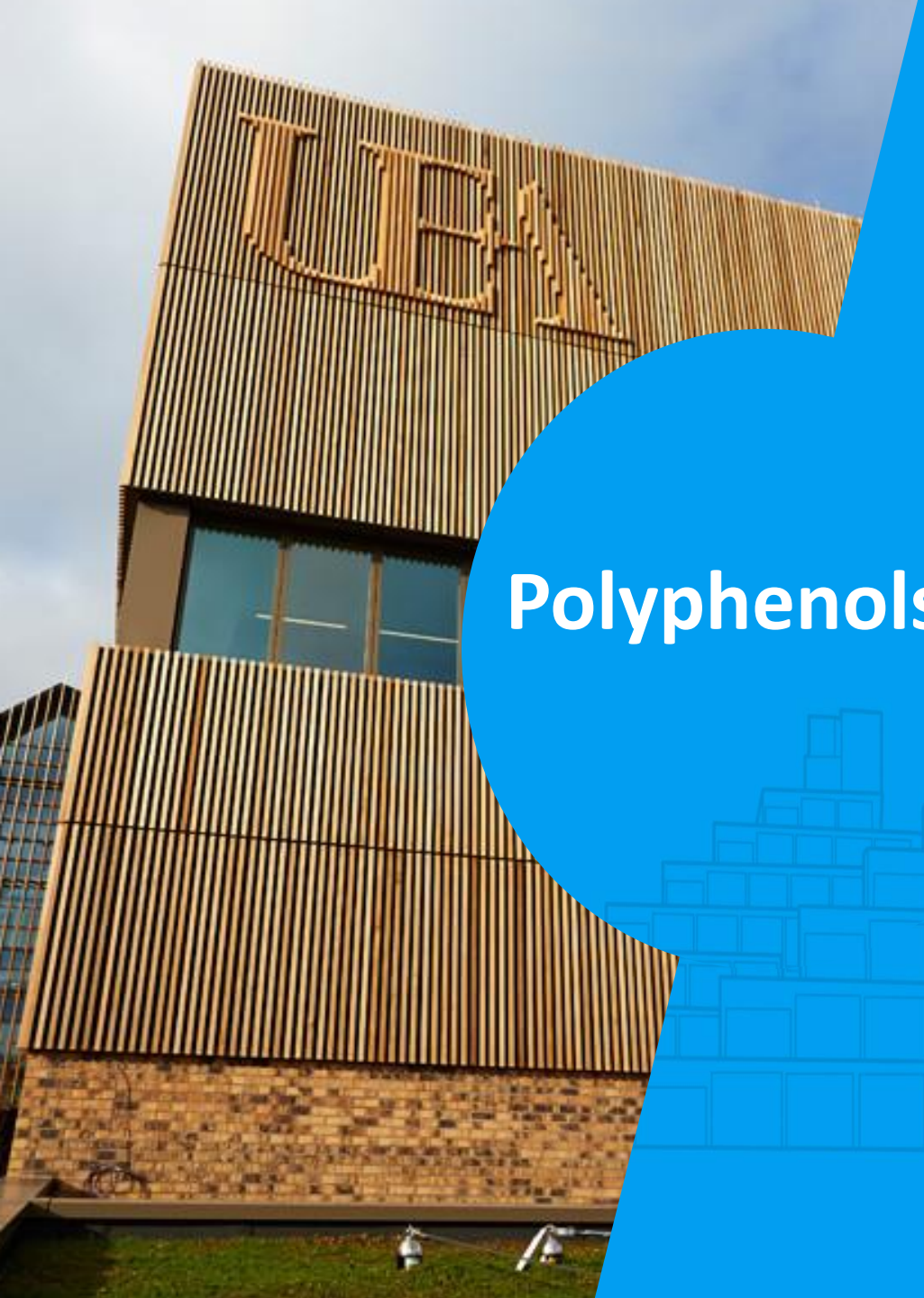

Polyphenols for Cognitive Health

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Athena SWAN Silver Award

Disclosure

I have NO financial disclosure or conflicts of interest with the presented material in this presentation

Risk factors and brain vulnerability

Modifiable risk factors	Intermediate risk factors	Non modifiable risk factors
• **Unhealthy diet** • Physical inactivity • Tobacco/alcohol/drugs • Stress	• Cardiovascular disease • Obesity • Diabetes • Pulmonary disease • Mental Illness	• Age • Family history • Genetics

Vauzour D et al. Ageing Research Reviews. 2017, 35:222-240

Dietary Polyphenols/Flavonoids

A wide array of Fruits and vegetables

Green & Black Tea: (Flavanols)

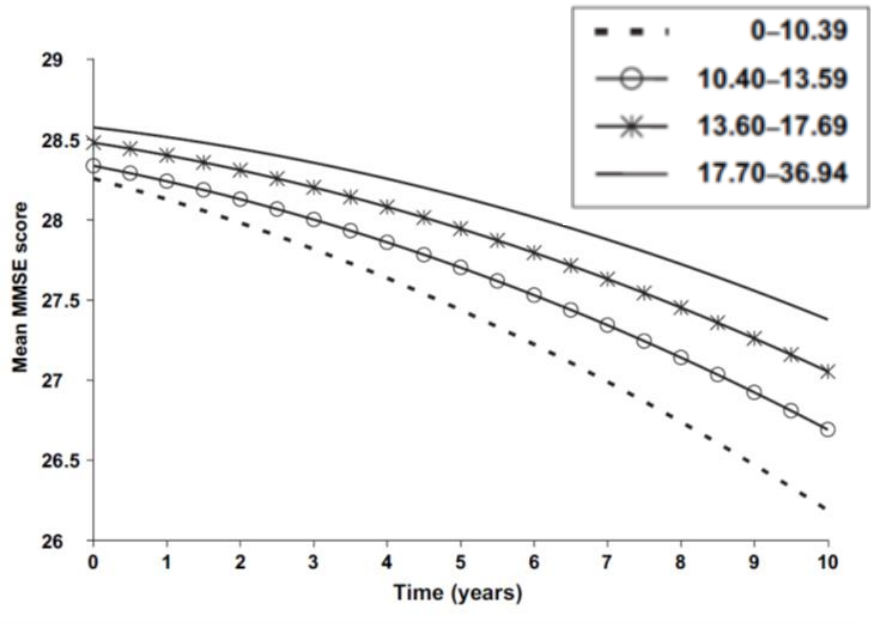
Red wine: (Flavanol, Flavonols)

Citrus: (Flavanone)

Cocoa: (Flavanols and procyanidins)

Berries: (Anthocyanins)

Reduction in global cognitive decline with increasing daily flavonoid intake



PAQUID Study

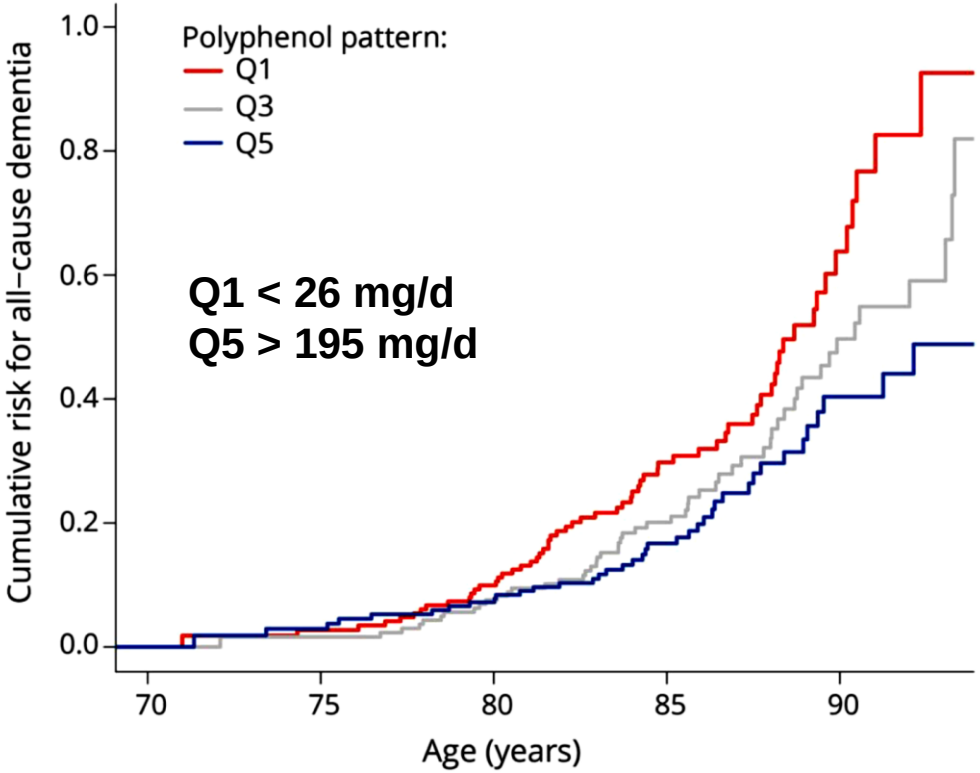
Letenneur L et al. American Journal of Epidemiology. (2007);165(12):1364–1371

Framingham Offspring Cohort

Shishtar E et al. Public Health Nutrition. (2020); 23(9), 1576-1588.

	Flavonoid quartiles								
	Quartile 1		Quartile 2		Quartile 3		Quartile 4		
Flavonoid class	Mean	(95% CIs)	Mean	(95% CIs)	Mean	(95% CIs)	Mean	(95% CIs)	*P*-trend[‡]
Total flavonoids[§]	−18.5	(−22.8,−14.1)	−18.3	(−22.3,−14.3)	−14.8	(−18.9,−10.6)	−14.9	(−19.1,−10.7)	0.19
Flavonols	−20.1	(−24.4,−15.9)	−17.8	(−21.9,−13.7)	−14.8	(−18.9,−10.7)	−13.9	(−18.0,−9.7)	0.04
Flavones	−16.0	(−20.2,−11.9)	−16.1	(−20.1,−12.0)	−16.8	(−20.9,−12.7)	−17.6	(−21.8,−13.4)	0.58
Flavanones	−15.4	(−19.5,−11.3)	−15.7	(−19.7,−11.6)	−17.9	(−21.9,−13.8)	−17.6	(−22.0,−13.3)	0.36
Flavan-3-ols	−20.6	(−24.8,−16.3)	−17.0	(−21.0,−12.9)	−15.3	(−19.4,−11.2)	−13.7	(−17.8,−9.6)	0.04
Anthocyanins	−15.9	(−20.3,−11.5)	−16.3	(−20.4,−12.2)	−17.3	(−21.3,−13.3)	−16.9	(−20.9,−12.9)	0.77
Flavonoid polymers	−18.4	(−22.8,−14.0)	−20.0	(−24.0,−16.0)	−13.5	(−17.6,−9.5)	−14.6	(−18.7,−10.5)	0.10

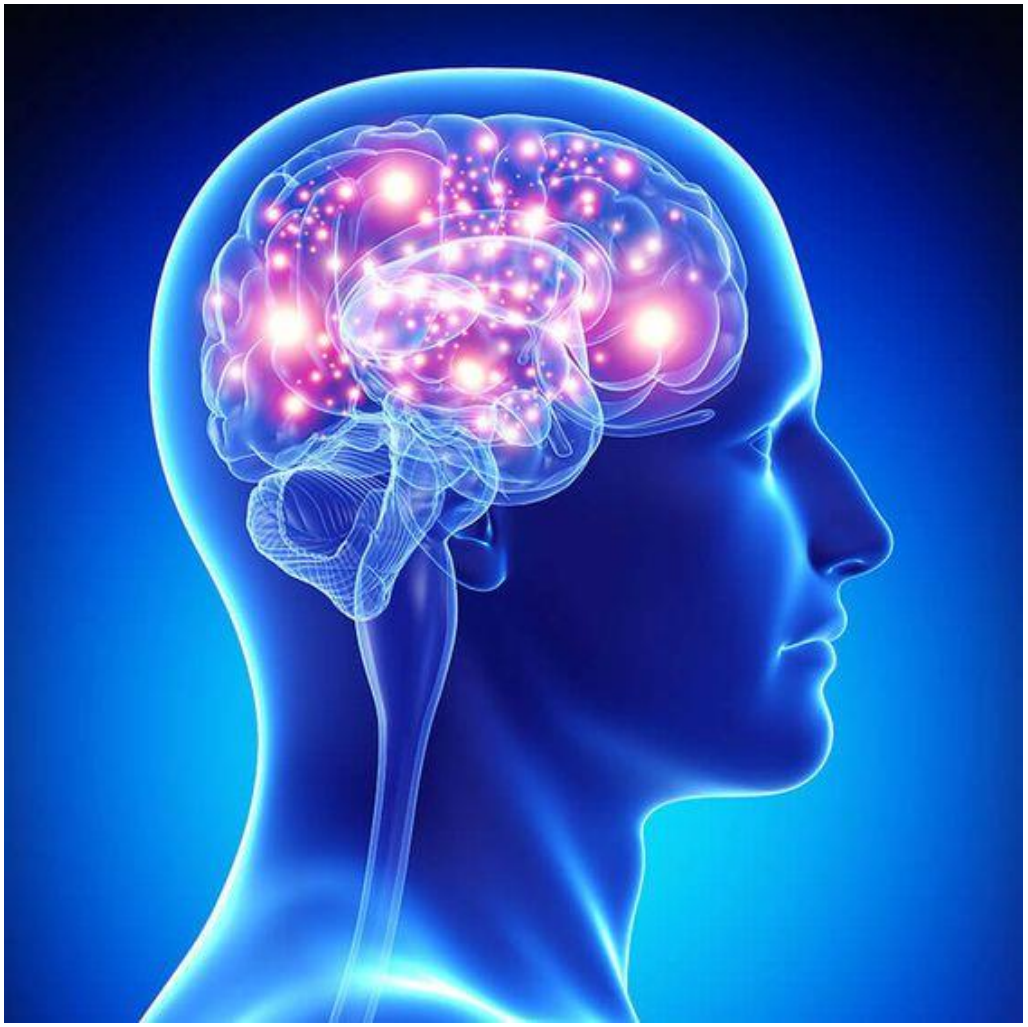
Decrease risk of incident all-cause dementia by quintiles of the polyphenol pattern



Compared with participants in the lower quintile of pattern score, those in the higher quintile had a 50% lower risk of dementia

Sophie Lefèvre-Arbogast S et al. Neurology. (2018); 90 (22) e1979-e1988

How do polyphenols exert their beneficial effects?



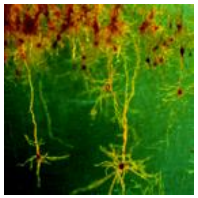
Interactions with the architecture of memory and cognition

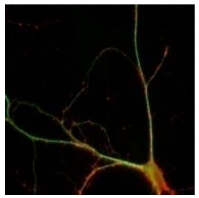
Polyphenols

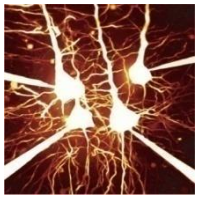
Cell Signalling and Gene Expression

Neuronal Morphology

Increased neuronal communication (synaptic plasticity)

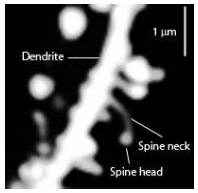


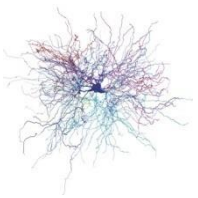


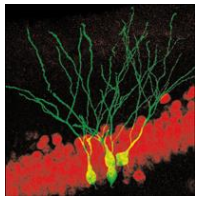


Vascular Effects

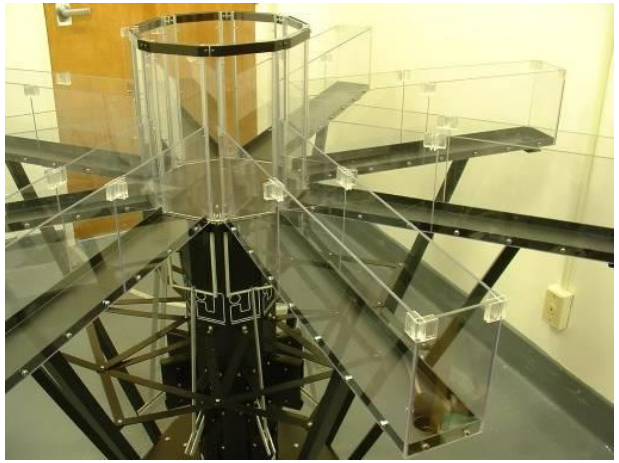
New nerve cell growth (neurogenesis)

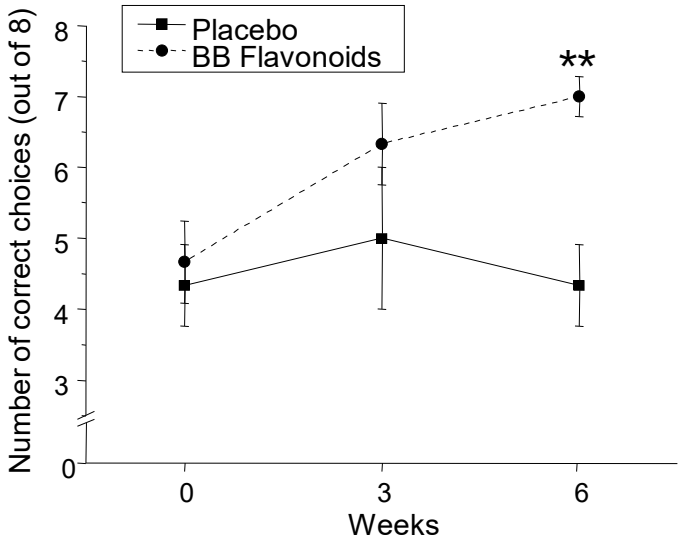


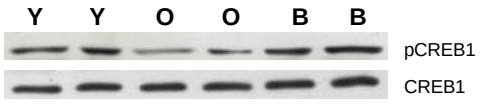


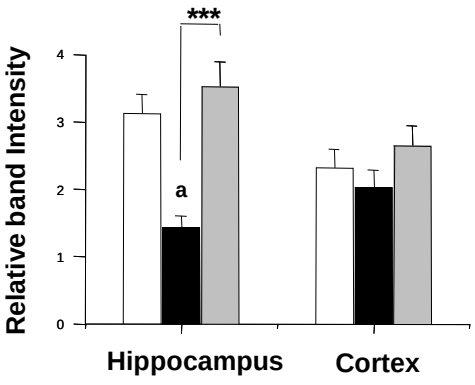


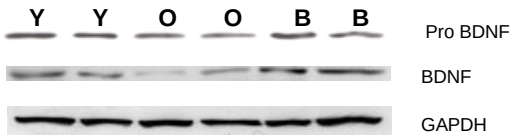
Impact of berry polyphenols on cognitive performances

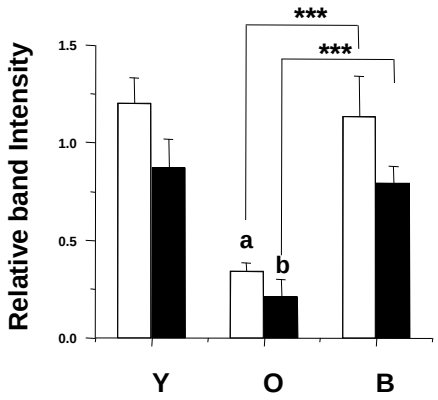


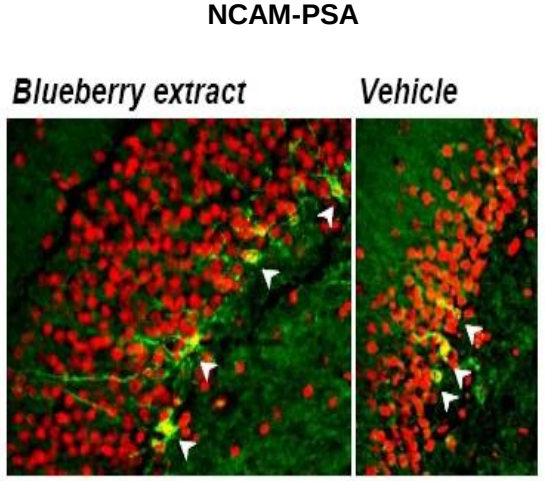










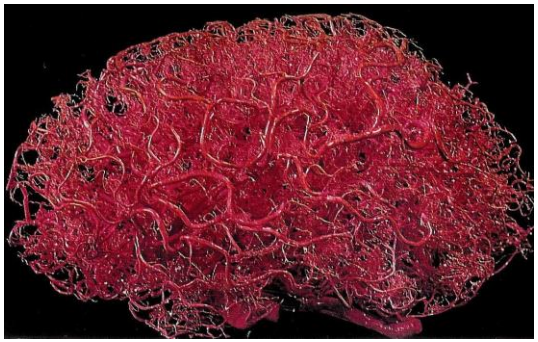


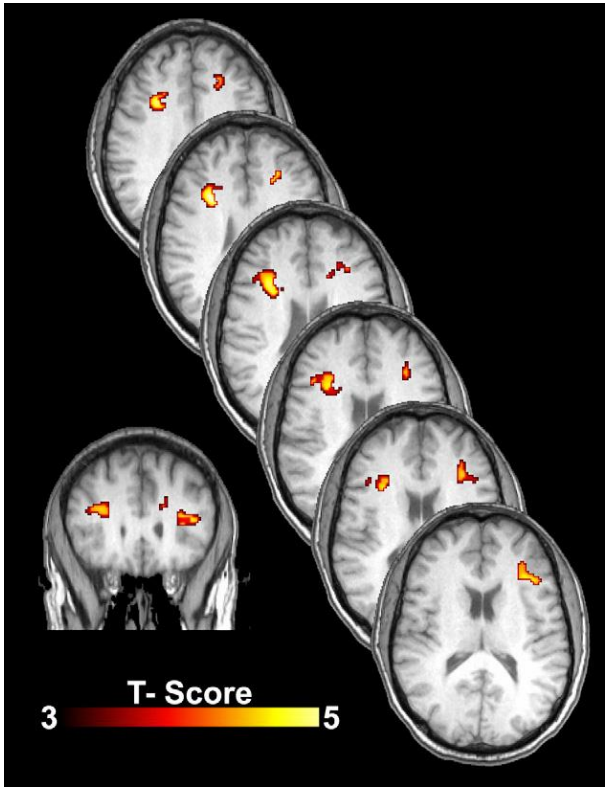
Williams CM, El Mohsen MA, Vauzour D *et al.* Free Radic Biol Med. 2008 Aug 1;45(3):295-305.

Cerebrovascular blood flow and cognition

ASL: arterial spin labelling

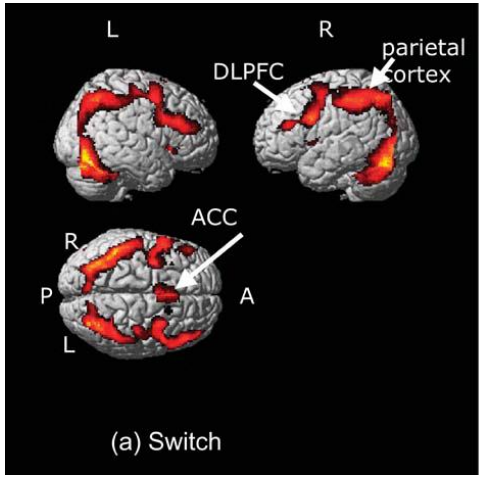
- measuring cerebral blood flow (CBF) in vivo

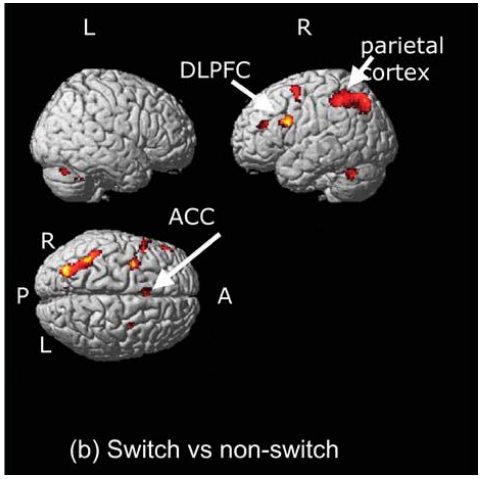




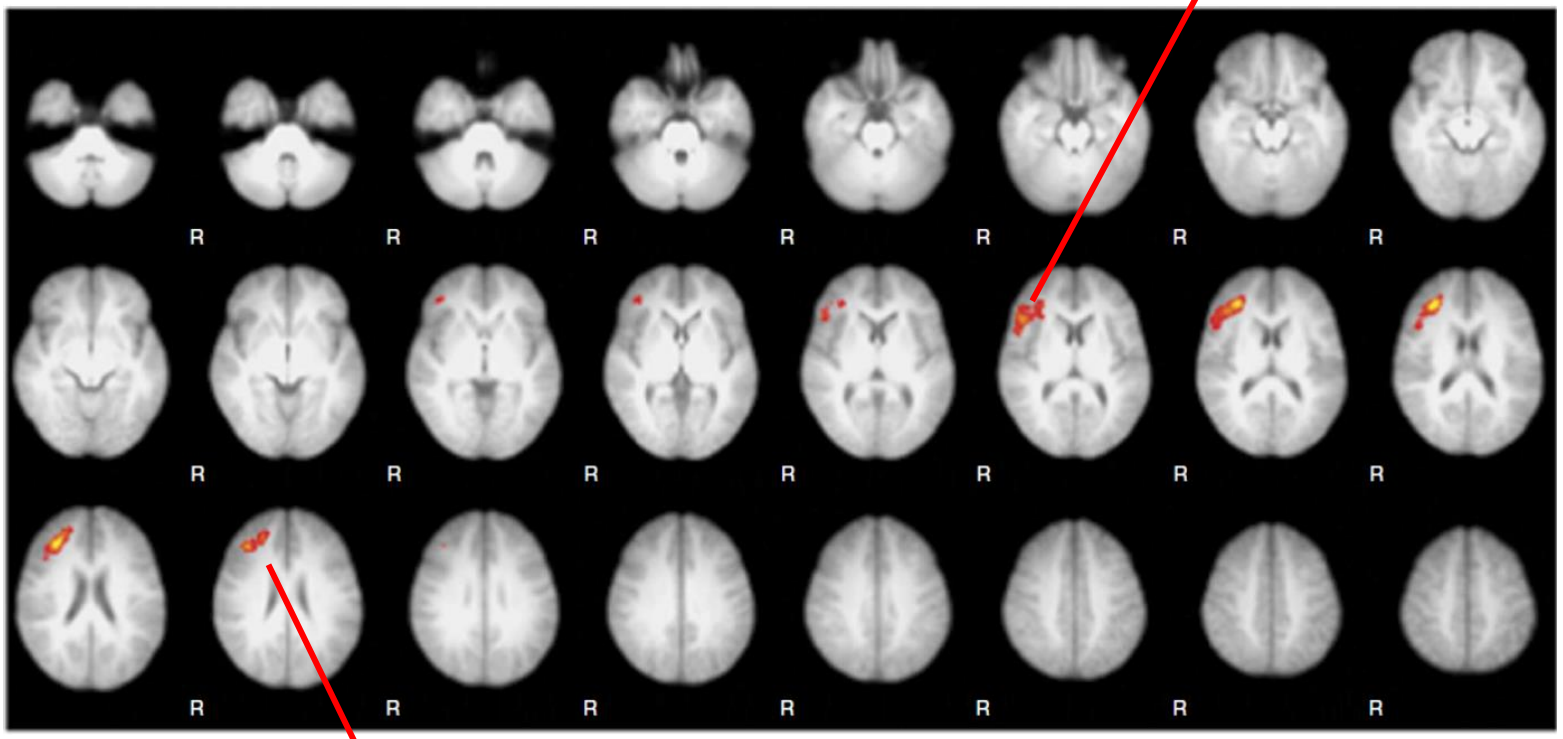
fMRI: functional MRI

- haemodynamic response (change in blood flow) related to neural activity in the brain



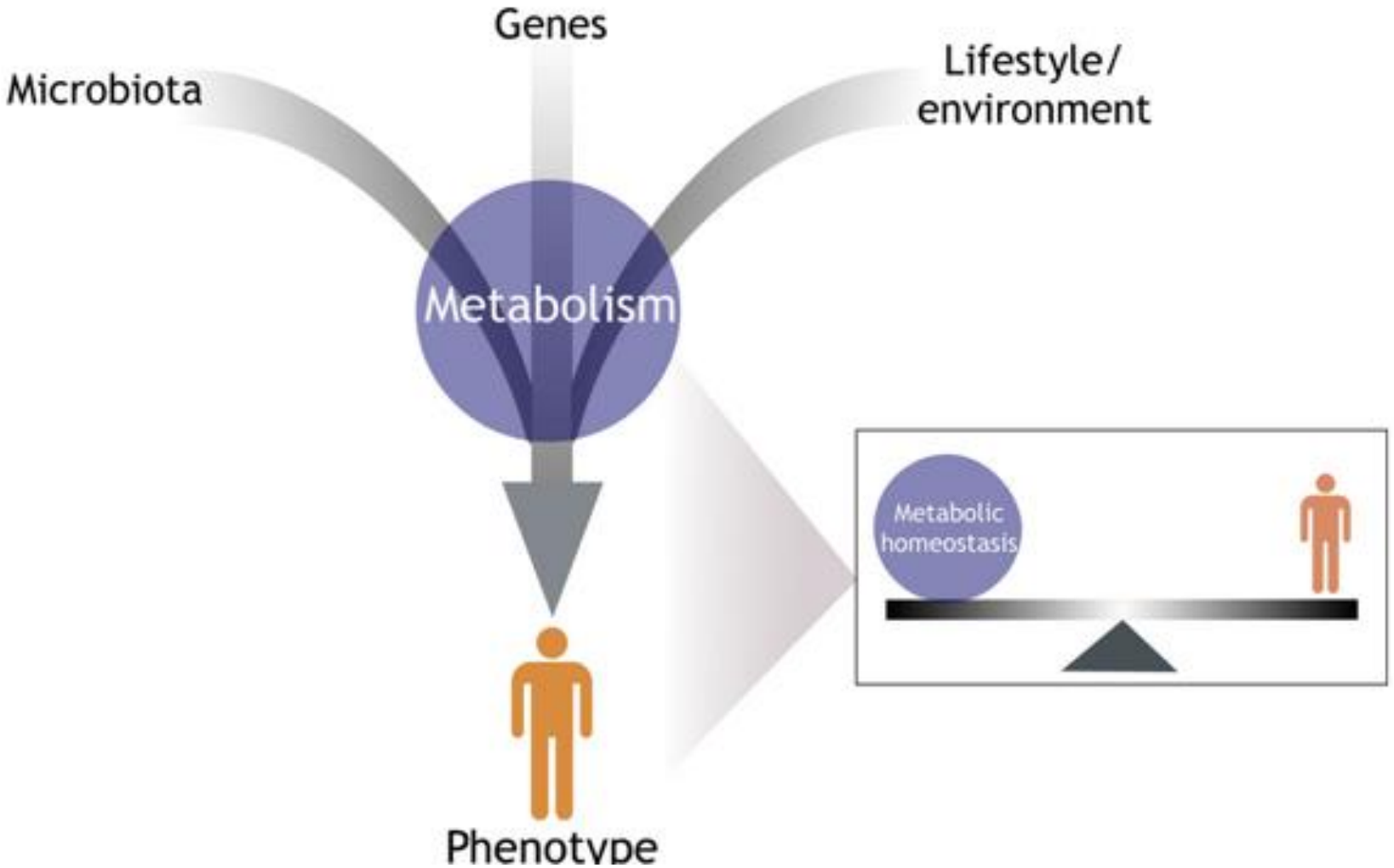


Time-series analysis on resting state ASL data
- high-flavanone drink intervention: baseline to 2h

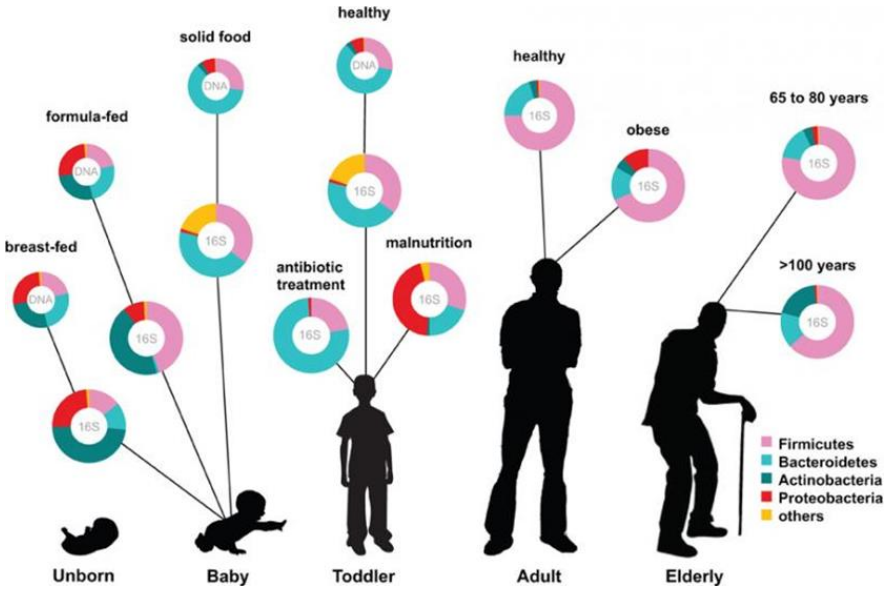


Lamport et al. British Journal of Nutrition (2017)

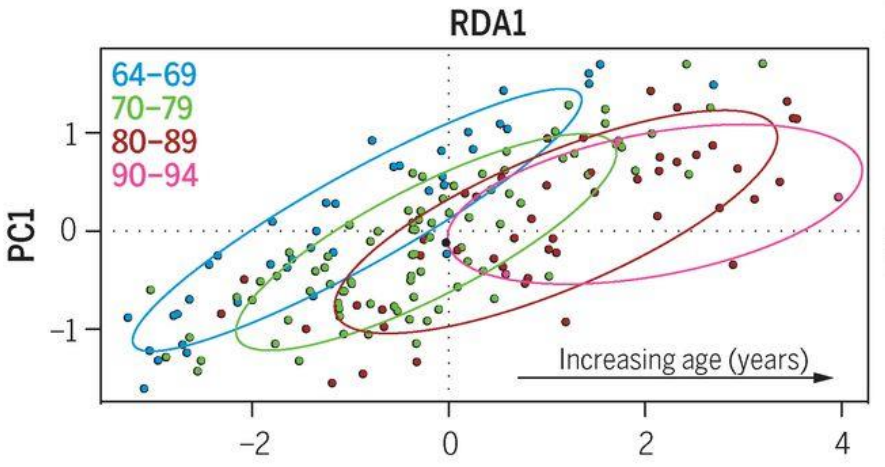
A more complex picture: The exposome, a lifelong process



Our microbiome is changing as we age



Ottman N et al. Front. Cell. Infect. Microbiol. 2012

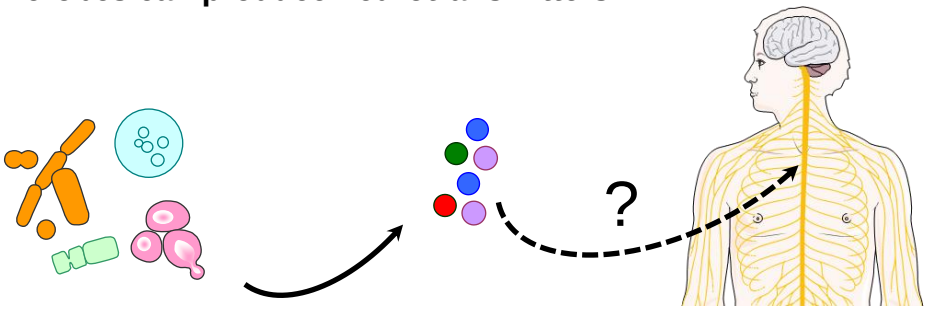


O'Toole P and Jeffery I.B. Science (2015); 350(6265):p214-1215

The brain and our body closely interact through the gut-brain axis

DA
Tryptophan
5-HT
GABA
Ach

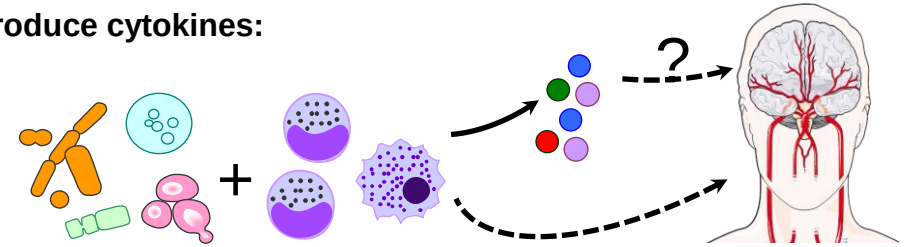
Gut microbes can produce neurotransmitters:



These neurotransmitters might signal the brain via the vagus nerve

Microbiota maintains microglia functionality

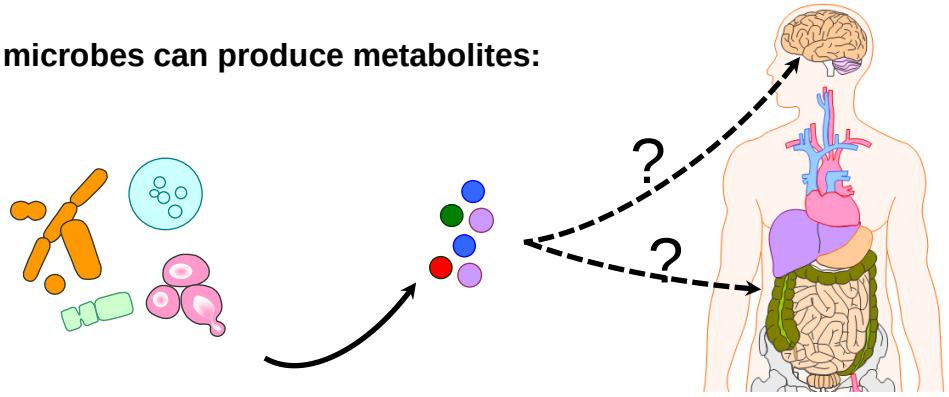
Gut microbes can stimulate immune cells to produce cytokines:



These cytokines might travel to the brain via blood vessels of the circulatory system

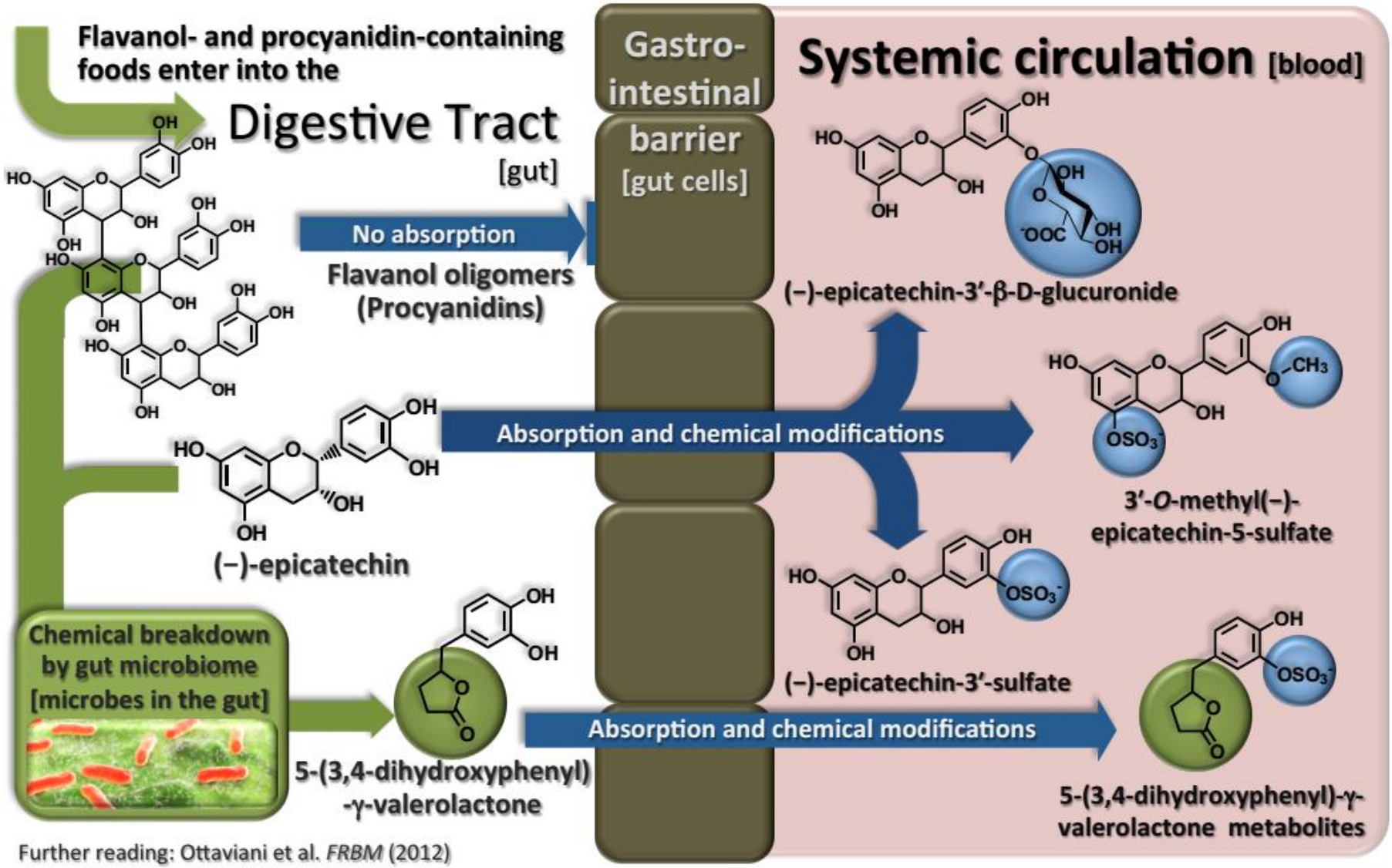
Microbial fermentation end-products (SCFA, butyrate regulate **epigenetic** synthesis of BDNF

Gut microbes can produce metabolites:



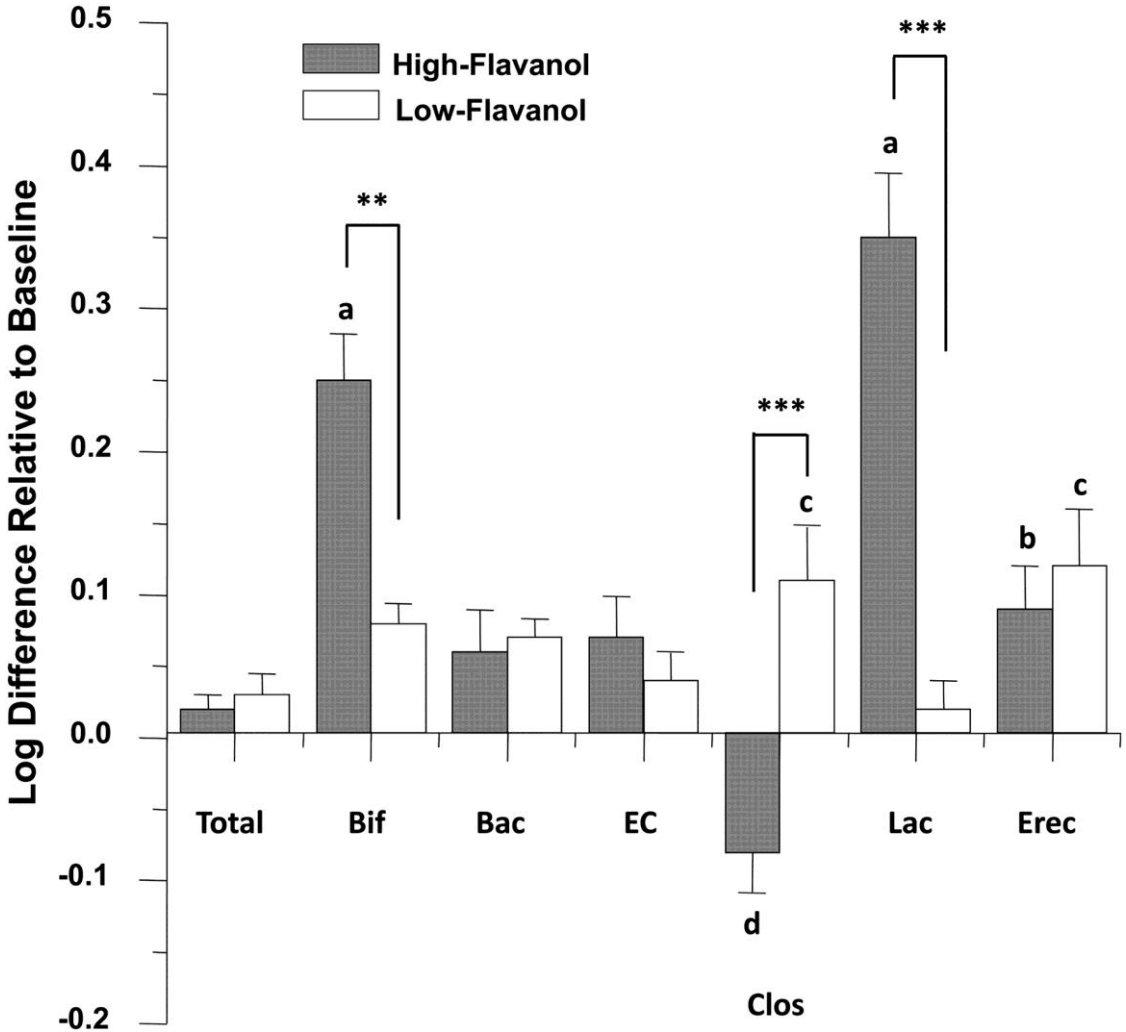
These metabolites might travel to the brain via blood vessels or stimulate gut epithelial cells to produce neurotransmitters that activate the vagus nerve

Polyphenol metabolism: example for procyanidins



Further reading: Ottaviani et al. *FRBM* (2012)

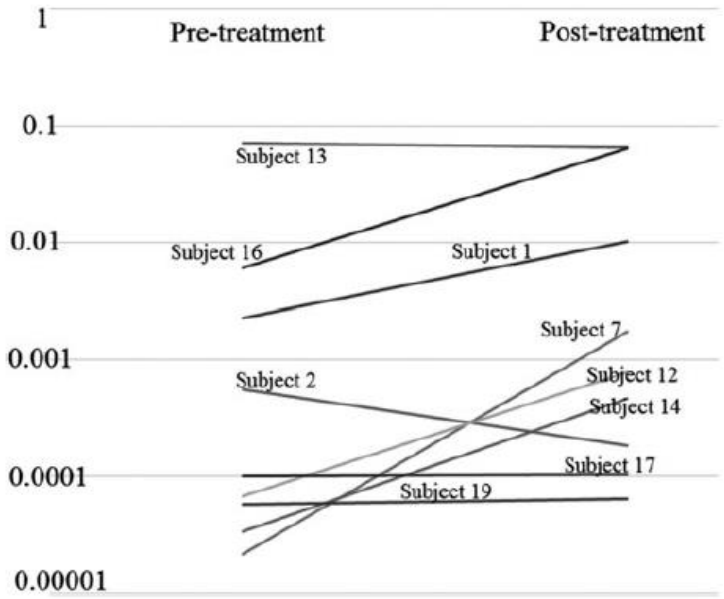
Cocoa flavanols affect gut microbiota diversity



Xenofon Tzounis et al. Am J Clin Nutr 2010;93:62-72

Cranberry flavonoids affect gut microbiota structure

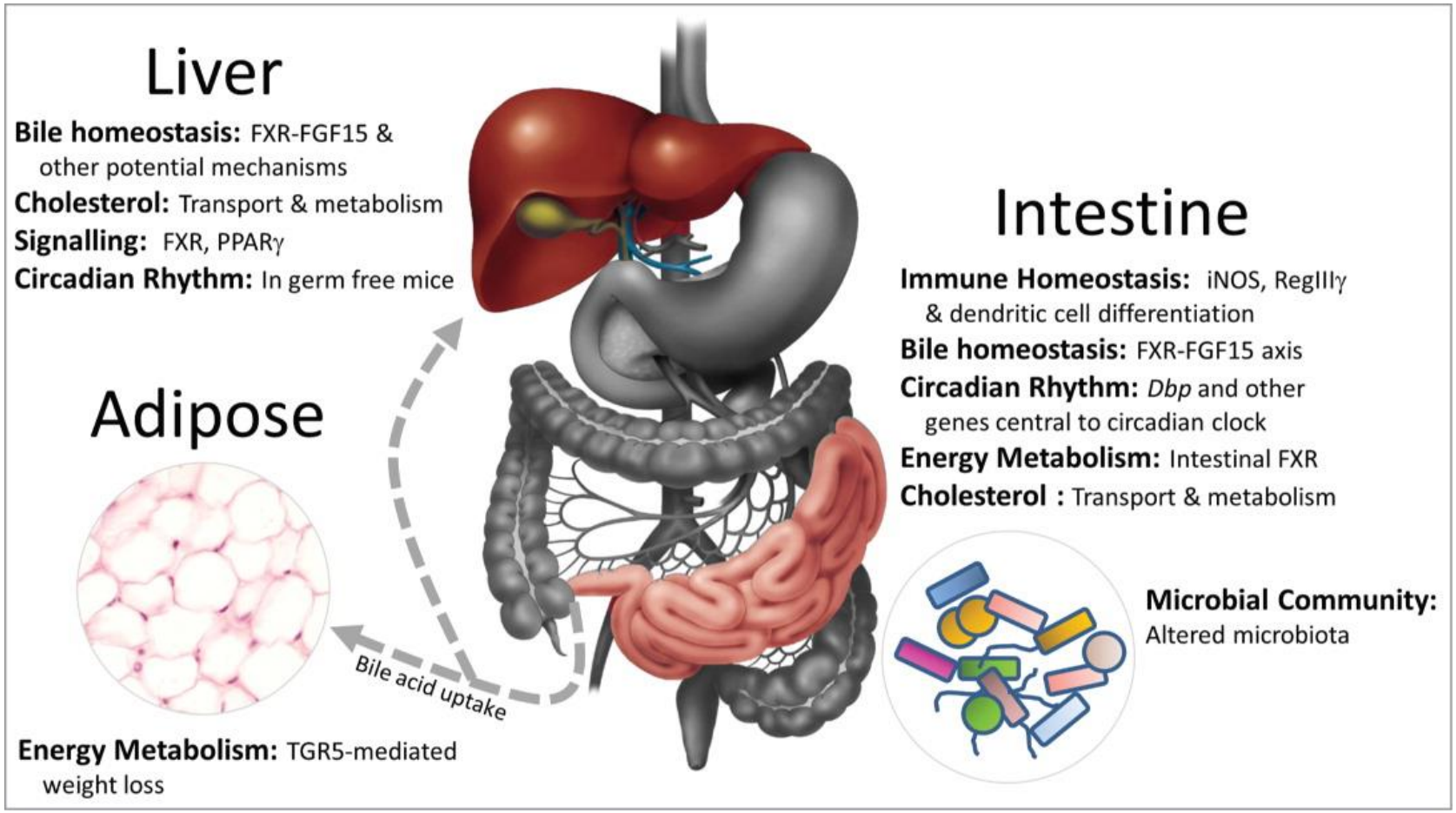
Weighted Unifrac distance
Subjects tend to cluster with themselves



Cranberries increase *Akkermansia* levels

Bekiares N *et al. Journal of Integrative Biology, 2017*

Role of bile acids for the gut/microbiota-liver axis



Impact of flavonoids on bile acid metabolism

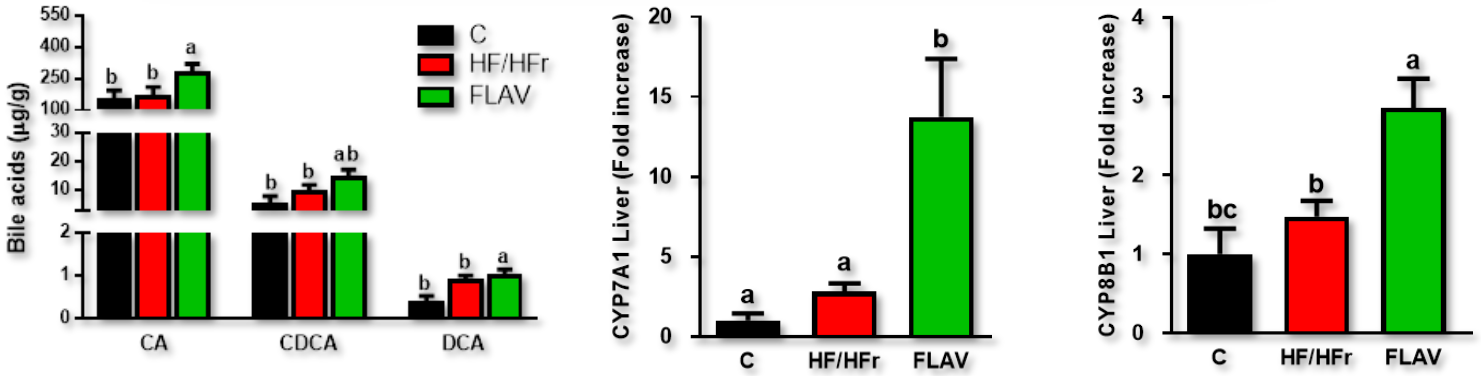
Contents lists available at ScienceDirect

BBA - Molecular Basis of Disease

journal homepage: www.elsevier.com/locate/bbadis

n-3 Fatty acids combined with flavan-3-ols prevent steatosis and liver injury in a murine model of NAFLD

David Vauzour[a,*,1], Ildefonso Rodriguez-Ramiro[a,1], Simon Rushbrook[b], Ignacio R. Ipharraguerre[c], Damon Bevan[a,d], Susan Davies[e], Noemi Tejera[a], Pedro Mena[f], Sonia de Pascual-Teresa[g], Daniele Del Rio[f], Jelena Gavrilovic[d], Anne Marie Minihane[a]



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Dr. John Walshaw
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BBSRC bioscience for the future
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