* p<0.05) in alertness rating between the two conditions at 6 hours post consumption.]

Alharbi et al. under review
Chronic 8 week orange juice intervention

Placebo controlled, crossover design
305mg flavonoids day for 8 weeks
N = 37 healthy older adults (mean age 67 years)

A. Global function

B. Executive function

Kean et al. under review
**Flavonoid-rich Cocoa**

Acute, Crossover, double-blind. HF = 494mg  LF = 23mg  330ml dairy based cocoa drinks  
Equicaloric (113kcal), matched for theobrom. & caffein  
N = 63 healthy older adults, aged 65-80 yrs

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**Executive Function**  
*z*-score from 5 tests

**Episodic memory**  
*z*-score from 4 tests

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Saunders et al. under review
Flavonoid-rich Cocoa - chronic

Cognitive benefits observed but only if baseline flavanol intake is low

Improvement in ‘executive function’ in the lowest tertile: \( p = 0.03 \)

- Tertile 1: 45-256 mg/day, \( n = 21 \)
- Tertile 2: 256-439 mg/day, \( n = 21 \)
- Tertile 3: 439-918 mg/day, \( n = 21 \)
How do they exert such actions in the brain?

Flavonoids

Cell Signalling and Gene Expression

Changes in cerebrovascular blood flow

Modulation of synaptic plasticity

Inhibition of Neuroinflammation
Blueberry consumption & enhanced vascular function

Rodriguez-Mateos et al
AJCN 2013
Brain imaging using fMRI

ASL: arterial spin labelling
- measuring cerebral blood flow (CBF) in vivo

fMRI: functional MRI
- haemodynamic response (change in blood flow) related to neural activity in the brain
Cocoa flavonoids and increased cerebral blood flow (ASL)

The HF – LF contrast analysis revealed significantly increased regional perfusion 2 hrs post consumption of the HF drink relative to the LF drink.

1. anterior cingulate gyrus
2. central opercular cortex of the left parietal lobe down to a sub-cluster in the temporal pole

Lamport et al. under review
Citrus Juices and increased cerebral blood flow (ASL)

Axial slices: sig. greater perfusion flow after the grapefruit and orange juice drink compared with the control drink at 2 hrs post consumption (p<0.05)

Lamport et al. under review
How do they exert such actions in the brain?

Flavonoids

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Modulation of synaptic plasticity

Inhibition of Neuroinflammation
Blueberries associated with increased Brain Derived Neurotrophic Factor (BDNF)

N=17 young healthy adults
Blueberry powder, the equivalent of 200g blueberries, with semi-skimmed milk

BDNF is a secreted protein and part of the neurotrophin family of growth factors which supports the survival and growth of neurons in the brain, and is a biomarker of learning and memory

Dodd 2013 PhD thesis
Mechanisms

Flavonoids/phenolic acids metabolites

ERK1/2, Akt/PKB

eNOS

eNOS

Vascular endothelium

Increased brain blood perfusion

Peripheral & Cerebrovascular blood flow

BBB

Neuron

Akt/ERK

CREB

BDNF, NRF, Arc

VEGF-B, nNOS

Neuronal Morphology

Dendritic spine growth

Neuronal communication

Synaptic plasticity

Angiogenesis/Neurogenesis

Oxygen/nutrient delivery

Enhancement of Memory and Cognition
Effects of Flavonoids on Health

- **Reduction of oxidative stress and inflammation**
  - Asgary, S 2014. ISRN Nutrition 405867-7

- **Reduces Blood Pressure**
  - Morand, C 2011. Am Clin Nutr vol. 93 no. 1 73-80
  - Asgary & Keshvari 2013. ARYA Atheroscler 9-1

- **Lower stroke risk**

- **Improves blood lipid profile**
  - Kurowska et al 2000. Am J Clin Nutr. 72 no. 5 1095-1100

- **Cognition and psychological condition**

- **Improves endothelial function**
  - Morand, C 2011. Am Clin Nutr vol. 93 no. 1 73-80
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