Cérebro 40+ - A importância da suplementação para atrasar o neuroenvelhecimento.

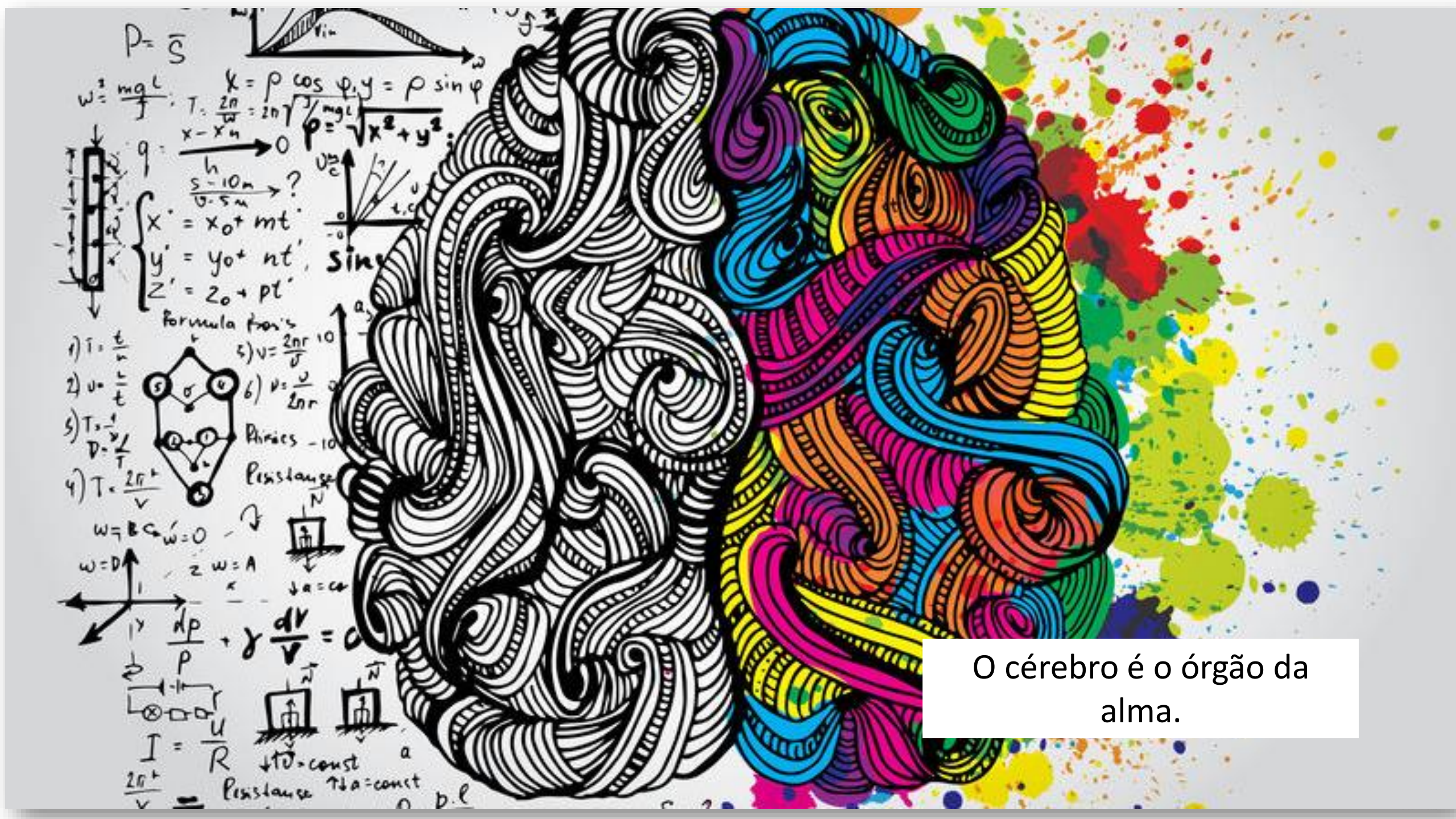
Prof. Dr. Fabrício Assini

Farmacêutico (UFSC-2000)

Mestre em Psicofarmacologia (UFSC-2005)

Doutor em Psicofarmacologia (UFSC-2011)

Diretor Científico da Escola de Neurosuplementação


O cérebro é o órgão da alma.

Journal of Diabetes Science and Technology
Volume 2, Issue 6, November 2008

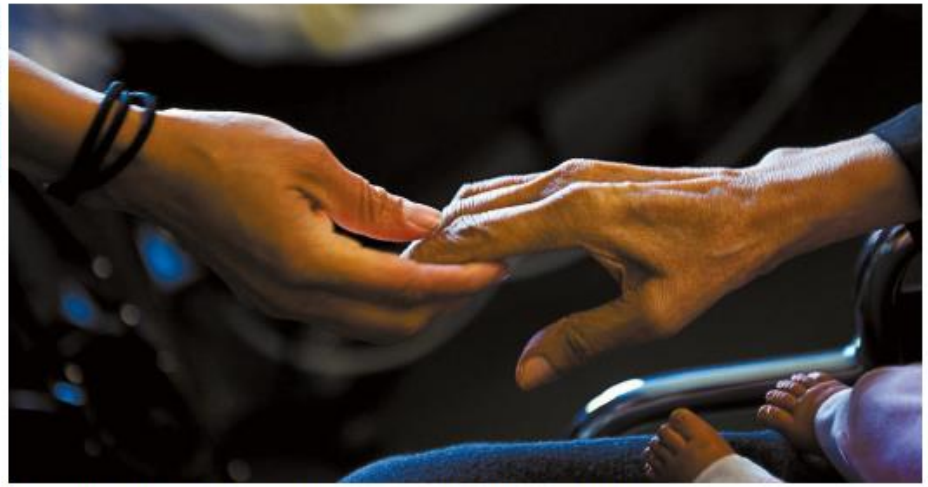
REVIEW ARTICLE

Alzheimer's Disease Is Type 3 Diabetes—Evidence Reviewed

Suzanne M. de la Monte, M.D., M.P.H.[1–3] and Jack R. Wands, M.D.[3]

Estamos errados ao chamar o Alzheimer de Diabetes do Tipo 3?

COMMENT



KATHERINE FREYTHE/WASHINGTON POST

The number of people living with Alzheimer's is on the rise — one in ten people aged 65 or over now has the disease.

Stop Alzheimer's before it starts

Success in the hunt for drugs to halt Alzheimer's disease has remained elusive; it's time to stop the disease before it gets started, urge **Eric McDade** and **Randall J. Bateman**.

In 2015, the global cost of Alzheimer's disease was US$818 billion. That's similar to the gross domestic product of the world's 18th-largest economy. By 2030, the number of people with the disease is expected to rise to more than 70 million worldwide (see 'Staying ahead').

Unless there is a breakthrough in treatment, nearly one in every 2–3 people over 85 will have Alzheimer's. Even those who escape the disease will have at least one close friend or relative who can no longer converse with them, has no recollection of what happened minutes before and is reliant on round-the-clock care.

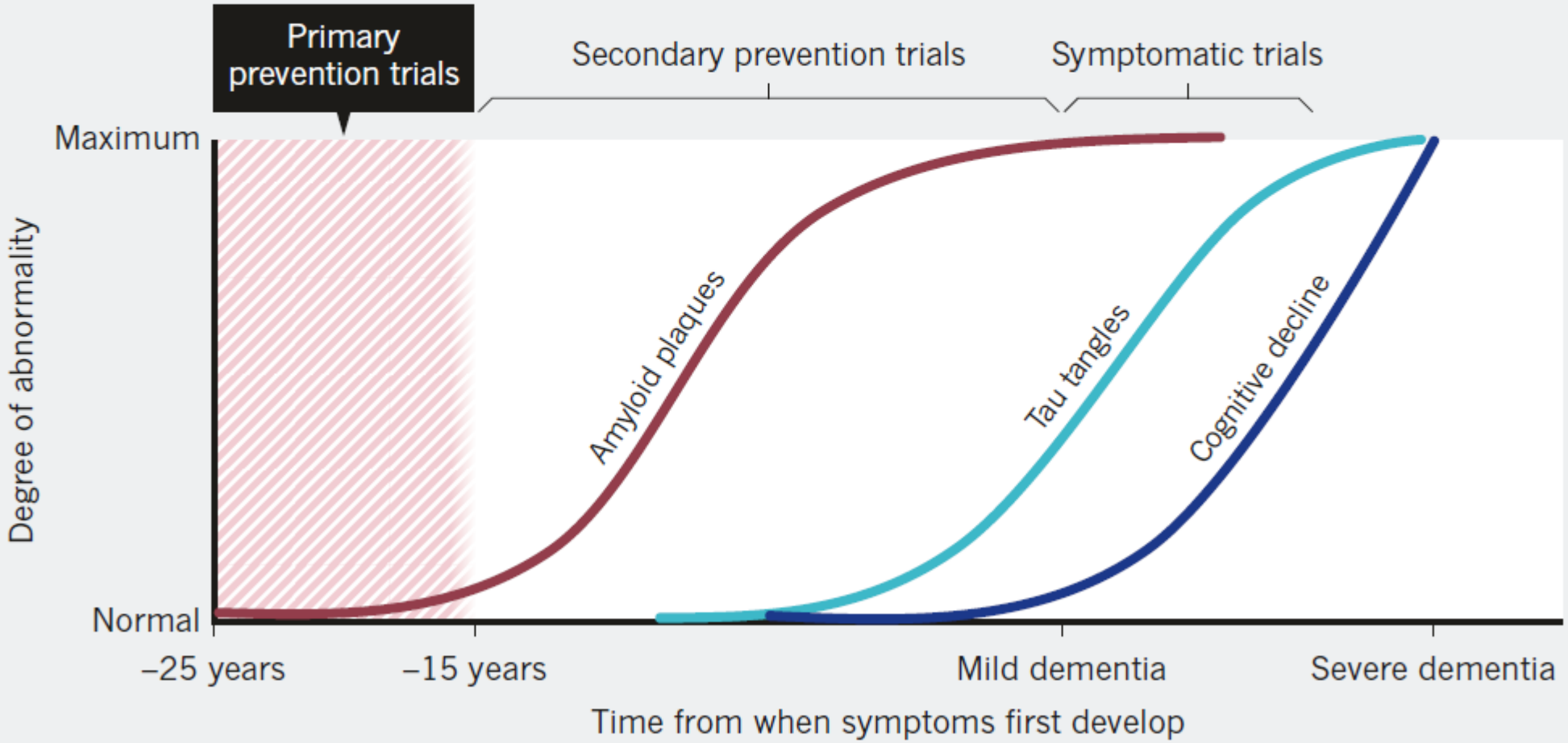
Clinical trials have predominantly focused on therapies aimed at treating people who have developed symptoms (memory loss, confusion and difficulties communicating) and begun to lose independence. In the past five years, investigators have started trials at an earlier stage — when memory loss is mild or absent but brain scans reveal the hallmark pathology of amyloid-β protein plaques. However, we think that the clock should be turned back even further — to when the signature brain pathology hasn't yet appeared.

An important precedent for such 'primary prevention' is statins. In the early 1980s, these now-widespread medications were shown to lower blood cholesterol in people with a rare genetic disorder that severely elevates it. People with the condition (around 0.005% of the population) typically develop cardiovascular symptoms as adolescents or young adults. Without treatment, they typically die in their 30s[1]. But when statins are given to such people in childhood, the onset of heart disease and stroke is delayed by decades, and lifespan prolonged by between 15 and 30 years.

The search for an Alzheimer's 'statin' is ▶

STAYING AHEAD

Primary prevention trials would investigate drugs designed to treat Alzheimer's disease before brain pathology, such as amyloid-β plaques and tau tangles, or cognitive symptoms develop.



Fonte: Nature (153) vol 547 | 2017

STAYING AHEAD

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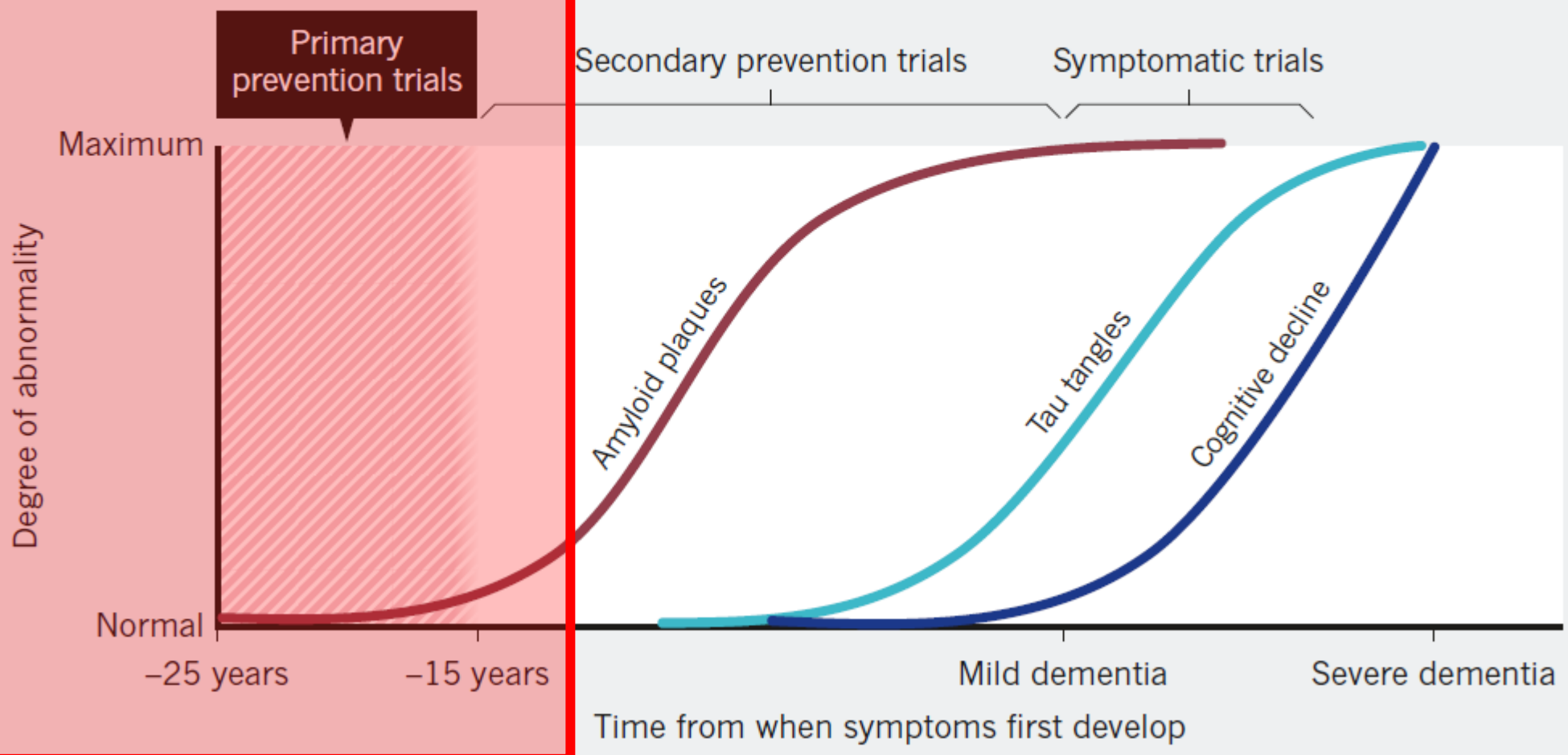


Fonte: Nature (153) vol 547 | 2017

Mantenha-se à frente

Estamos errados ao chamar o Alzheimer de Diabetes do Tipo 3?

Estamos errados ao chamar o Alzheimer de Diabetes do Tipo 3?

Sim ou pelo menos colocando o problema numa **escala temporal equivocada** ou ainda, com **foco muito específico**.

Porque prevenir o neuroenvelhecimento envolve estimular a saúde emocional e cognitiva de adultos.

Xie et al. BMC Geriatrics (2022) 22:494
https://doi.org/10.1186/s12877-022-03181-6

BMC Geriatrics

RESEARCH Open Access

Association between childhood friendship and cognitive ageing trajectory in later life: evidence from the China Health and Retirement Longitudinal Study (CHARLS)

Jinzhao Xie[1†], Xiaoyan Fan[2†], Ping Yin[1], Jing Gu[1,3,4*] and Chengwu Yang[5,6]

Abstract

Background: Childhood experience has been suggested to affect cognitive function in later life. However, the association between childhood friendship status and cognitive ageing trajectory in middle-aged and older adults has not been fully assessed. This study examined the association between childhood friendship status and cognitive ageing trajectory and identified factors modifying this association.

Methods: We used four waves of data from the China Health and Retirement Longitudinal Study (CHARLS), a national representative longitudinal study of adults aged 45 years or older, 2011–2018. The CHARLS included surveys on childhood friendship and cognitive assessments. Childhood friendship status was categorised as poor, fair, and good. To examine the association between childhood friendship and cognitive ageing trajectory in later life, we applied multilevel linear regression models, and explored potential influences of sociodemographic factors, health status and behaviours, and childhood conditions on this association.

Results: Of the 4,350 participants, 1,919 (44.1%) were women. The mean age was 56.29 ± 7.80 years. We found childhood friendship was significantly associated with cognitive ageing trajectory in later life, with a dose–response relationship. After adjusting for covariates, comparing to participants with poor childhood friendships, those with better childhood friendships had lower rates of cognitive decline (β = 0.12, 95% confidence interval [CI]: 0.03 to 0.22 [interaction term of fair friendship and time]; β = 0.19, 95% CI: 0.10 to 0.28 [interaction term of good friendship and time]) and higher level of cognitive functions (β = 0.40, 95% CI: 0.22 to 0.58 [fair friendships]; β = 0.61, 95% CI: 0.43 to 0.79 [good friendships]). These associations were stronger for those who were female, less educated, and had experienced more adverse childhood experiences.

Conclusions: Childhood friendship is associated with cognitive ageing in later life. Enhancing childhood friendships can play an important role to promote healthy ageing in the future.

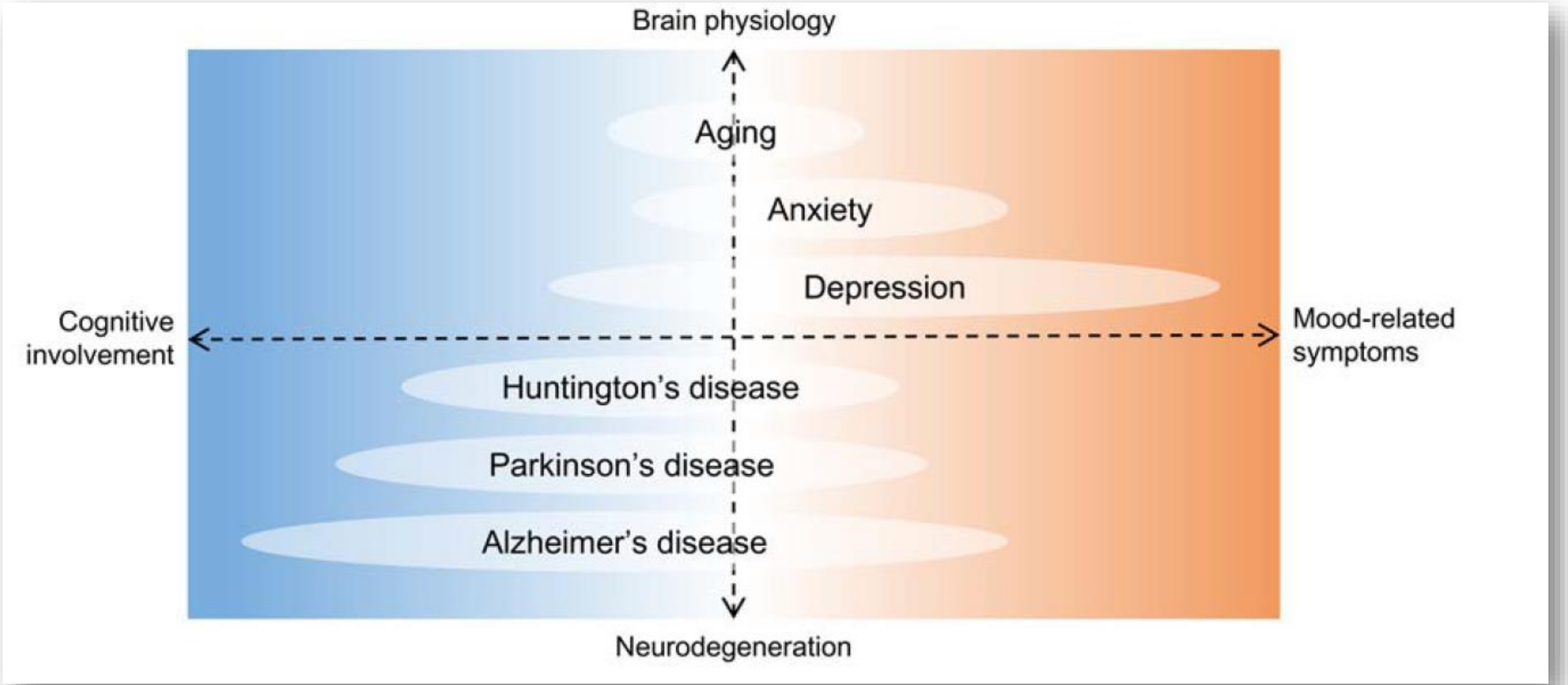
Keywords: Cognitive ageing, Childhood friendship, Multilevel model, China

Current Nutrition Reports
https://doi.org/10.1007/s13668-019-0276-z

NUTRITION AND THE BRAIN (J NASSER, SECTION EDITOR)

Impact of Brain Insulin Signaling on Dopamine Function, Food Intake, Reward, and Emotional Behavior

André Kleinridders [1,2] · Emmanuel N. Pothos [3]



Fonte: Front. Neuroanat. 12:44. doi: 10.3389/fnana.2018.00044

Existe envelhecimento NORMAL do SNC?

Published in final edited form as:

J Neurochem. 2018 March ; 144(5): 595–608. doi:10.1111/jnc.14234.

Cerebral Blood Flow in Normal Aging Adults: Cardiovascular Determinants, Clinical Implications, and Aerobic Fitness

Takashi Tarumi[a,b] and **Rong Zhang**[a,b,c]

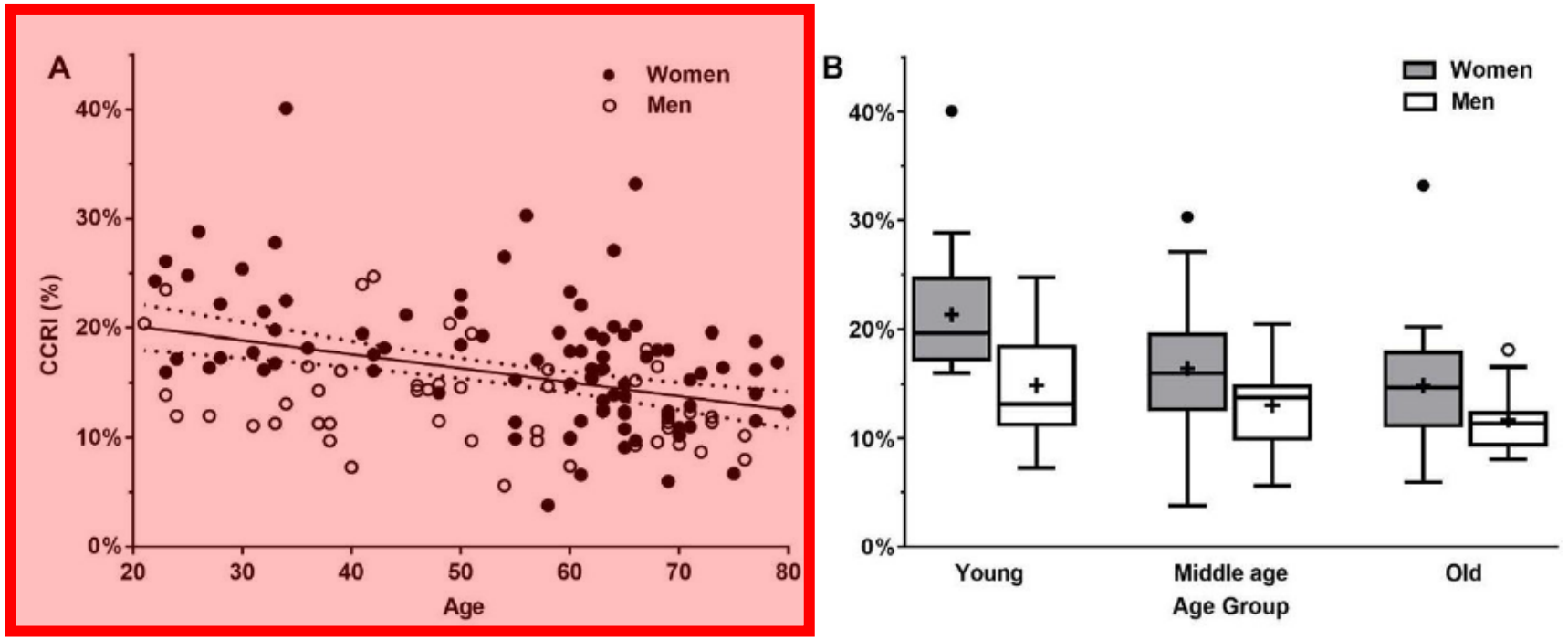
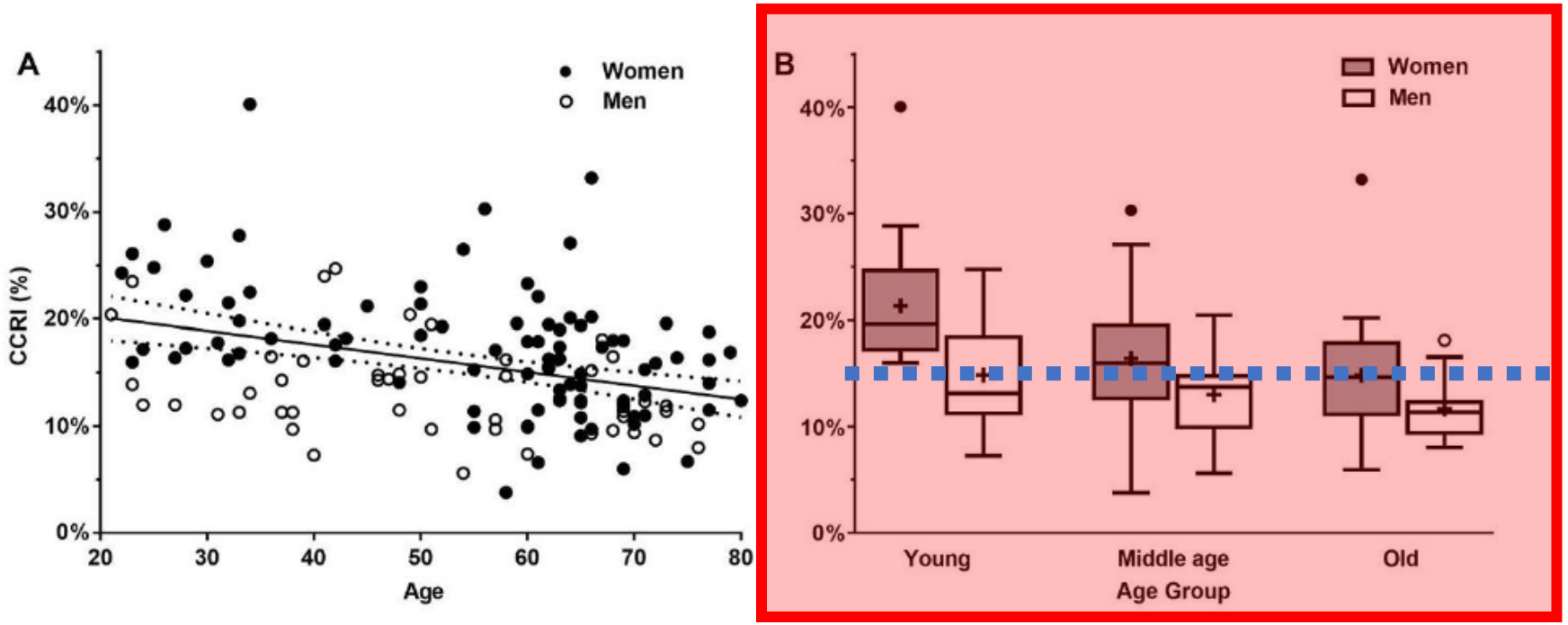


Figure 2.

Association between age and the proportion of cardiac output distributed to the brain (n=139). The CCRI represents the cerebral blood flow to cardiac output ratio index. Panel A shows the linear decline of CCRI with increasing age (CCRI=−0.127%×age+22.72% with R^2=0.13, P<0.001). Panel B shows the association between age and CCRI in men and women separately (P<0.001 for age group, P<0.001 for sex, and P=0.26 for age and sex interaction). Young=21–45 years; middle age=45–65 years; and old=66–80 years. Error bars



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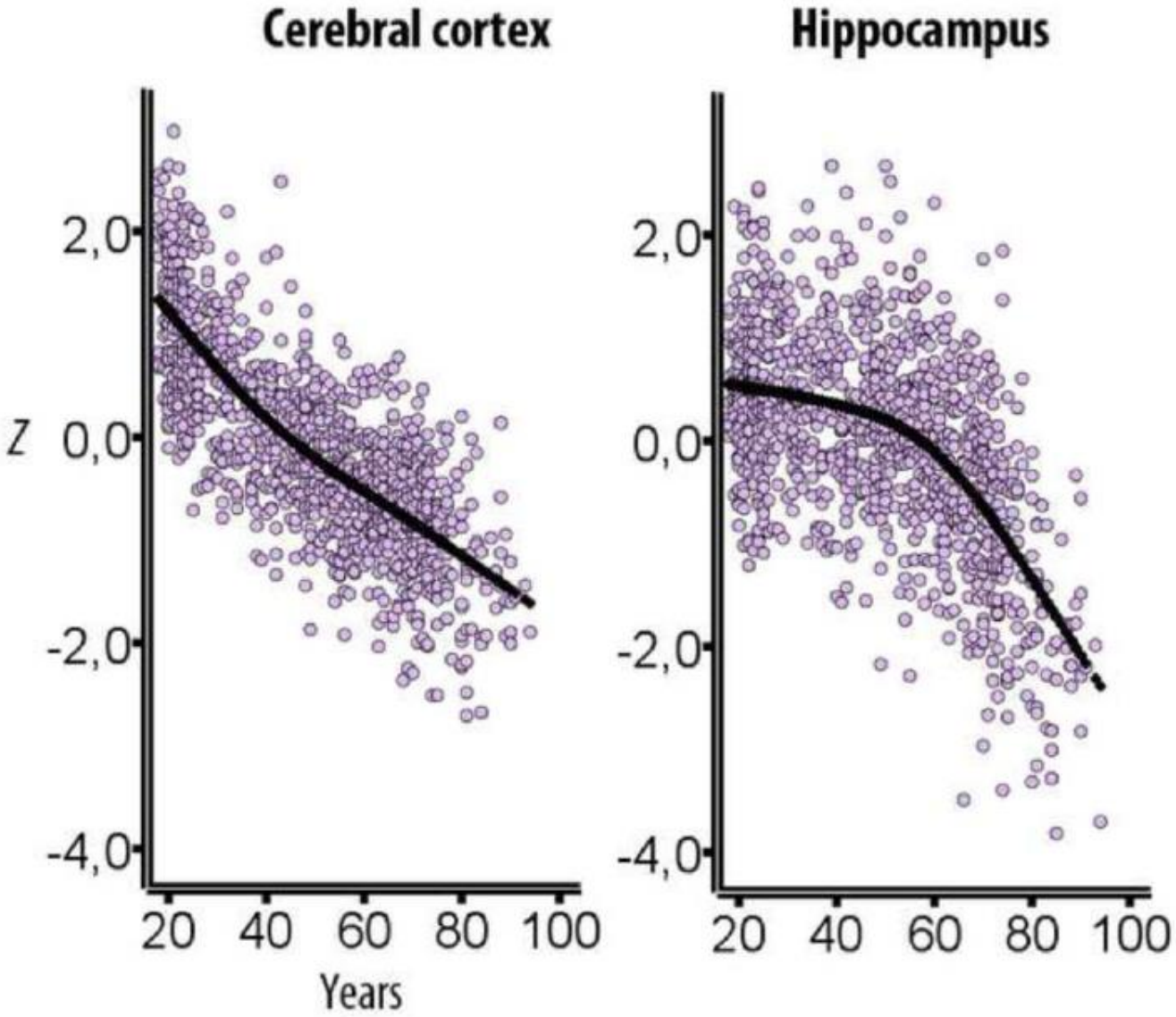
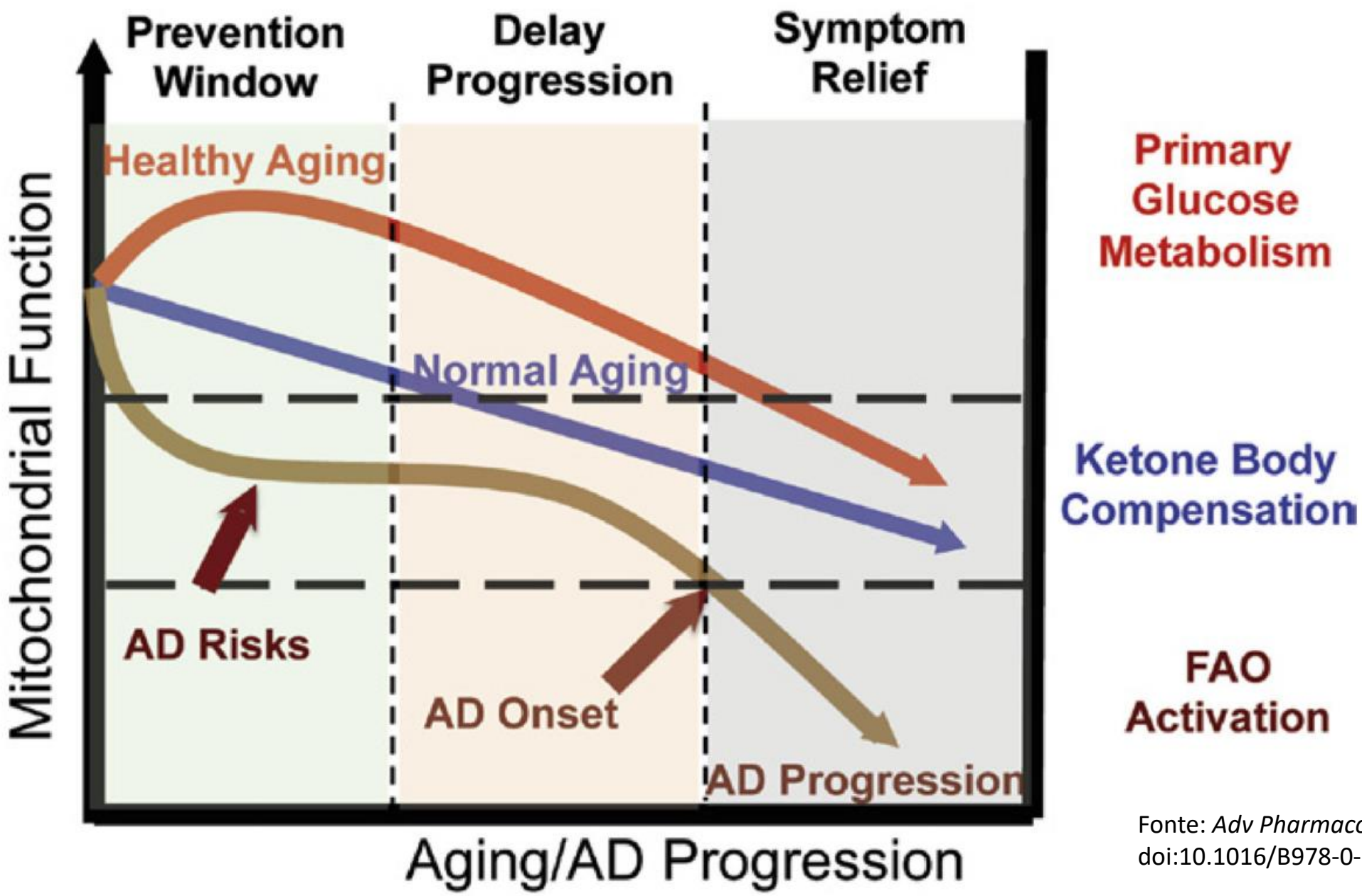


Figure 5. Life-span trajectories of volumetric reductions
Cross-sectional estimates of adult life-span trajectories of total cerebral cortex volume and total hippocampal volume. Volume is expressed in units of standard deviations. Data from (Fjell et al., 2013c).

Fonte: *Prog Neurobiol*. 2014 June ; 117: 20–40. doi:10.1016/j.pneurobio.2014.02.004



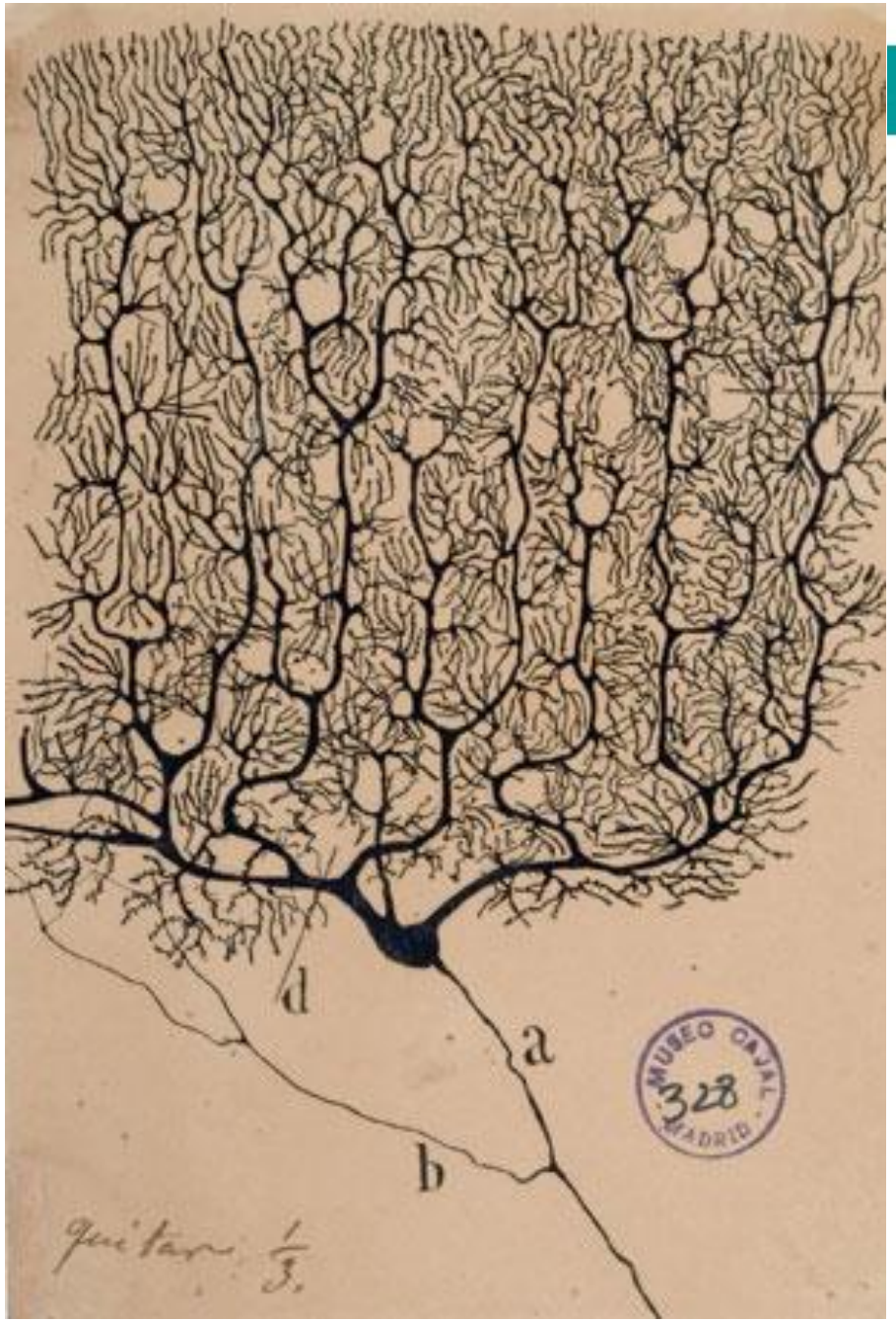
Fonte: *Adv Pharmacol*. 2012 ; 64: 327–371. doi:10.1016/B978-0-12-394816-8.00010-6.

Existe uma atrofia normal durante o envelhecimento do cérebro, essa diminuição acontece tanto na *substância cinzenta quanto branca* e também está associada com o crescimento dos *ventrículos*. Drayer BP. Imaging of the aging brain. Part I Normal findings. Radiology. 1988; 166:785–796.

- Análises histológicas sugerem que a atrofia esteja **relacionada com a regressão de dendritos** e morte neuronal. Dumitriu D, J Neurosci. 2010; 30:7507–7515

“Cada neurônio faz em média 10.000 sinapses. Podendo chegar ao extremo de 200.000 nos dendritos das células de Purkinje do cerebelo”

(Roberto Lent, 100 bilhões de neurônios).



Ramón y Cajal, S. Degeneration and Regeneration of the Nervous System (Trans. Day, R. M., from the 1913 Spanish edn) (Oxford Univ. Press, London, 1928).

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(Roberto Lent, 100 bilhões de neurônios).

E dai?!

Psychiatry Research: Neuroimaging 266 (2017) 1–9

Contents lists available at ScienceDirect

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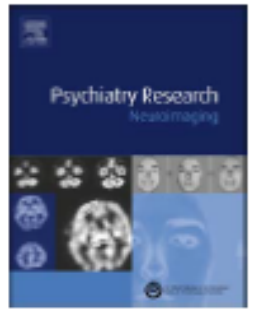


Frontal and subcortical grey matter reductions in PTSD

Daniel C.M. O'Doherty[a,*], Ashleigh Tickell[a], Will Ryder[a], Charles Chan[a], Daniel F. Hermens[a], Maxwell R. Bennett[a], Jim Lagopoulos[b]

Brain Atrophy in Multiple Sclerosis

Clinical Relevance and Technical Aspects

Jaume Sastre-Garriga, MD, PhD[a,*], Deborah Pareto, PhD[b,c], Àlex Rovira, MD[b,c]

Neuroimag Clin N Am ■ (2017) ■–■
http://dx.doi.org/10.1016/j.nic.2017.01.002

Psychological Medicine (2015), **45**, 1931–1944.
doi:10.1017/S0033291714003055

ORIGINAL

Depression, depressive symptoms, and rate of hippocampal atrophy in a longitudinal cohort of older men and women

GENÉTICA

G1, G2, G3

Epigenética

AMBIENTE

Estresse, traumas, relações interpessoais...

- Tristeza e sentimento de culpa;
- Anedonia;
- Agitação/ lentidão;
- Tendências suicidas;
- Alterações de sono;
- Atenção e foco;
- Aprendizado e memória

Por onde começar?

3 passos essenciais para ajustar a neuroquímica e promover saúde emocional e cognitiva

Esteja atento para os fatores de risco durante a anamnese;

Garanta a síntese de ATP;

Pense de maneira integrativa.

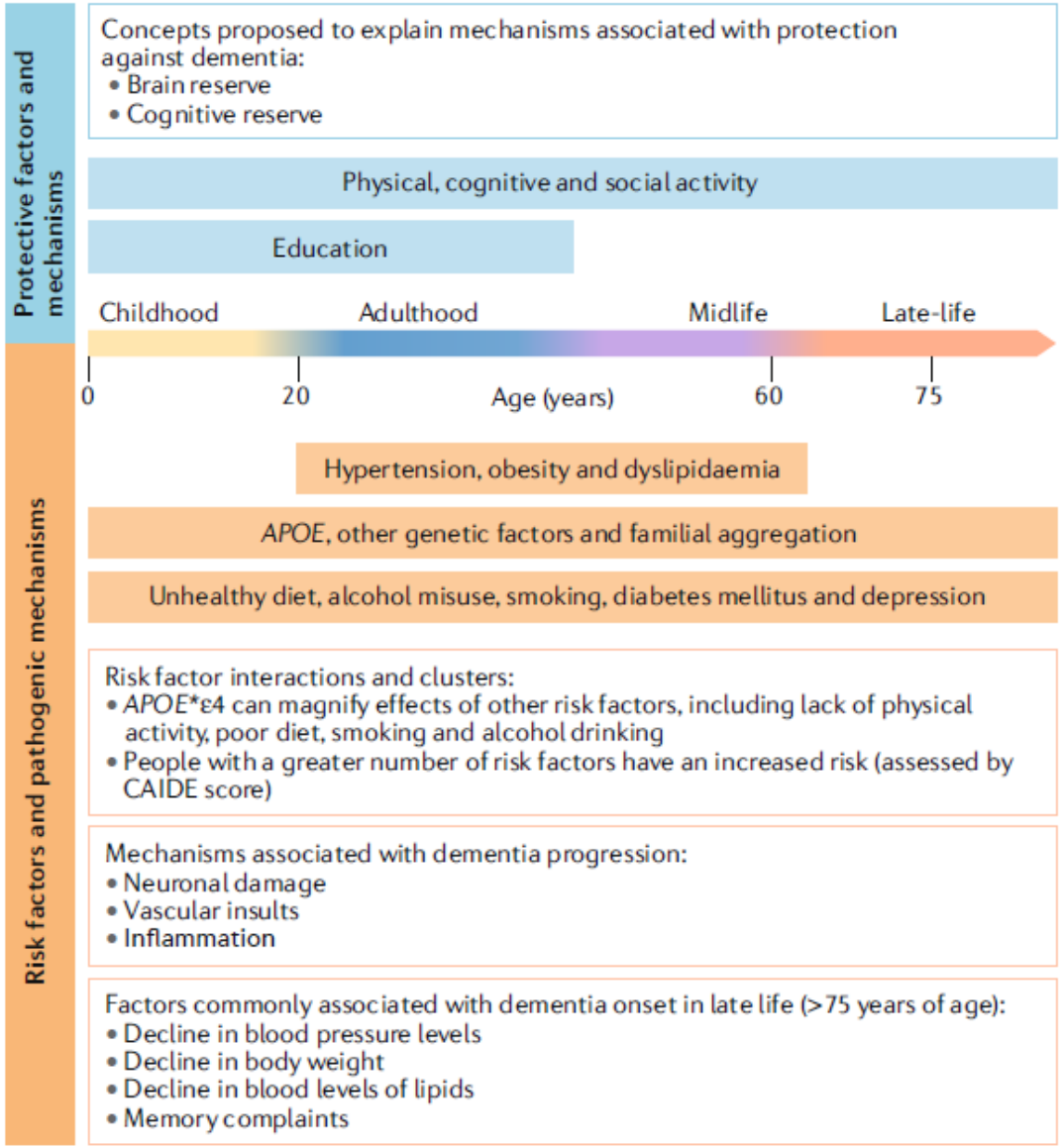
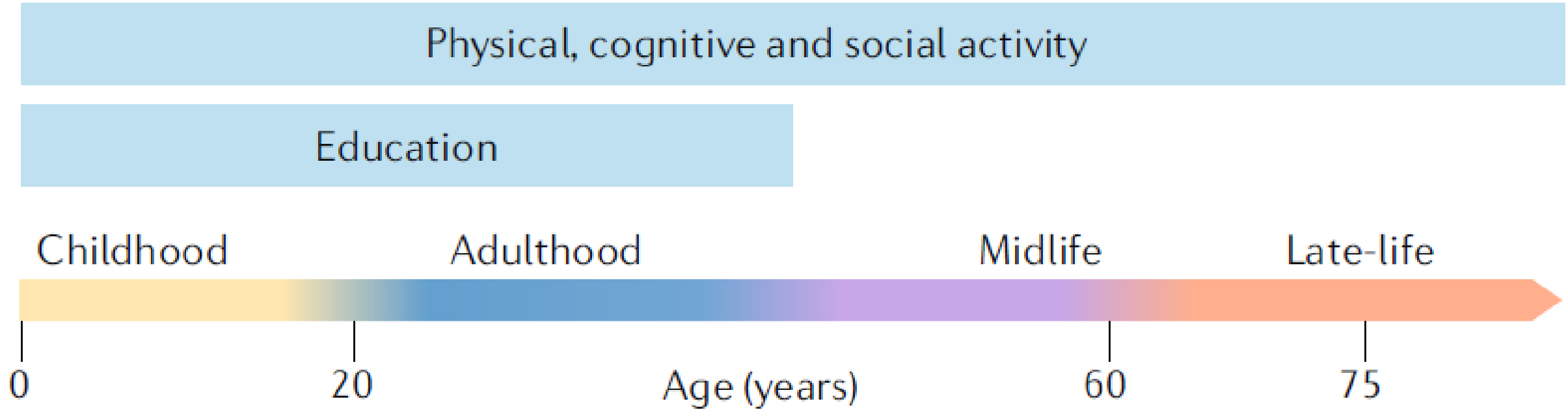


Fig. 1 | **Risk and protective factors for dementia and Alzheimer disease across the lifespan.** Some factors can differentially affect the risk of dementia and Alzheimer disease in an individual depending on the time of exposure within the life course. For example, hypertension, obesity and dyslipidaemia increase dementia risk when a person is exposed during midlife. By contrast, other factors such diet affect risk across the lifespan. CAIDE, Cardiovascular Risk Factors, Aging and Dementia.

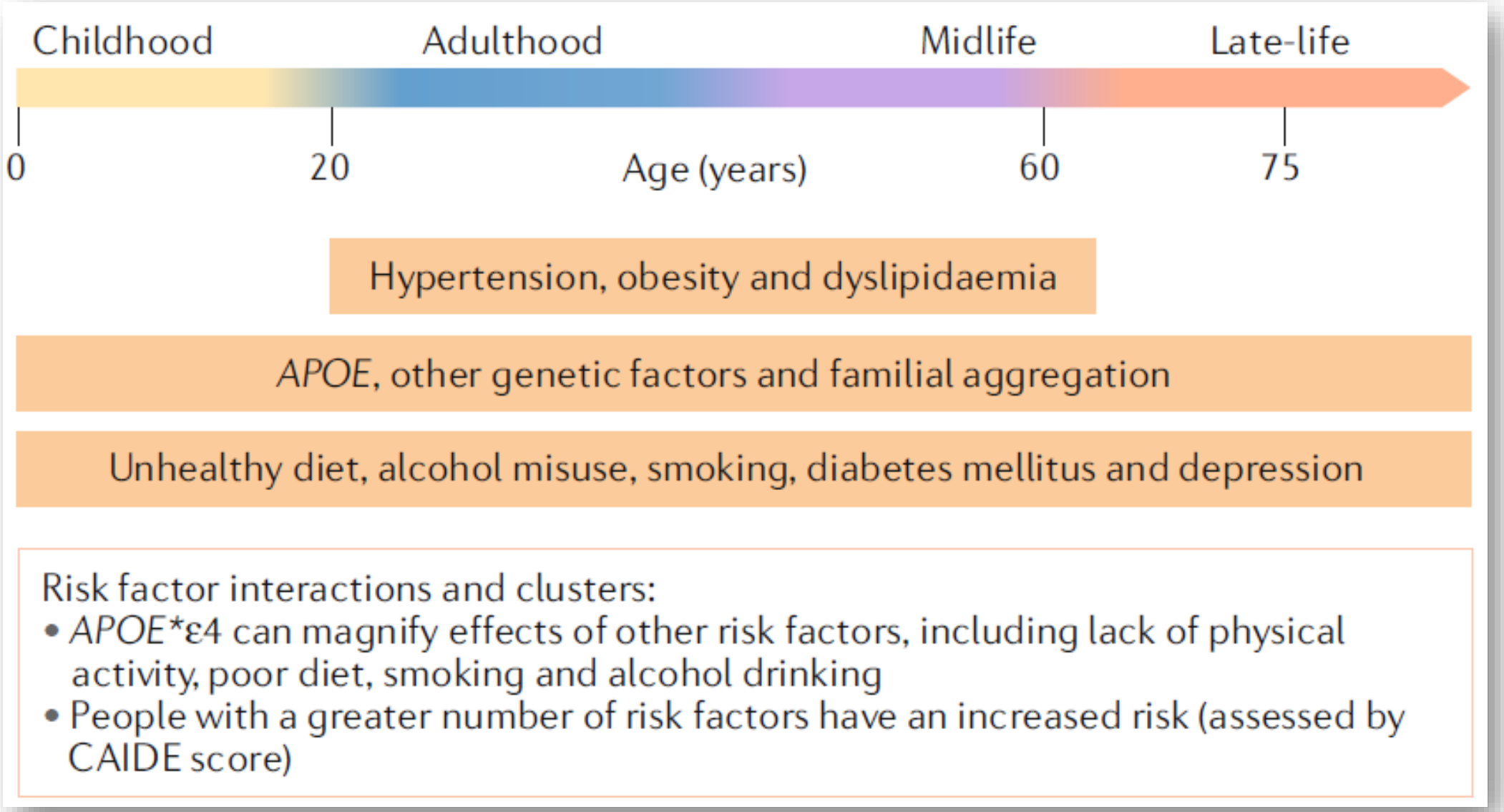
Fonte: Nat Rev Neurol. 2018 Nov; 14(11):653-666.
doi: 10.1038/s41582-018-0070-3.

Concepts proposed to explain mechanisms associated with protection against dementia:

- Brain reserve
- Cognitive reserve



Fonte: Nat Rev Neurol. 2018 Nov;14(11):653-666. doi: 10.1038/s41582-018-0070-3.



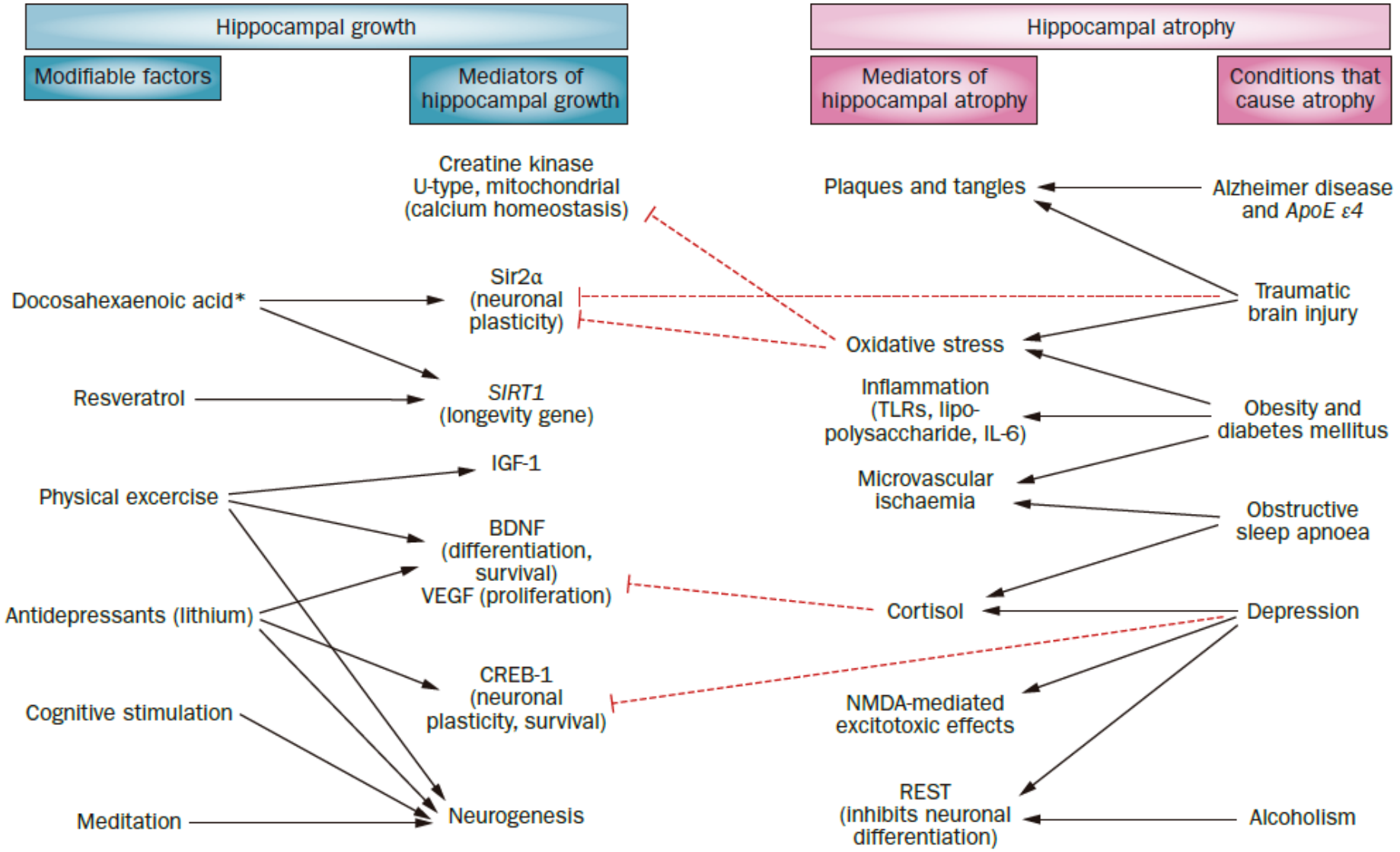
Fonte: Nat Rev Neurol. 2018 Nov;14(11):653-666. doi: 10.1038/s41582-018-0070-3.

Table 1
Current evidence for preventive strategies, targeting risk and protective factors, and the underlying biological mechanisms.

Preventive strategies	Risk and protective factors	Biological mechanisms				
		Neurodegeneration	Brain resilience	Vascular damage	Inflammation	Oxidative stress
Targeting the body to protect the brain	Systemic and cerebral atherosclerosis	[c]		[a]	[a]	[c]
	Atrial fibrillation	[c]		[a]	[b]	[c]
	Heart failure	[c]		[a]	[b]	[c]
	Ischemic heart disease	[c]		[a]	[b]	[c]
	Mid-life hypertension	[b]		[a]	[b]	[c]
	Diabetes	[b]		[a]	[b]	[b]
	Mid-life obesity	[c]				
Interventions to counteract brain aging	High education		[b]			
	Work complexity		[b]			[c] (Reduced)
	Leisure-time mentally, socially and physically stimulating activities		[b]	[b] (Reduced)	[b] (Reduced)	[c] (Reduced)
Lifespan health promotion to reduce dementia risk	Physical inactivity	[b]	[b]	[a]	[b]	[c]
	Smoking	[c]		[a]	[b]	[c]
	Excessive alcohol consumption	[c]		[a]	[b]	[c]
	Unhealthy/imbalanced diet	[c]		[a]	[b]	[c]

[a] Strong evidence (i.e. evidence from meta-analyses, RCTs, well designed cohort studies with consistent findings).
[b] Emerging evidence (i.e. less consistent findings).
[c] Limited evidence (i.e. limited number of studies).

Fonte: Ageing Research Reviews Volume 64, December 2020, 101045 https://doi.org/10.1016/j.arr.2020.101045



Fonte: Fotuhi, M. *et al. Nat. Rev. Neurol.* 8, 189–202 (2012); doi:10.1038/nrneurol.2012.27

The CAIDE dementia risk score

Risk factor		Points
Age	<47 years	0
	47–53 years	3
	>53 years	4
Education	≥10 years	0
	7–9 years	2
	<7 years	3
Sex	Female	0
	Male	1
Blood pressure	≤140 mmHg	0
	>140 mmHg	2
BMI	≤30 kg/m ^{2}	0
	>30 kg/m ^{2}	2
Total cholesterol	≤6.5 mmol/l	0
251,5 mg/dL	>6.5 mmol/l	2
Physical activity	Yes	0
	No	1

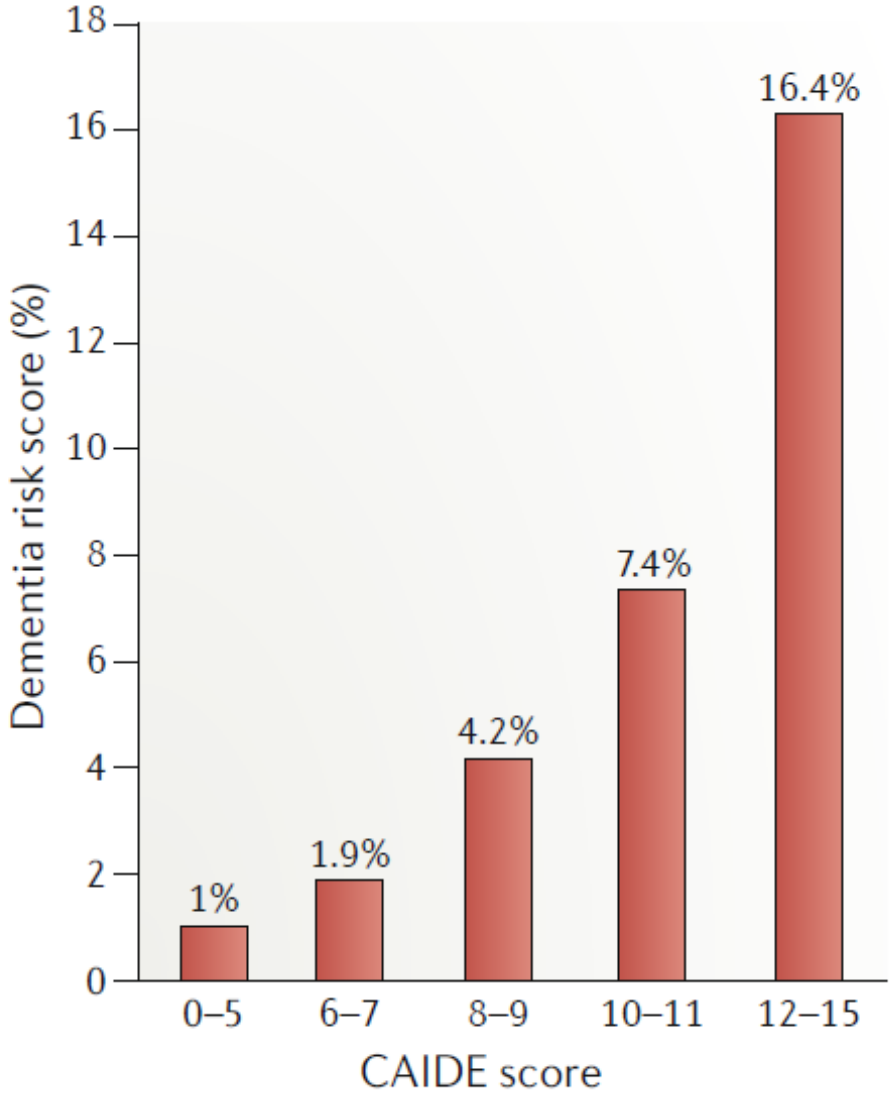
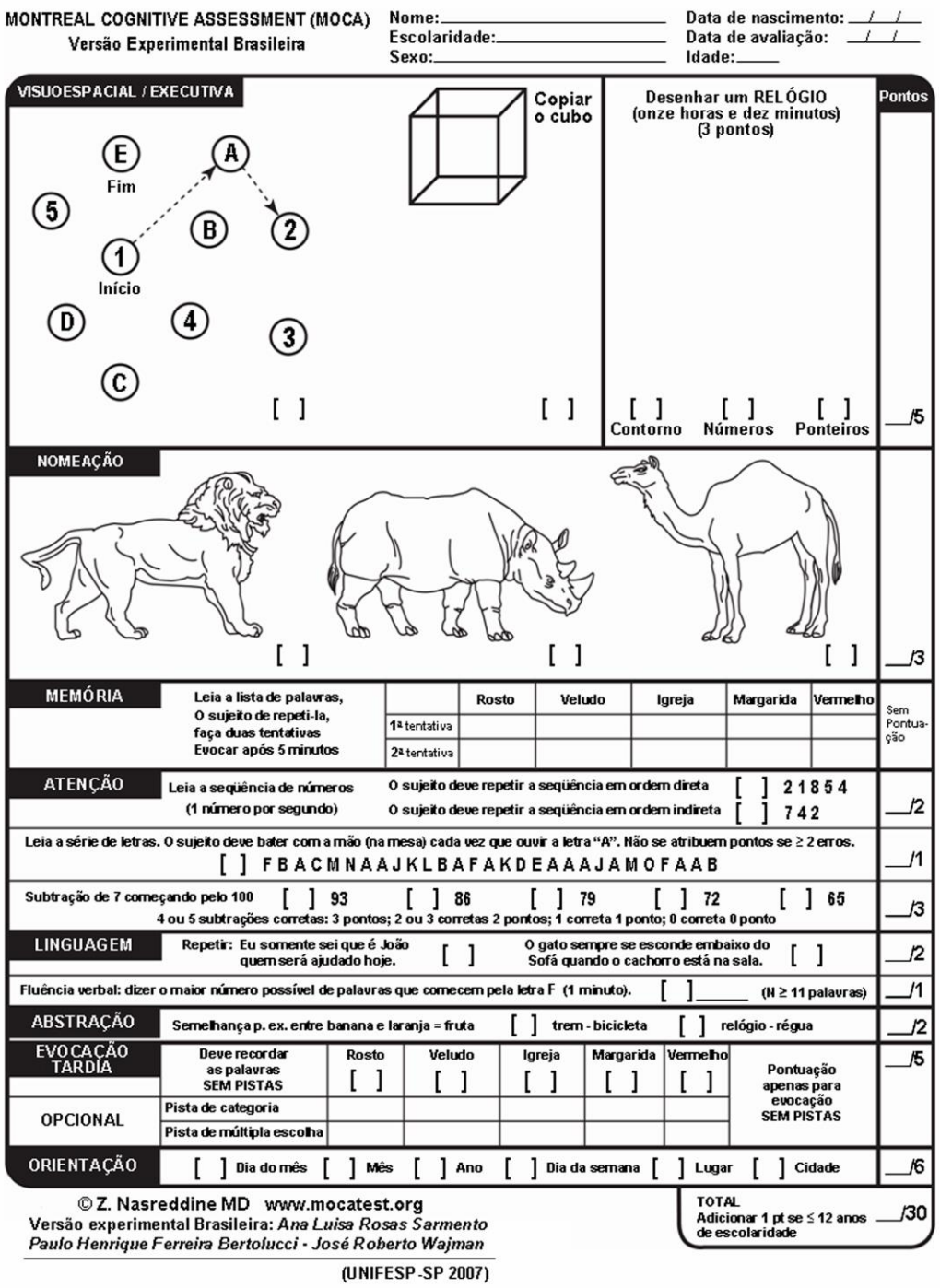


Fig. 2 | **CAIDE risk score.** The Cardiovascular Risk Factors, Aging and Dementia (CAIDE) risk score enables the prediction of the later risk of dementia on the basis of the risk factor profile present in midlife (age 40–65 years).

Montreal Cognitive Assessment (MOCA) test

Valores abaixo de 26 indicam prejuízo cognitivo leve.



MONTREAL COGNITIVE ASSESSMENT (MOCA)
Versão Experimental Brasileira

Nome: _____ Data de nascimento: __/__/__
Escolaridade: _____ Data de avaliação: __/__/__
Sexo: _____ Idade: ____

VISUOESPACIAL / EXECUTIVA — Pontos

Copiar o cubo

E Fim · A · 5 · B · 2 · 1 Início · D · 4 · 3 · C

[ ] [ ]

Desenhar um RELÓGIO (onze horas e dez minutos) (3 pontos)

[ ] Contorno [ ] Números [ ] Ponteiros

__/5

NOMEAÇÃO

[ ] [ ] [ ]

__/3

MEMÓRIA — Leia a lista de palavras, O sujeito de repeti-la, faça duas tentativas. Evocar após 5 minutos

	Rosto	Veludo	Igreja	Margarida	Vermelho
1ª tentativa					
2ª tentativa					

Sem Pontuação

ATENÇÃO

Leia a seqüência de números (1 número por segundo)

O sujeito deve repetir a seqüência em ordem direta [ ] 2 1 8 5 4

O sujeito deve repetir a seqüência em ordem indireta [ ] 7 4 2

__/2

Leia a série de letras. O sujeito deve bater com a mão (na mesa) cada vez que ouvir a letra "A". Não se atribuem pontos se ≥ 2 erros.

[ ] F B A C M N A A J K L B A F A K D E A A A J A M O F A A B

__/1

Subtração de 7 começando pelo 100 [ ] 93 [ ] 86 [ ] 79 [ ] 72 [ ] 65

4 ou 5 subtrações corretas: 3 pontos; 2 ou 3 corretas 2 pontos; 1 correta 1 ponto; 0 correta 0 ponto

__/3

LINGUAGEM

Repetir: Eu somente sei que é João quem será ajudado hoje. [ ]

O gato sempre se esconde embaixo do Sofá quando o cachorro está na sala. [ ]

__/2

Fluência verbal: dizer o maior número possível de palavras que comecem pela letra F (1 minuto). [ ]_____ (N ≥ 11 palavras)

__/1

ABSTRAÇÃO

Semelhança p. ex. entre banana e laranja = fruta [ ] trem - bicicleta [ ] relógio - régua

__/2

EVOCAÇÃO TARDIA

	Deve recordar as palavras SEM PISTAS	Rosto	Veludo	Igreja	Margarida	Vermelho	Pontuação apenas para evocação SEM PISTAS
		[ ]	[ ]	[ ]	[ ]	[ ]	
OPCIONAL	Pista de categoria						
	Pista de múltipla escolha						

__/5

ORIENTAÇÃO

[ ] Dia do mês [ ] Mês [ ] Ano [ ] Dia da semana [ ] Lugar [ ] Cidade

__/6

© Z. Nasreddine MD www.mocatest.org
Versão experimental Brasileira: *Ana Luisa Rosas Sarmento, Paulo Henrique Ferreira Bertolucci - José Roberto Wajman*
(UNIFESP-SP 2007)

TOTAL
Adicionar 1 pt se ≤ 12 anos de escolaridade __/30

Linha do tempo para o diagnóstico do prejuízo cognitivo:

1 – Declínio cognitivos subjetivos (“normais” ao envelhecimento);

Atividade cognitiva menos eficiente; Desbalanço fisiológico;

2 – Prejuízo cognitivo leve;

Desequilíbrio metabólicos; Início da neurodegeneração; Depressão, ansiedade, fadiga crônicas;

3) Demências;

Prejuízo das atividades diárias causadas pela neurodegeneração ou demência metabólica.

Fatores de risco para a saúde emocional e cognitiva:

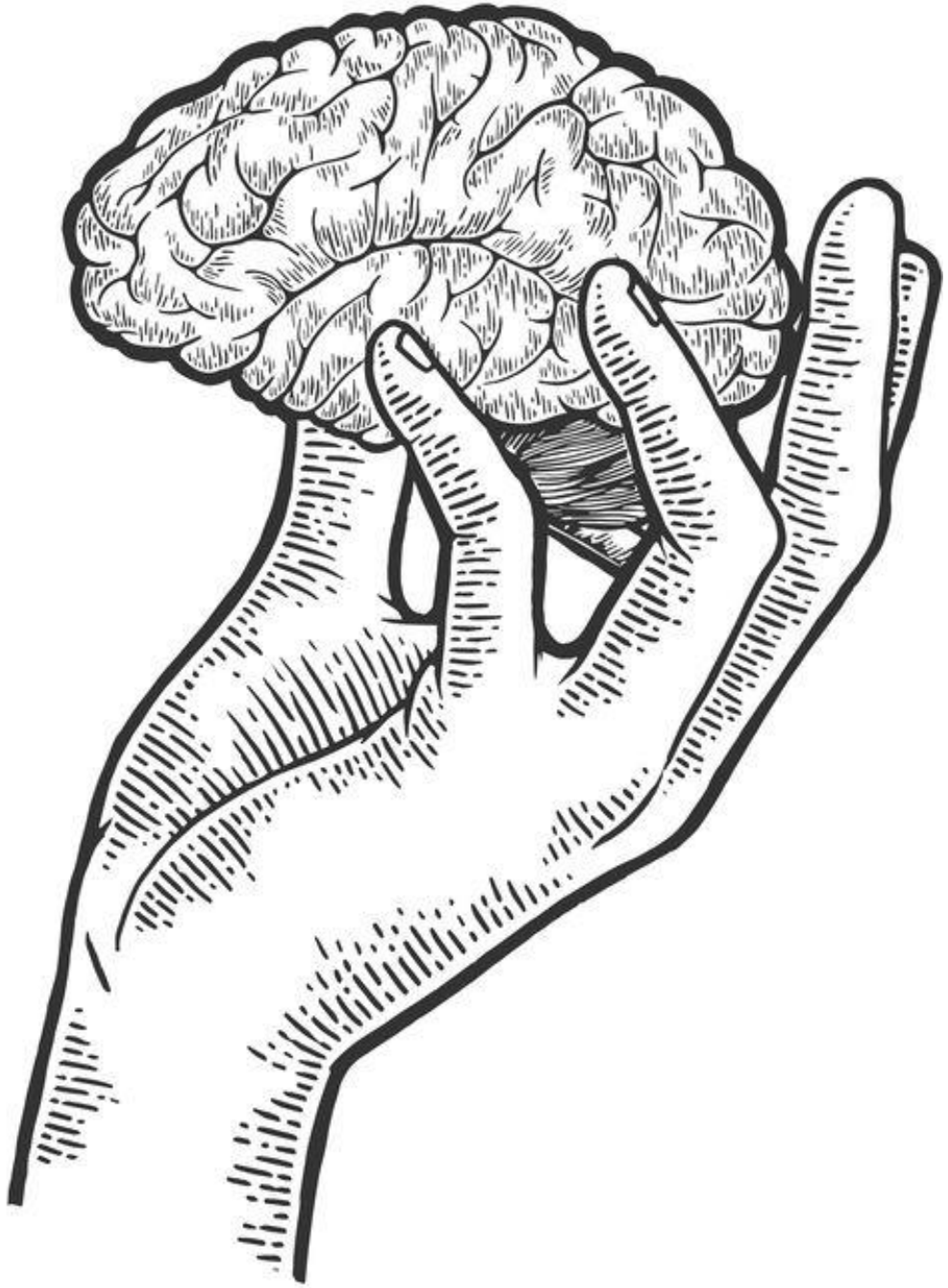
- Sedentarismo, baixa escolaridade, falta de estímulos cognitivos, tabagismo, má alimentação;
- Abuso de álcool (+ de 14 doses para homens ou + 7 doses mulheres por semana)
- Hipertensão, obesidade, dislipidemia, Diabetes
- Depressão
- Polimorfismo APOE4
- Aterosclerose sistêmica e cerebral
- Fibrilação atrial, falência cardíaca, Doença isquêmica coronária
- Apneia obstrutiva do sono
- Traumas encefálicos
- MOCA teste abaixo de 26
- CAIDE escore acima de 12

3 passos essenciais para ajustar a neuroquímica e promover saúde emocional e cognitiva

Esteja atento para os fatores de risco durante a anamnese;

Garanta a síntese de ATP;

Pense de maneira integrativa.



2% do peso corporal

20% do débito cardíaco

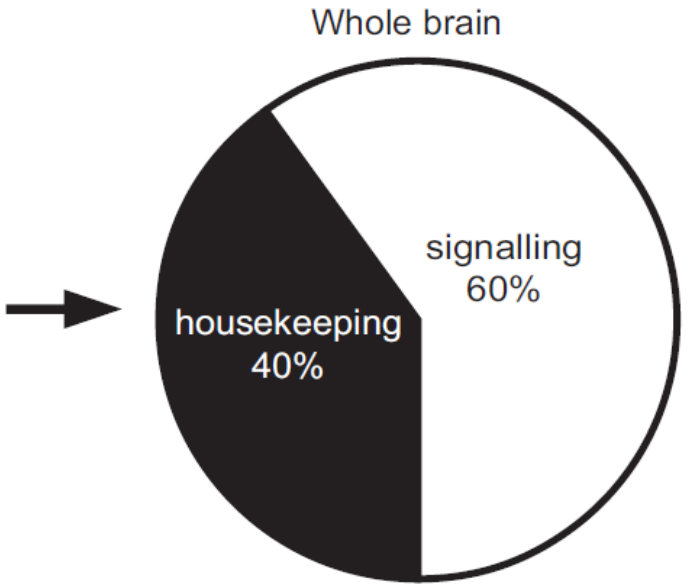
20% do consumo de ATP/diário

Fonte: Cells **2021**, 10, 2531.
https://doi.org/10.3390/cells10102531

O cérebro consome 20% do ATP diário

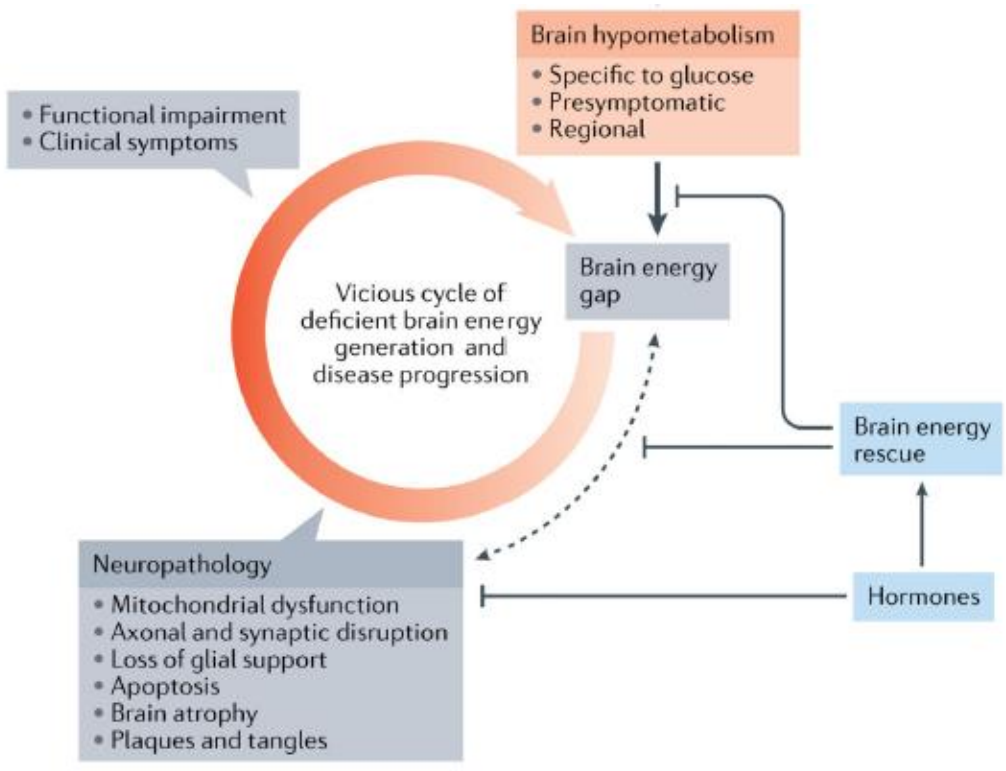
'Housekeeping' process	% of total brain energy use
Actin treadmilling	<1% (M) - 50% (E)
Microtubule dynamic instability	<< 1% (M)
Protein synthesis	1.3% (M)
Lipid turnover	13% - 25% (E+M)
Microglial motility	?
Mitochondrial proton leak	20% (E+M)

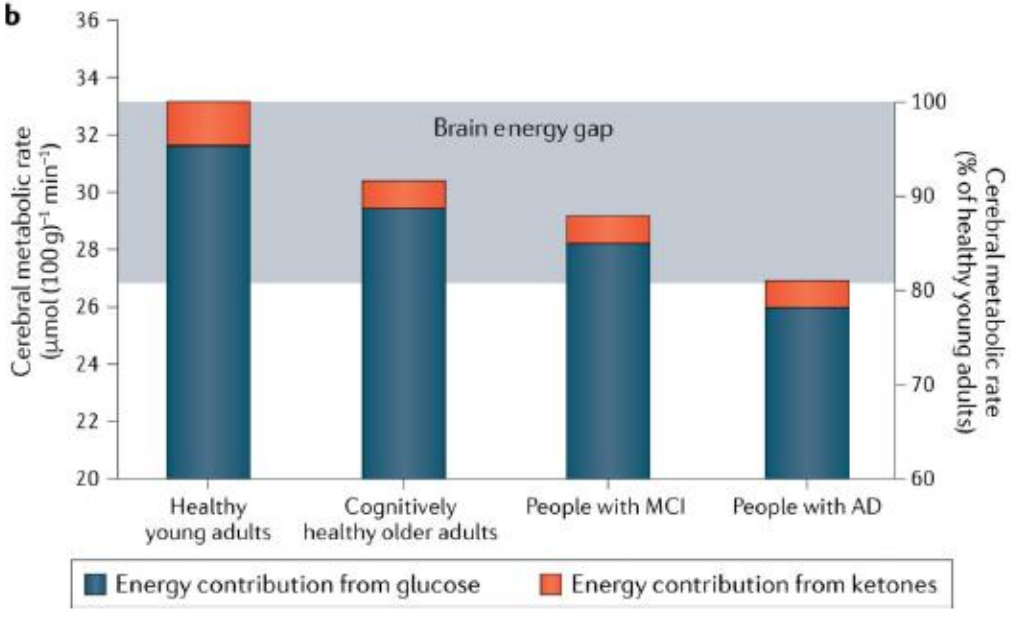
Energetic cost:	Estimate obtained by:
Undecided	Experiment (E)
Likely 'cheap'	Modelling (M)
Likely 'expensive'	



Distribuição do consumo energético no cérebro.

Fonte: *J Physiol* 593.16 (2015) pp 3417–3429





Fonte: Nat Rev Drug Discov. 2020 September ; 19(9): 609–633. doi:10.1038/s41573-020-0072-x.

Molecular Psychiatry

www.nature.com/mp

EXPERT REVIEW

Schizophrenia: a disorder of broken brain bioenergetics

Nicholas D. Henkel[1]✉, Xiajoun Wu[1], Sinead M. O'Donovan[1], Emily A. Devine[1], Jessica M. Jiron[1], Laura M. Rowland[2], Zoltan Sarnyai[3], Amy J. Ramsey[4], Zhexing Wen[5], Margaret K. Hahn[6] and Robert E. McCullumsmith[1,7]

Quanta energia gasta o cérebro de alguém que pensa demais?

nature > news > article

NEWS | 11 August 2022

Why thinking hard makes us feel tired

Difficult tasks can lead to build-up of a signalling molecule in the brain, triggering fatigue.

Heidi Ledford

Para ir além, veja: Wiehler, A., Branzoli, F., Adanyeguh, I., Mochel, F. & Pessiglione, M. *Curr. Biol*. https://doi.org/10.1016/j.cub.2022.07.010 (2022).

Suplementação Neuroenergética:

- **Creatina 3-6g/dia**
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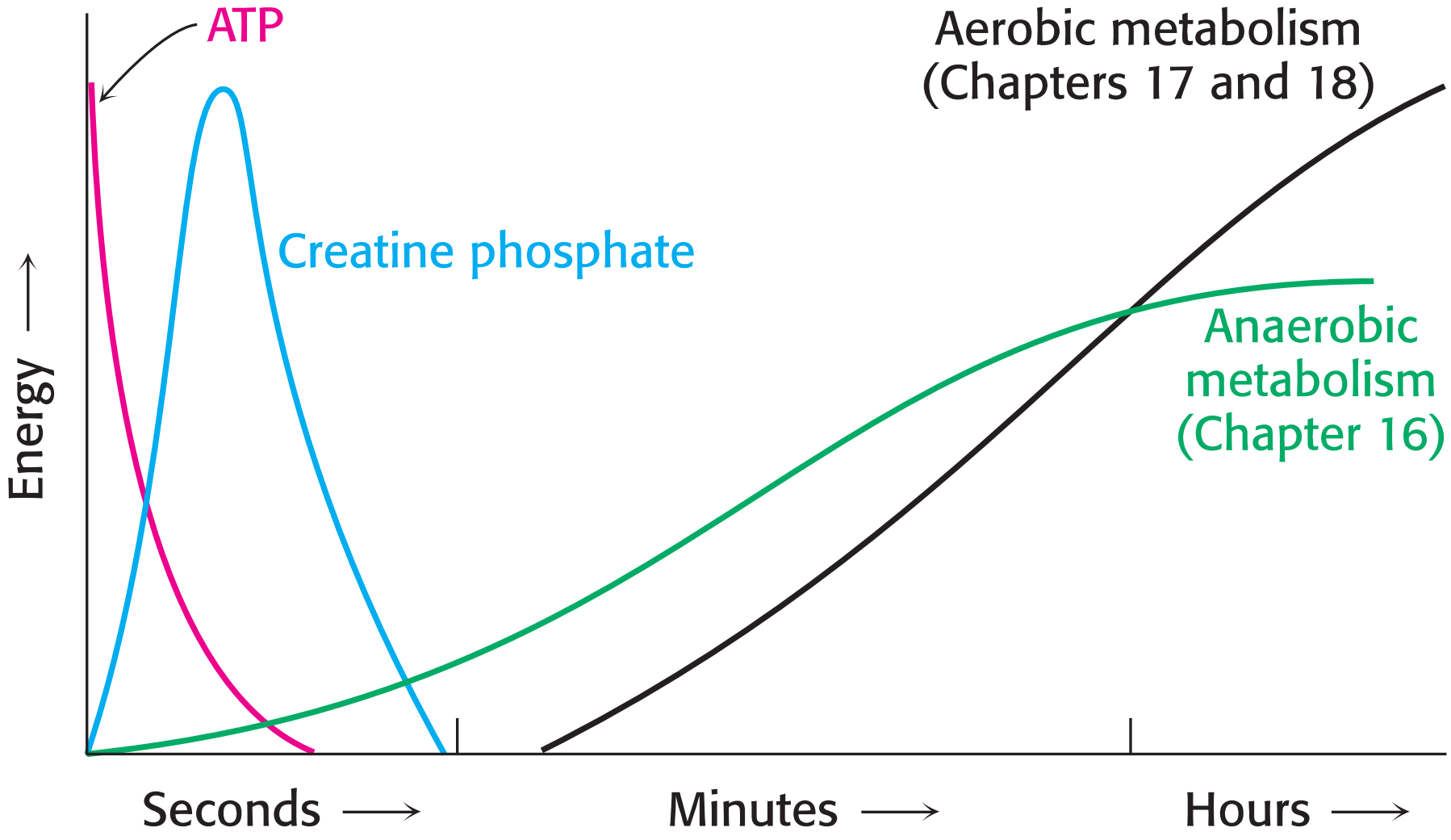
- **Solução composta pela associação de C8 (60%) e C10 (40%) fornecendo 30g/dia dos TCM**

Divididos em 2-3 tomadas diárias



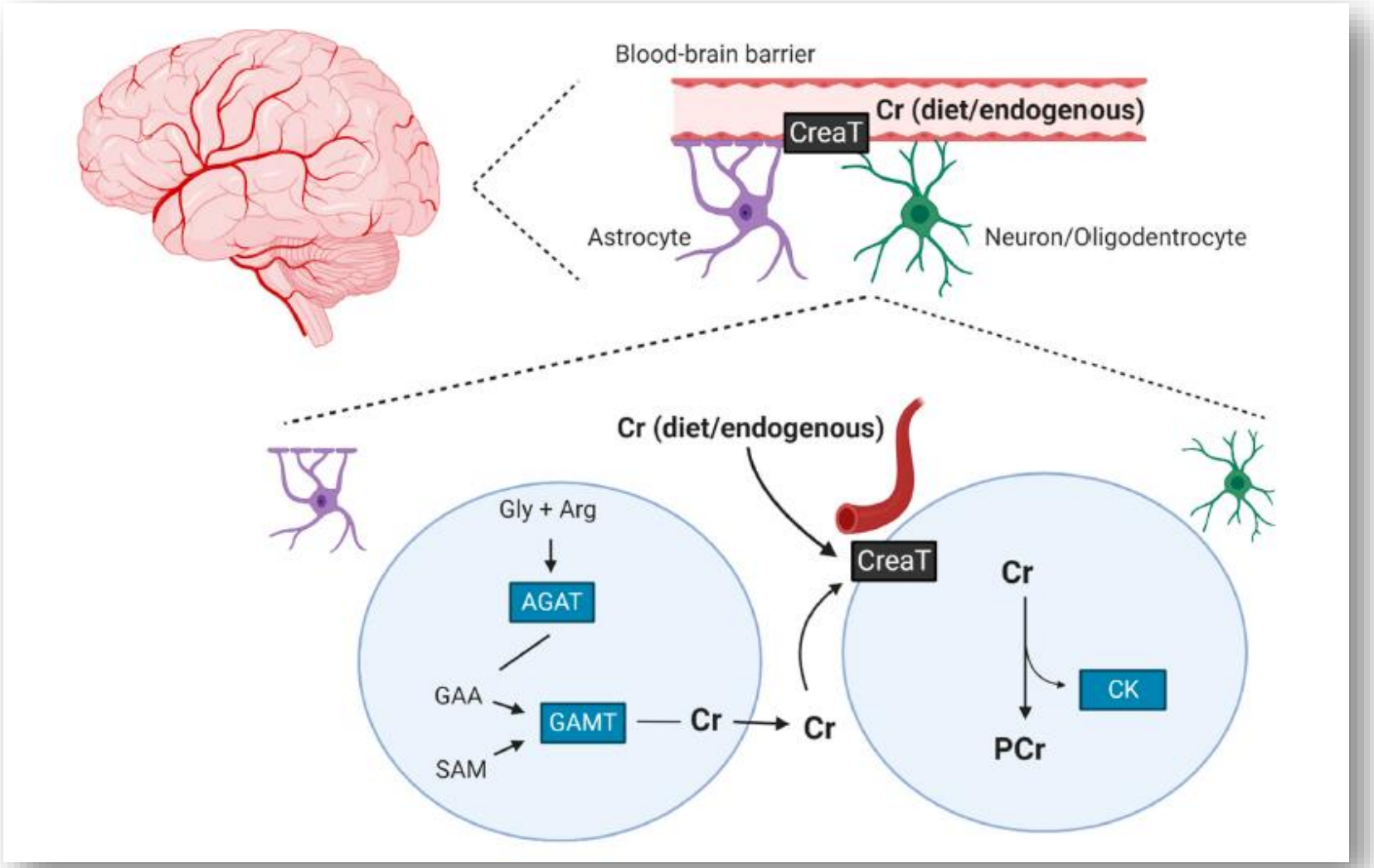
Fonte: Stryer, Bioquimica, 6ed.

Table 1. Summary of human studies (excluding CCDS) describing low tissue creatine levels.

Pathology	Refs.
Autism spectrum disorder	[40–45]
Concussion and mild traumatic brain injury	[13,46]
Multiple sclerosis	[47–51]
Gyrate atrophy of the choroid and retina	[15,52]
Post-viral fatigue syndrome	[53,54]
Primary and secondary brain tumors	[17,18]
Neuromuscular disease	[19]
Facioscapulohumeral muscular dystrophy	[20]
Dilated cardiomyopathy	[21,24,25]
Aortic valve disease	[22]
Heart transplantation	[23]
Coronary disease	[26]
Chronic obstructive pulmonary disease	[27,28]
Lung cancer	[29]
Pancreatic cancer	[30]
Hepatitis C	[31]
Chronic HIV infection	[32]
Infant malnutrition	[33]

Fonte: Ostojic, S.M. Low Tissue Creatine: A Therapeutic Target in Clinical Nutrition. Nutrients **2022**, 14, 1230. https://doi.org/10.3390/nu14061230

Transporte da creatina para o SNC

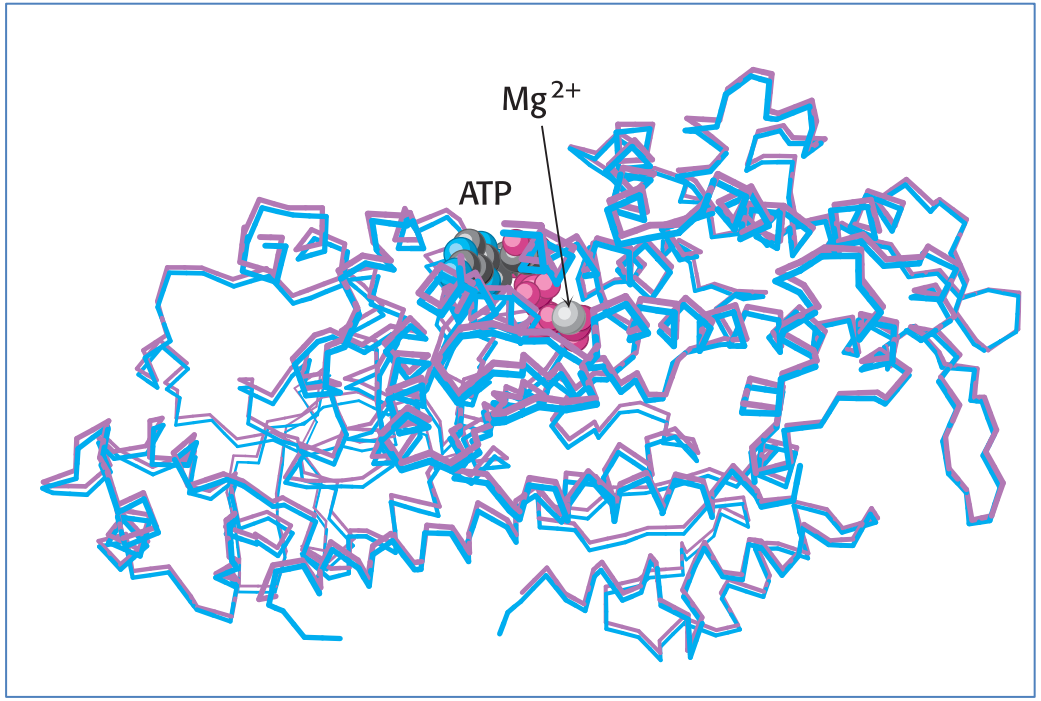


Fonte: Nutrients **2021**, 13, 586. https://doi.org/10.3390/nu13020586

A relação entre ATP e Mg^2

- A forma ativa do ATP é um complexo com Mg^{2+} ;
- Existe, no citoplasma de uma célula normal, uma relação 1:1 nas concentrações de ATP:Mg;
- Os complexos de Mg^{2+} com os nucleosídeos trifosfatos são substratos para todas as enzimas dependentes de NTPs;
- Outros NTPs: guanosina trifosfato (GTP), uridina trifosfato (UTP) e citidina trifosfato (CTP).

Fonte: Stryer, Bioquimica, 6ed.



Estrutura do complexo ATP-miosina em *Dictyostelium discoideum.*

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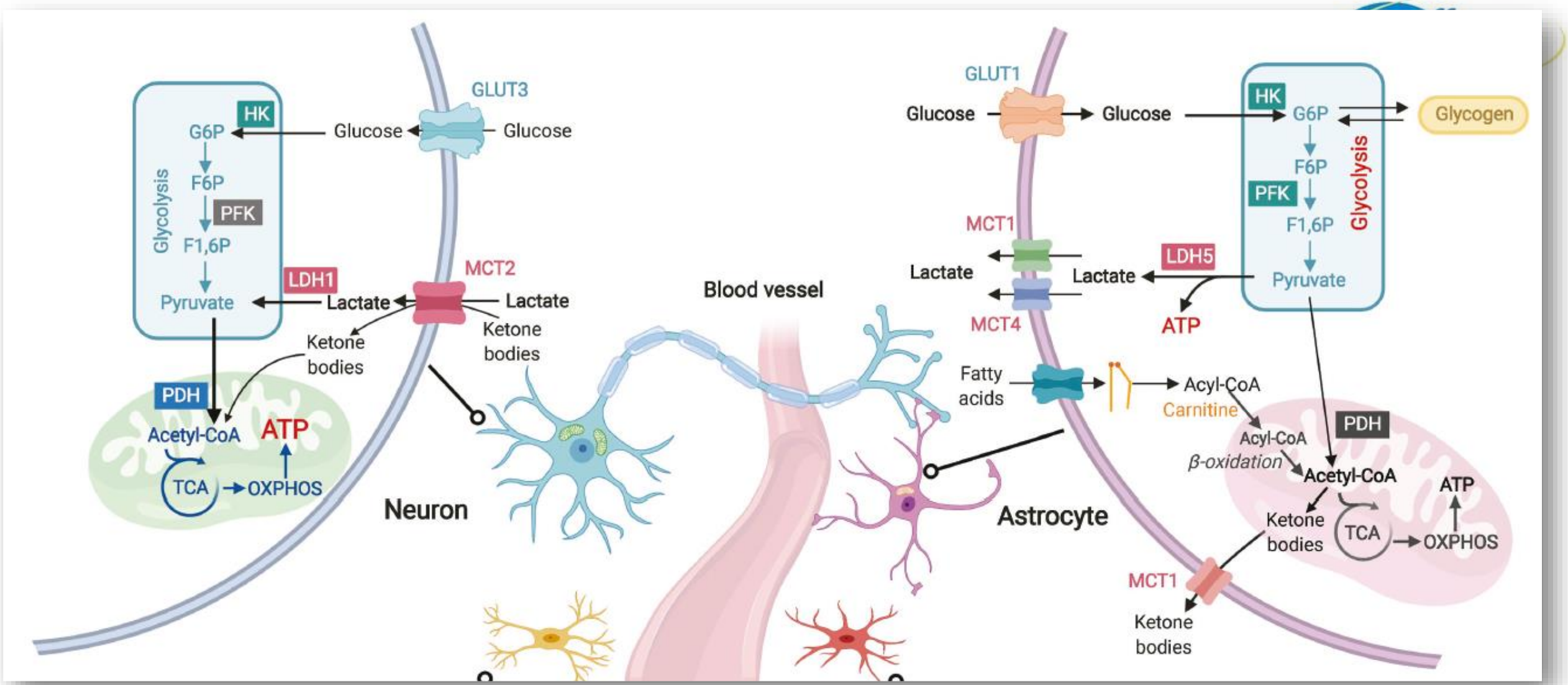
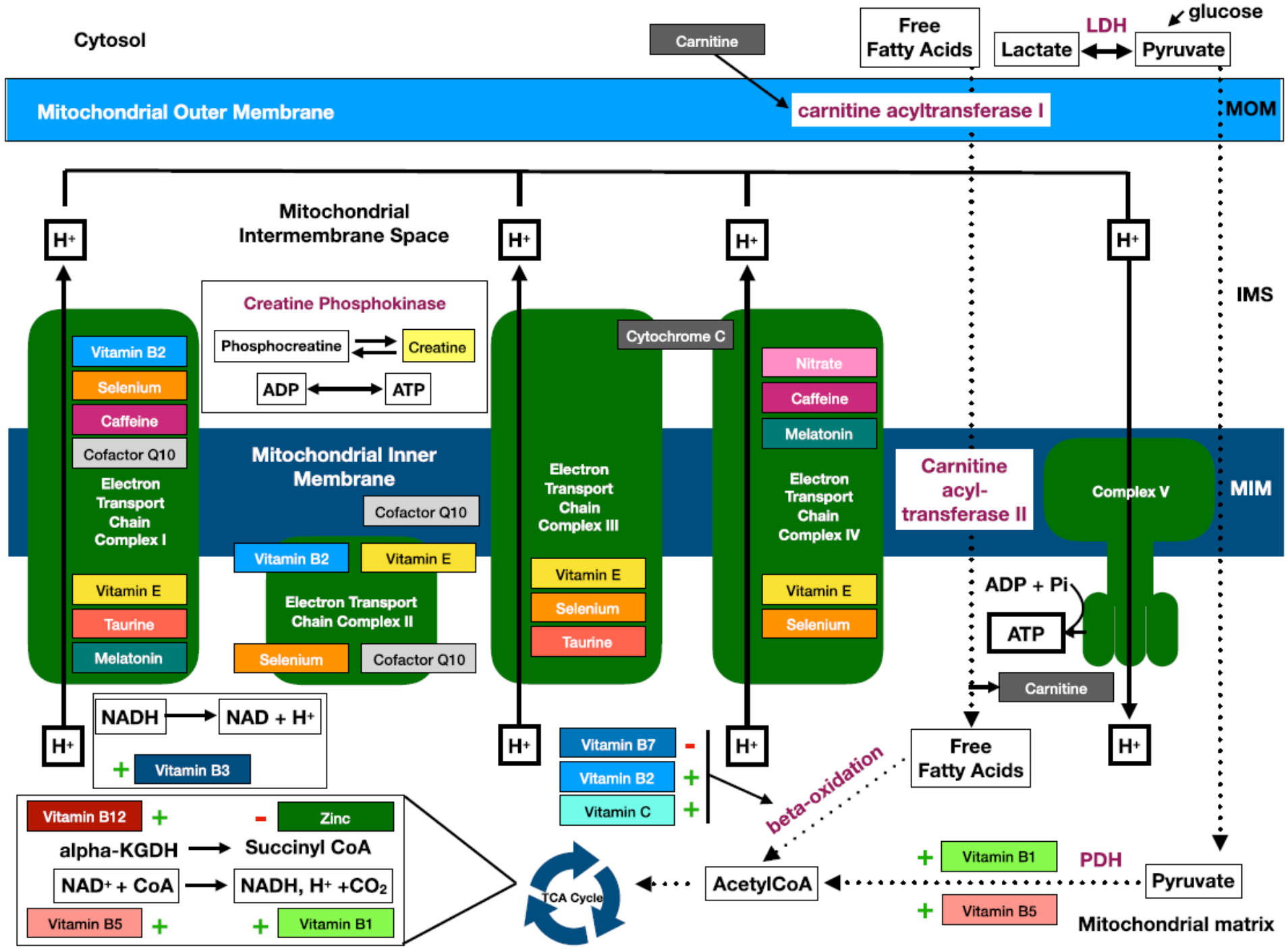


Fonte:*Qi G, Mi Y and Yin F (2020) Cellular Specificity and Inter-cellular Coordination in the Brain Bioenergetic System: Implications for Aging and Neurodegeneration. Front. Physiol. 10:1531. doi: 10.3389/fphys.2019.01531*

A glicólise não é uma via importante para a geração de piruvato em neurônios;

O lactato proveniente do astrócito é uma importante fonte de piruvato para a formação de acetil-CoA;

A principal fonte de ATP é a fosforilação oxidativa porque neurônios fazem pouca beta-oxidação;



Fonte: Clinical Nutrition 38 (2019) 982e995

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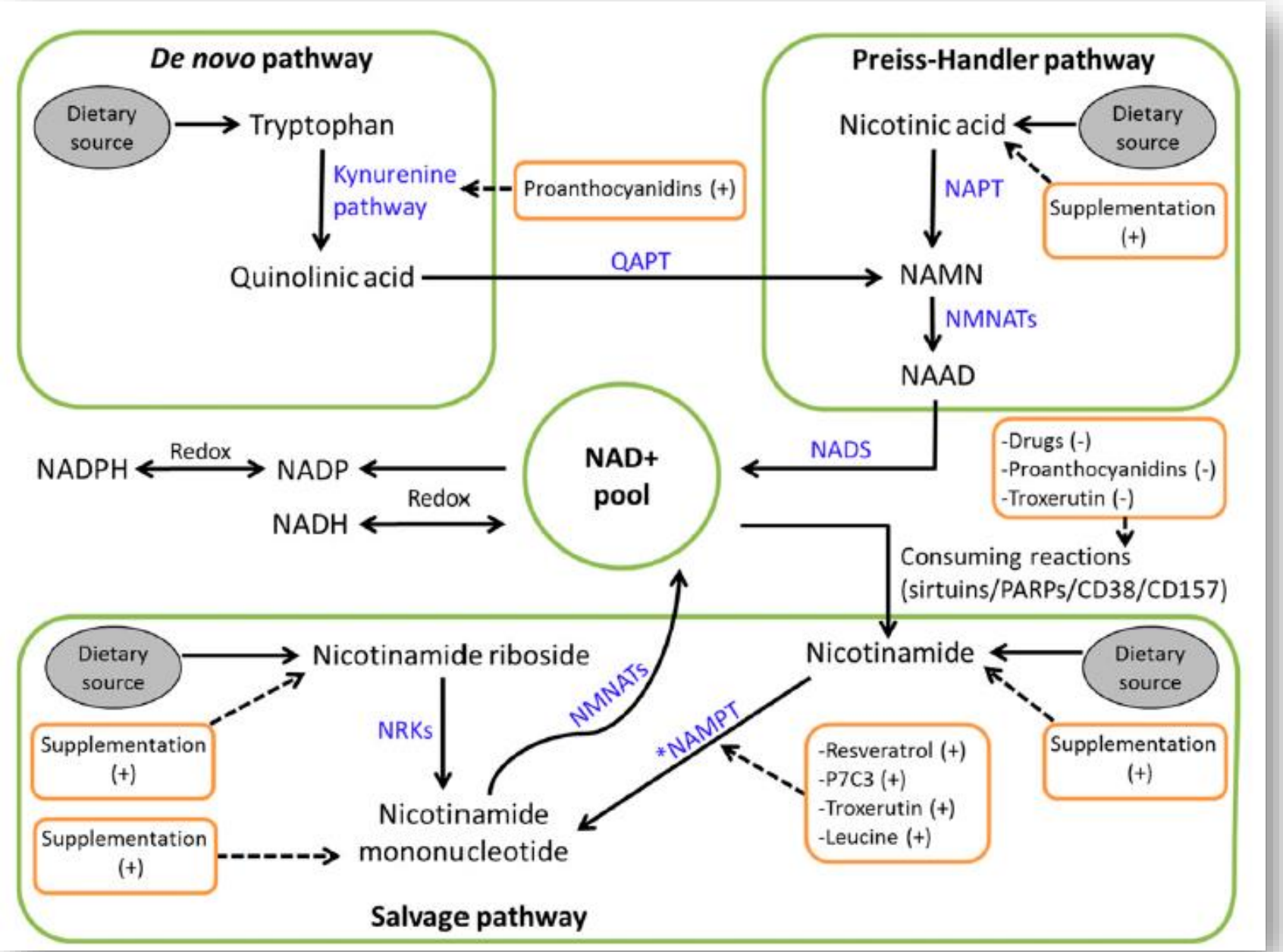
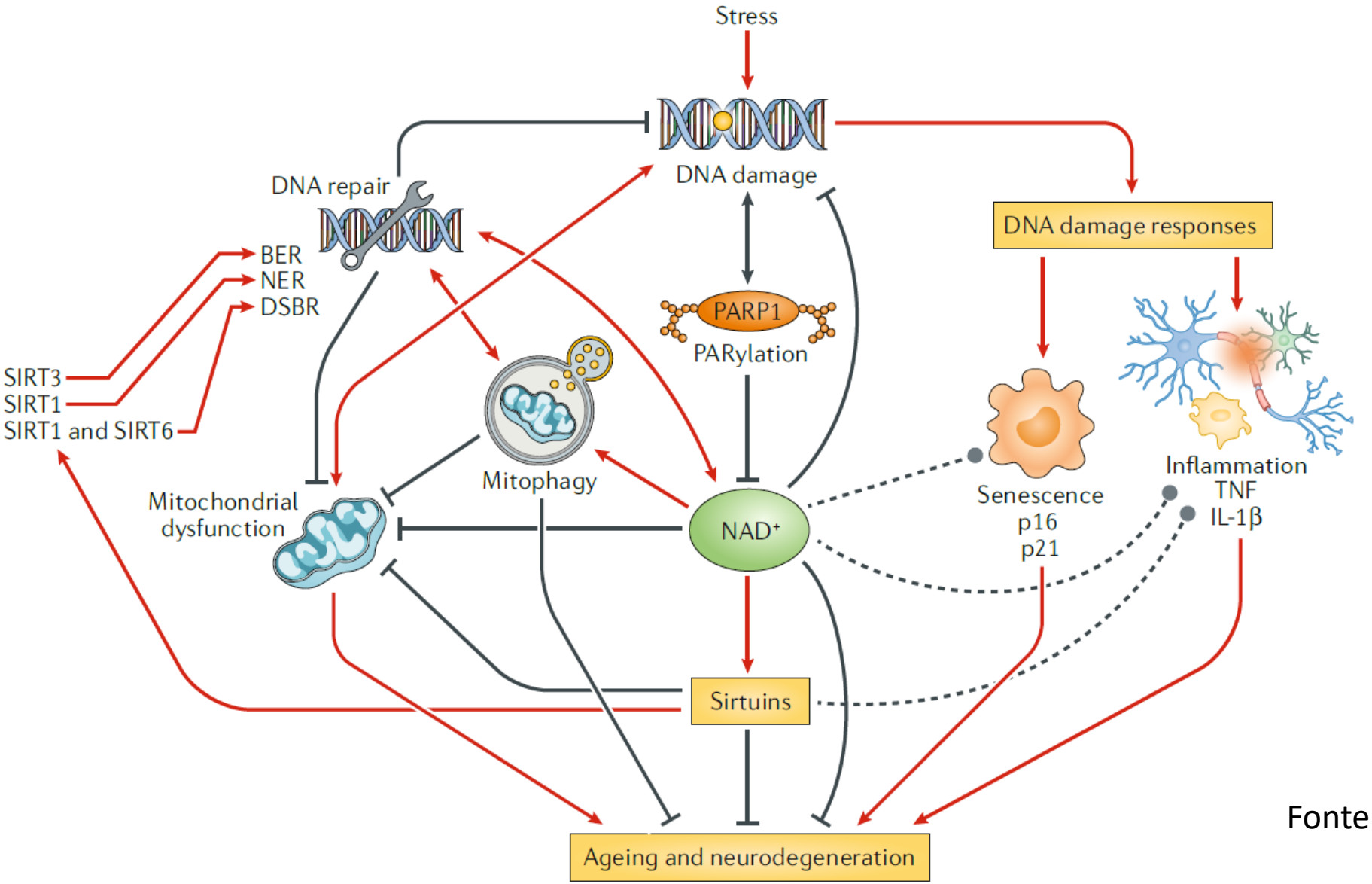


Vias de síntese do NAD

Fonte: doi: 10.1210/js.2017-00092 | Journal of the Endocrine Society | 816–835



Fonte: Nature Reviews, **Neurology,** https://doi.org/10.1038/s41582-019-0244-7

Bellacqua
FARMÁCIA DE MANIPULAÇÃO

Perceba o NAD como uma molécula chave na relação núcleo x mitocôndria X inflamação.

FASSINI

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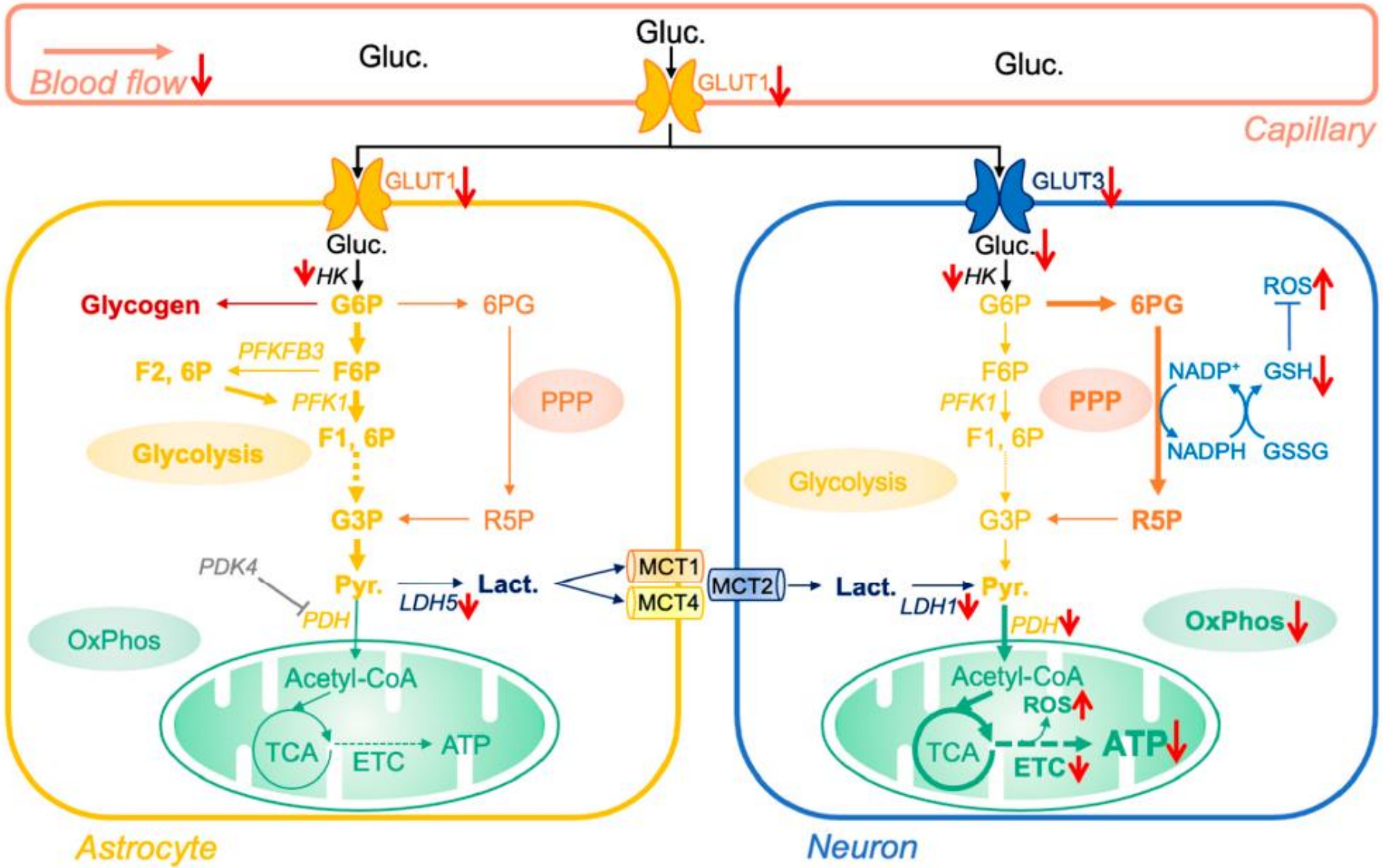
Impacto do envelhecimento sobre o metabolismo da glicose no cérebro



Fonte: Cells **2021**, 10, 2531. https://doi.org/10.3390/cells10102531

A via das pentoses é relevante na bioenergética neuronal e fundamental para a formação de NADPH.

Este último, essencial para a formação de GLUTATIONA REDUZIDA (o principal antioxidante de neurônios);

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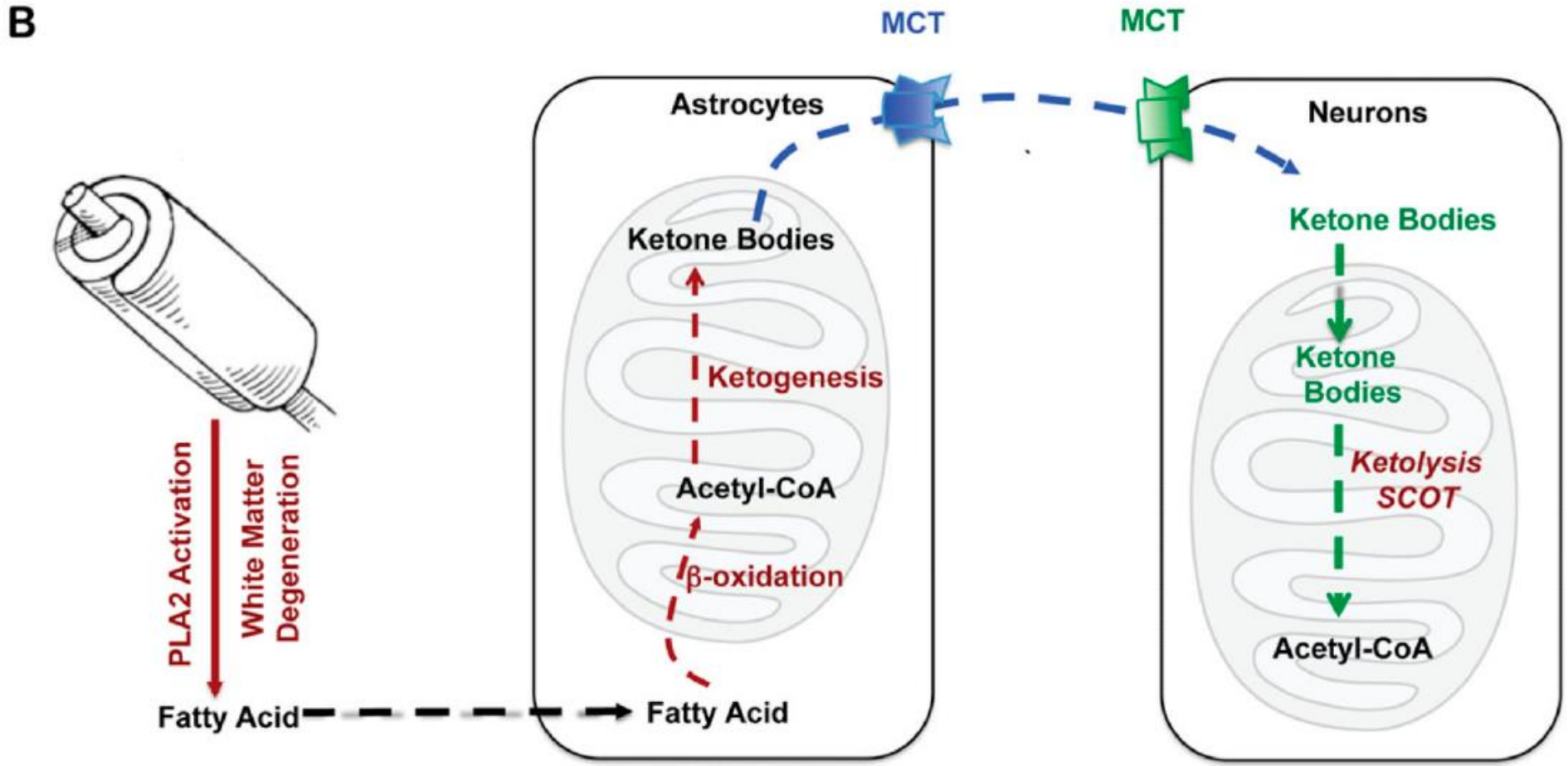


Figure 1. Bioenergetic substrate and catalytic compensatory adaptations to sustain metabolic demand of the brain

Fonte: *Adv Pharmacol*. 2012 ; 64: 327–371. doi:10.1016/B978-0-12-394816-8.00010-6.

frontiers in Aging Neuroscience

ORIGINAL RESEARCH
published: 15 February 2019
doi: 10.3389/fnagi.2019.00015

Links Between Metabolic and Structural Changes in the Brain of Cognitively Normal Older Adults: A 4-Year Longitudinal Follow-Up

Christian-Alexandre Castellano[1], Carol Hudon[2,3], Etienne Croteau[1,4], Mélanie Fortier[1], Valérie St-Pierre[1], Camille Vandenberghe[1], Scott Nugent[2], Sébastien Tremblay[5], Nancy Paquet[6], Martin Lepage[5,6,7], Tamàs Fülöp[1,8], Éric E. Turcotte[5,6,7], Isabelle J. Dionne[1,9], Olivier Potvin[2], Simon Duchesne[2,10] and Stephen C. Cunnane[1,4,8]*

We aimed to longitudinally assess the relationship between changing brain energy metabolism (glucose and acetoacetate) and cognition during healthy aging. Participants aged 71 ± 5 year underwent cognitive evaluation and quantitative positron emission tomography (PET) and magnetic resonance imaging (MRI) scans at baseline (N = 25) and two (N = 25) and four (N = 16) years later. During the follow-up, the rate constant for brain extraction of glucose (K_{glc}) declined by 6%–12% mainly in the temporo-parietal lobes and cingulate gyri ($p \leq 0.05$), whereas brain acetoacetate extraction (Kacac) and utilization remained unchanged in all brain regions ($p \geq 0.06$). Over the 4 years, cognitive results remained within the normal age range but an age-related decline was observed in processing speed. K_{glc} in the caudate was directly related to performance on several cognitive tests (r = +0.41 to +0.43, *all* $p \leq 0.04$). Peripheral insulin resistance assessed by the homeostasis model assessment of insulin resistance (HOMA-IR) was significantly inversely related to K_{glc} in the thalamus (r = –0.44, p = 0.04) and in the caudate (r = –0.43, p = 0.05), and also inversely related to executive function, attention and processing speed (r = –0.45 to –0.53, all $p \leq 0.03$). We confirm in a longitudinal setting that the age-related decline in K_{glc} is directly associated with declining performance on some tests of cognition but does not significantly affect Kacac.

Fonte: Castellano C-A et al., (2019) Links Between Metabolic and Structural Changes in the Brain of Cognitively Normal Older Adults: A 4-Year Longitudinal Follow-Up. Front. Aging Neurosci. 11:15. doi: 10.3389/fnagi.2019.00015

Tanto em momentos de demandas metabólicas aumentadas quanto com envelhecimento neuronal os corpos cetônicos passam a ter um papel importante na geração de ATP em neurônios.

Com a exaustão dos corpos cetônicos leva a degradação da bainha de mielina para o fornecimento de ácidos graxos para a beta-oxidação.

Published in final edited form as:

Ageing Res Rev. 2020 March ; 58: 101001. doi:10.1016/j.arr.2019.101001.

Medium Chain Triglycerides induce mild ketosis and may improve cognition in Alzheimer's disease. A systematic review and meta-analysis of human studies

Konstantinos I. Avgerinos[1], **Josephine M. Egan**[2], **Mark P. Mattson**[1], **Dimitrios Kapogiannis**[1,*]

[1]Laboratory of Neurosciences, Intramural Research Program, National Institute on Aging, National Institutes of Health, Baltimore, US

[2]Laboratory of Clinical Investigations, Intramural Research Program, National Institute on Aging, National Institutes of Health, Baltimore, US

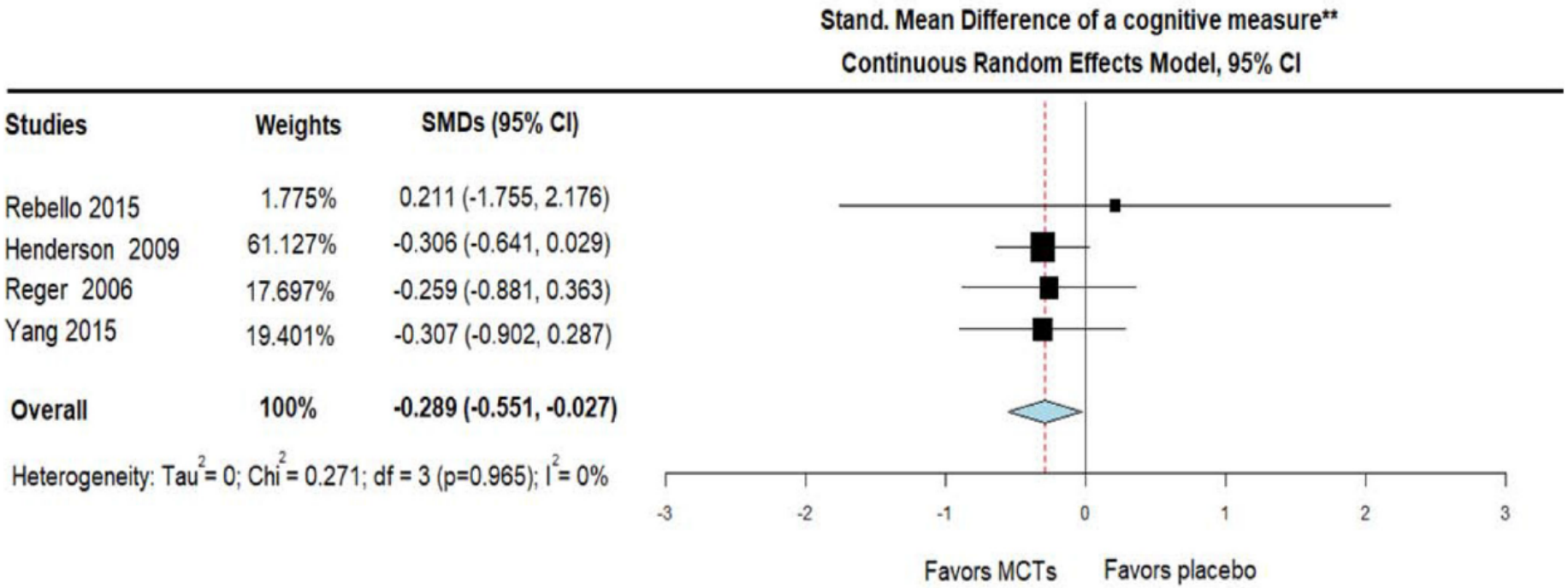
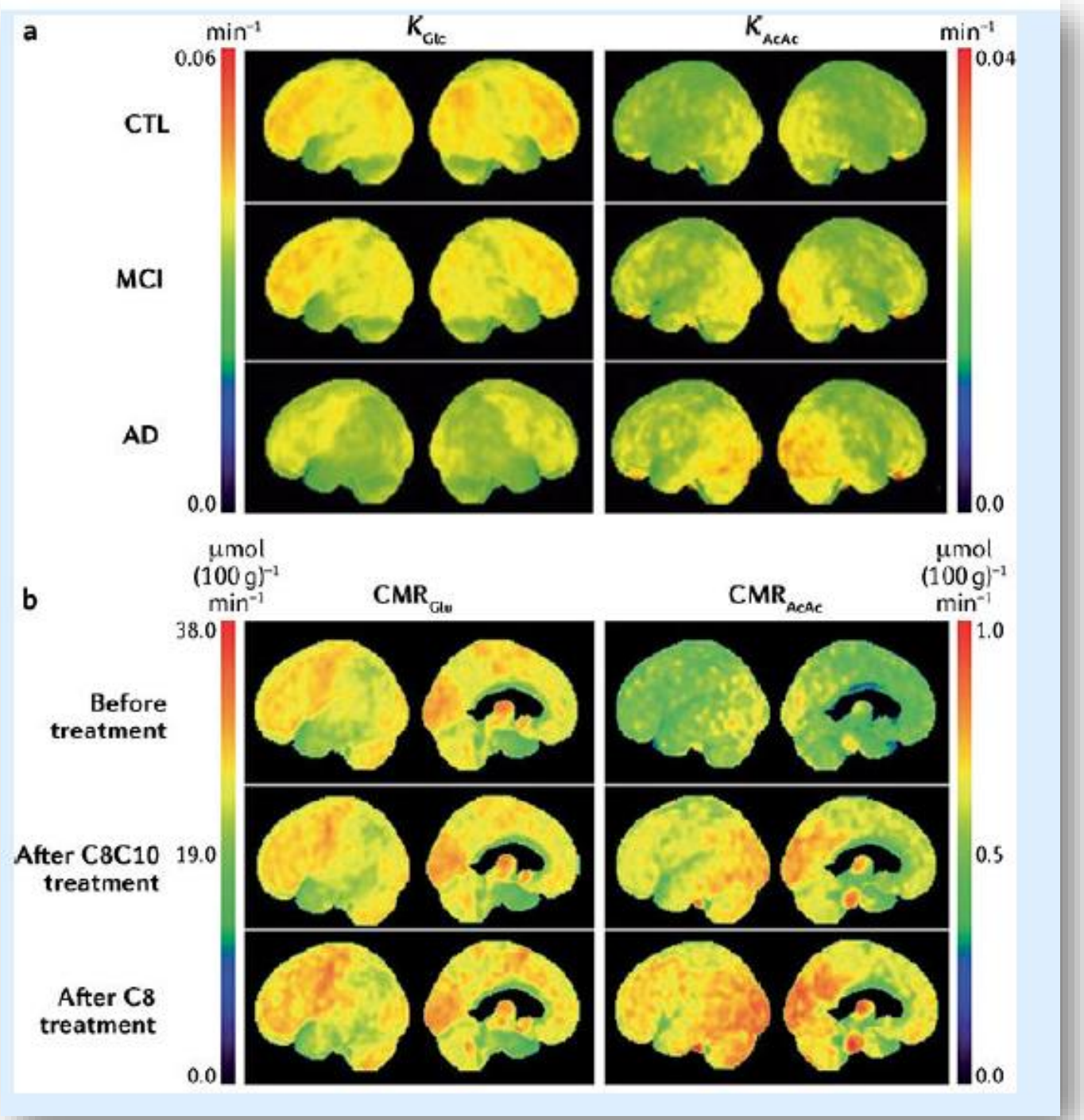
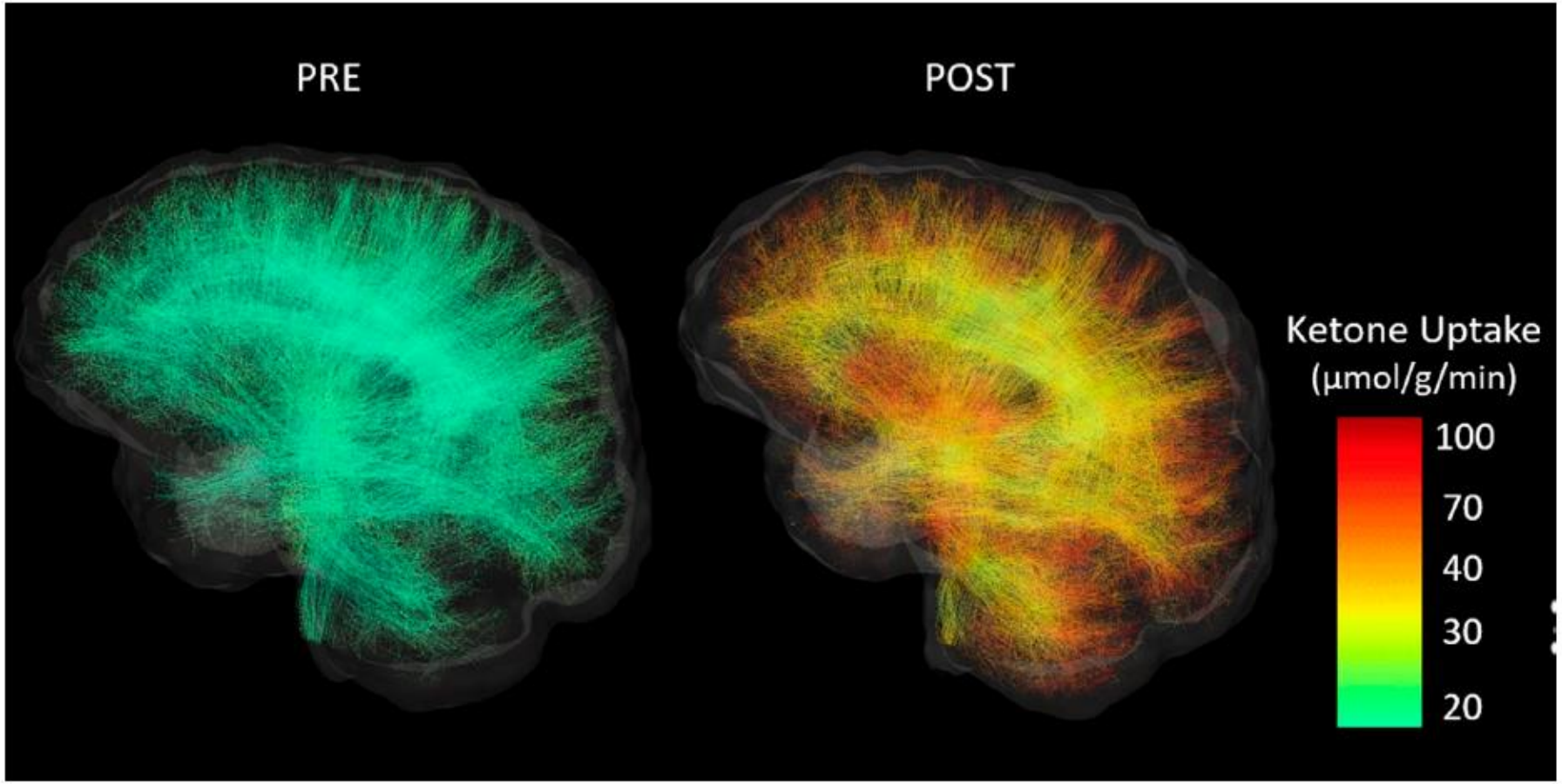


Figure 5B.

Forest plot showing cognitive performance (measured with Standardized Mean Difference derived from changes on (i) the Spanish version of MMSE in Yang et al study and (ii) ADAS-Cog for the rest studies). Results from meta-analysis of 4 Randomized Controlled Trials, using Continuous Random-Effects Model. Note that as with ADAS-Cog scale, negative changes here also indicate cognitive improvement



Fonte: Nat Rev Drug Discov. 2020 September ; 19(9): 609–633. doi:10.1038/s41573-020-0072-x.



Solução composta pela associação de C8 (60%) e C10 (40%) fornecendo 30g/dia dos TCM

FIGURE 1 Whole-brain white matter tractograms from a sample participant in the ketogenic medium chain triglyceride (kMCT) group before (PRE) and after (POST) the 6-month intervention. Streamlines are colored according to their acetoacetate metabolic rate (µmol/g/min). Subsets of 10,000 streamlines per whole-brain tractogram are shown.

Fonte: *Alzheimer's Dement*. 2021;7:e12217. https://doi.org/10.1002/trc2.12217

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3 passos essenciais para ajustar a neuroquímica e promover saúde emocional e cognitiva

Esteja atento para os fatores de risco durante a anamnese;

Garanta a síntese de ATP;

Pense de maneira integrativa.

GENÉTICA

G1, G2, G3

Epigenética

AMBIENTE

Estresse, traumas, relações interpessoais...

- Tristeza e sentimento de culpa;
- Anedonia;
- Agitação/ lentidão;
- Tendências suicidas;
- Alterações de sono;
- Atenção e foco;
- Aprendizado e memória

O **Suplemento é o vento a favor** para quem já entendeu a **necessidade de pedalar!**

ARTICLE

Nutrients and bioactives in green leafy vegetables and cognitive decline

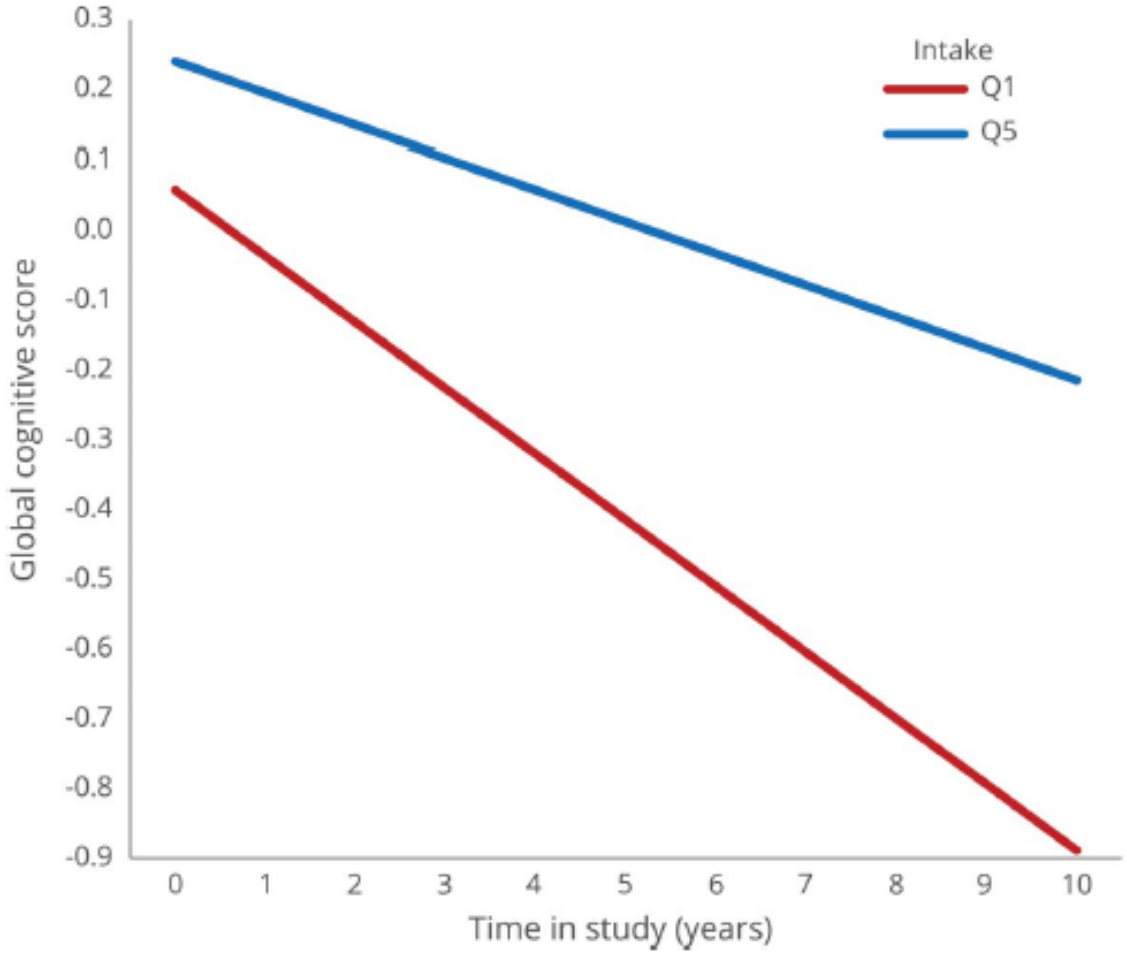
Prospective study

Martha Clare Morris, ScD, Yamin Wang, PhD, Lisa L. Barnes, PhD, David A. Bennett, MD, Bess Dawson-Hughes, MD, and Sarah L. Booth, PhD

Neurology® 2018;90:e214-e222. doi:10.1212/WNL.0000000000004815

Correspondence
Dr. Morris
Martha_C_Morris@rush.edu

Figure Rate of decline in global cognitive score for the top and the lowest quintile of intake of green leafy vegetables



Rate of decline in global cognitive score for the top quintile of intake of green leafy vegetables (median 1.3 servings/d) and the lowest quintile of intake (median 0.09 servings/d) based on mixed models adjusted for age, sex, education, energy intake, participation in cognitive activities, physical activity, smoking, and alcohol consumption in 960 Rush Memory and Aging Project participants, 2004–2014.

O consumo diário de verdes folhosos (equivalente a uma xícara por dia) irá deixar seu cérebro 10 anos mais jovem.

Fonte: Neurology® 2018;90:e214-e222. doi:10.1212/WNL.0000000000004815

nutrients

MDPI

Article

A High Polyphenol Diet Improves Psychological Well-Being: The Polyphenol Intervention Trial (PPhIT)

Fonte: Nutrients **2020**, 12, 2445; doi:10.3390/nu12082445

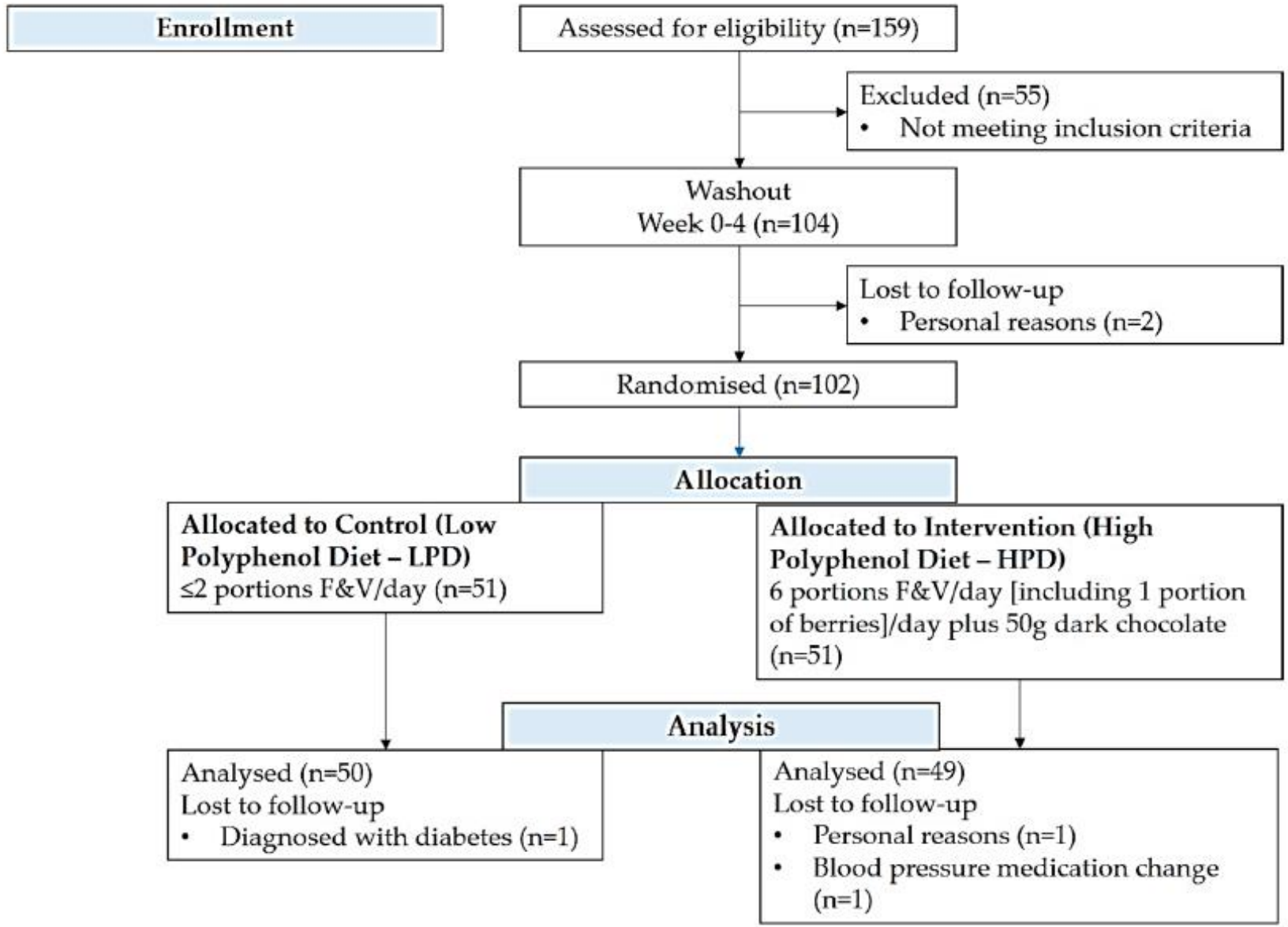


Figure 1. CONSORT diagram summarizing flow of participants through the study.

Table 3. Changes in mood, self-esteem, body image and quality of life indicators according to the Polyphenol Intervention Trial (PPhIT) study group allocation.

	Low Polyphenol Diet (n_{max} = 50)				High Polyphenol Diet (n_{max} = 49)				
	Week 0 [1]	Week 12	Median Change (IQR) [2]	Within Group Change (p Value) [3]	Week 0 [1]	Week 12	Median Change (IQR) [2]	Within Group Change (p Value) [3]	Between Group Change (p Value) [4]
BDI-II *	6.0 (2.0, 12.5)	7.0 (2.0, 11.0)	0.2 (−1.5, 1.9)	0.98	6.0 (3.0, 12.0)	2.0 (0.0, 6.0)	−3.4 (−5.4, −1.5)	**<0.001**	**0.01**
DASS-21 **									
Depression [5]	2.0 (0.0, 12.0)	6.0 (0.0, 10.5)	0 (−2.0, 6.0)	0.29	2.0 (0.0, 10.0)	0.0 (0.0, 6.0)	0 (−2.0, 0.0)	0.53	0.56
Anxiety [5]	4.0 (2.0, 9.0)	2.0 (0.0, 8.0)	0.0 (−3.0, 3.0)	0.86	4.0 (0.0, 10.0)	2.0 (0.0, 6.0)	0.0 (−2.0, 0.0)	0.16	0.8
Stress [5]	7.0 (2.0, 12.5)	8.0 (0.0, 16.0)	0 (−2.0, 4.0)	0.76	6.0 (2.0, 14.0)	4.0 (0.0, 10.0)	−2.0 (−6.0, 2.0)	**0.05**	0.14
PANAS ***									
Positive affect	29.9 (8.3)	30.4 (9.8)	0.5 (−1.5, 2.5)	0.63	33.0 (6.8)	35.2 (7.4)	2.2 (0.3, 4.1)	**0.03**	0.21
Negative affect	11.0 (10.0, 13.0)	11.0 (10.0, 13.0)	0.0 (−1.5, 1.5)	0.56	12.0 (10.0, 15.0)	10.0 (10.0, 14.0)	0.0 (−1.0, 0.5)	0.68	0.99
Rosenberg Self-Esteem Score †	26.0 (25.0, 28.0)	26.0 (25.0, 28.0)	0.0 (−2.0, 2.0)	0.74	26.0 (25.0, 27.0)	27.0 (24.0, 27.0)	0.0 (−2.0, 2.0)	0.68	0.53
MBSRQ-AS ††									
Appearance Evaluation	2.9 (2.4, 3.5)	3.0 (2.4, 3.6)	0.0 (−0.3, 0.4)	0.27	3.0 (2.5, 3.4)	3.1 (2.7, 3.6)	0.1 (−0.3, 0.4)	0.15	0.76
Appearance Orientation	3.0 (2.5, 3.7)	3.0 (2.5, 3.7)	0.0 (−0.3, 0.2)	0.35	3.2 (2.8, 3.5)	3.3 (2.9, 3.8)	0.2 (−0.2, 0.4)	0.16	0.1
Body areas Satisfaction	3.0 (2.7, 3.4)	3.3 (2.4, 3.7)	0.2 (−0.1, 0.4)	**0.03**	3.1 (2.7, 3.6)	3.3 (2.8, 3.8)	0.2 (−0.1, 0.3)	**0.02**	0.71
Overweight Preoccupation	2.3 (1.8, 2.8)	2.4 (1.8, 2.8)	0.0 (−0.3, 0.5)	0.87	2.5 (1.8, 3.3)	2.6 (1.8, 3.2)	0.0 (−0.5, 0.3)	0.45	0.72
Self-classified Weight [1]	4.0 (3.4, 4.0)	4.0 (3.0, 4.0)	0.0 (0.0, 0.0)	0.08	4.0 (3.5, 4.0)	4.0 (3.5, 4.0)	0.0 (0.0, 0.0)	0.43	0.5
SF-36 †††									
Physical Functioning	90 (75.0, 97.5)	90 (81.3, 100.0)	0 (0.0, 10.0)	0.07	95 (80.0, 100.0)	95 (85.0, 100.0)	0 (−5.0, 10.0)	0.15	0.44
Role limitations—physical health	100 (37.5, 100.0)	100 (37.5, 100.0)	0 (0.0, 25.0)	0.45	100 (75.0, 100.0)	100 (100.0, 100.0)	0 (0.0, 0.0)	**<0.001**	0.61
Pain	80 (47.5, 100.0)	80 (46.3, 100.0)	0 (−10.0, 10.0)	0.64	90 (60.0, 90.0)	90 (70.0, 100.0)	0 (−10.0, 22.5)	0.2	0.51
General health	65 (45.0, 75.0)	60 (50.0, 75.0)	0 (−10.0, 10.0)	0.47	65 (50.0, 75.0)	75 (65.0, 85.0)	10 (−5.0, 20.0)	**<0.001**	**0.03**
Physical health component	210.5 (168.5, 223.1)	200.9 (172.9, 217.2)	−6.4 (−17.0, 4.2)	0.09	213.2 (189.6, 225.1)	216.6 (201.4, 225.3)	2.2 (−8.1, 15.4)	0.2	**0.04**
Role limitations—emotional health	100 (100.0, 100.0)	100 (100.0, 100.0)	0 (0.0, 0.0)	0.99	100 (100.0, 100.0)	100 (100.0, 100.0)	0 (0.0, 0.0)	0.1	0.85
Energy/fatigue	55 (40.0, 72.5)	60 (45.0, 70.0)	5 (−5.0, 10.0)	0.39	60 (50.0, 80.0)	70 (60.0, 80.0)	5 (0.0, 20.0)	**<0.001**	**0.02**
Emotional well-being	76 (64.0, 84.0)	80 (62.0, 86.0)	0 (−8.0, 8.0)	0.73	80 (60.0, 88.0)	84 (72.0, 92.0)	4 (0.0, 16.0)	0	**0.01**
Social functioning	100 (75.0, 100.0)	100 (75.0, 100.0)	0 (−6.3, 0.0)	0.97	100 (75.0, 100.0)	100 (100.0, 100.0)	0 (0.0, 25.0)	**0.02**	0.08
Mental health component	209.1 (176.8, 222.3)	197.9 (175.0, 217.2)	−4.0 (−26.6, 8.1)	0.04	208 (181.4, 226.0)	218.3 (201.4, 226.8)	1.9 (−6.9, 19.1)	0.09	**0.01**

6 porções de frutas/vegetais ao dia (sendo uma porção de “berries” + 50g de chocolate 70% cacau por 2 meses exerceram efeito significativos sobre a saúde mental, bem estar e fadiga/energia.

Fonte: Nutrients **2020**, 12, 2445; doi:10.3390/nu12082445

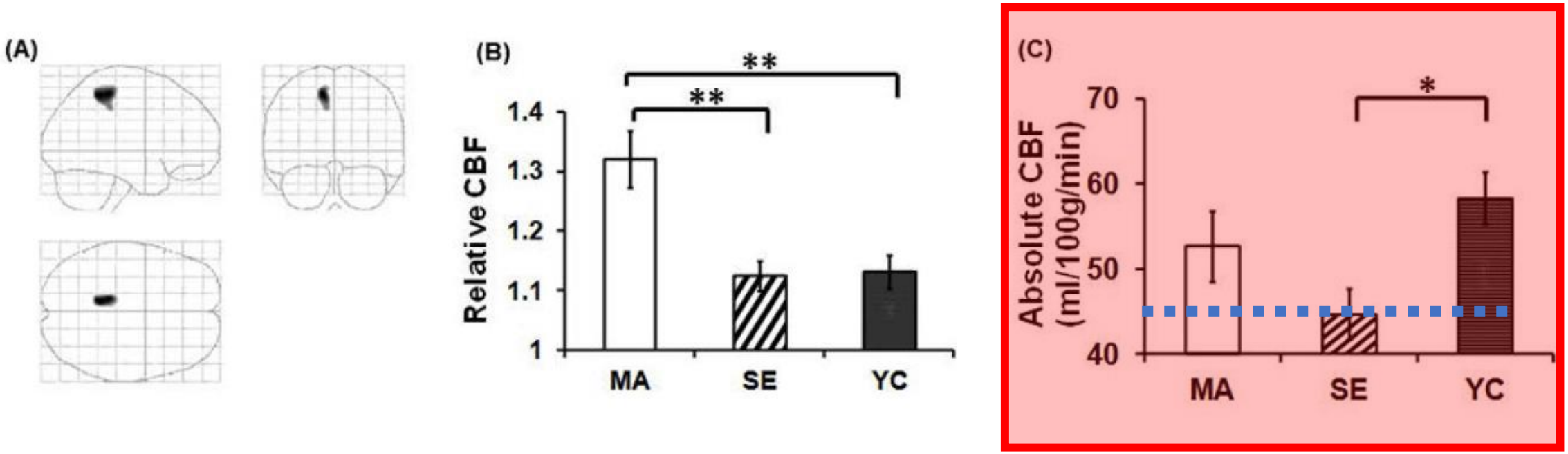
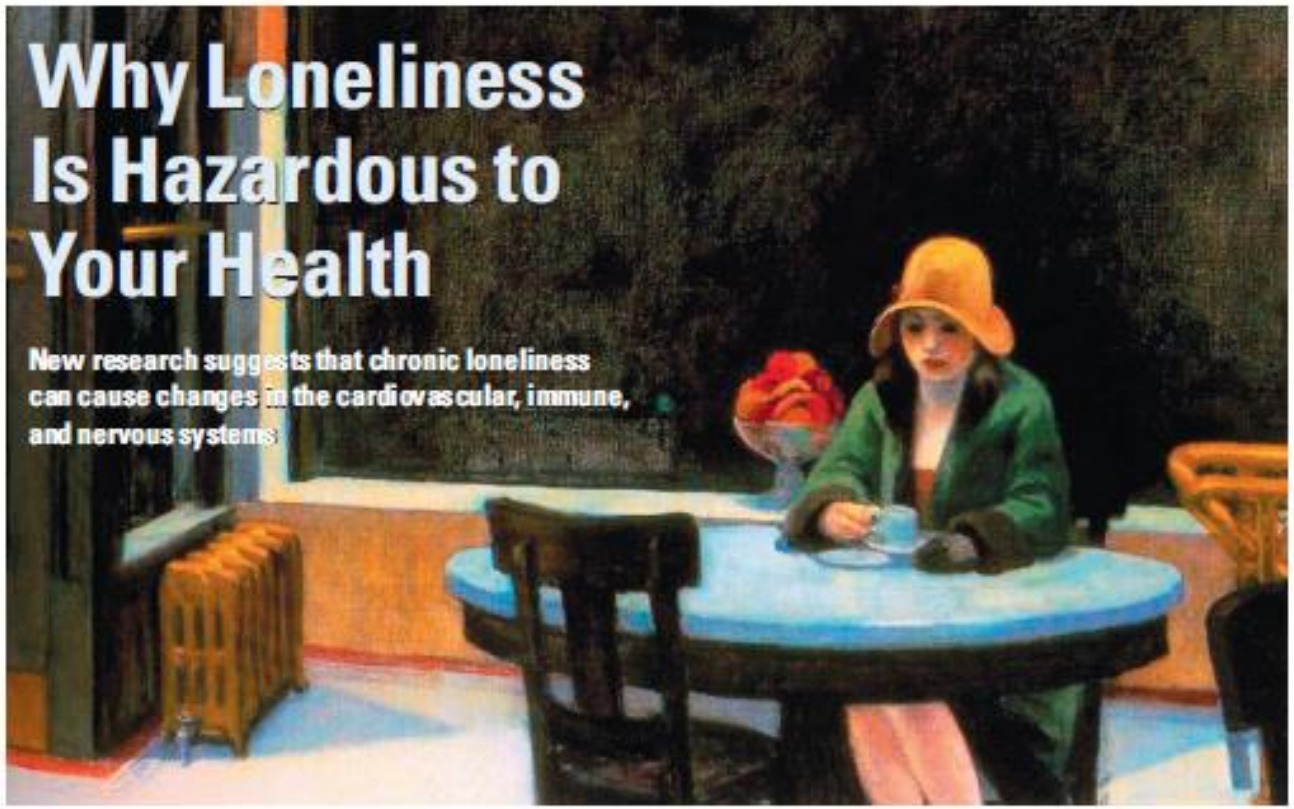
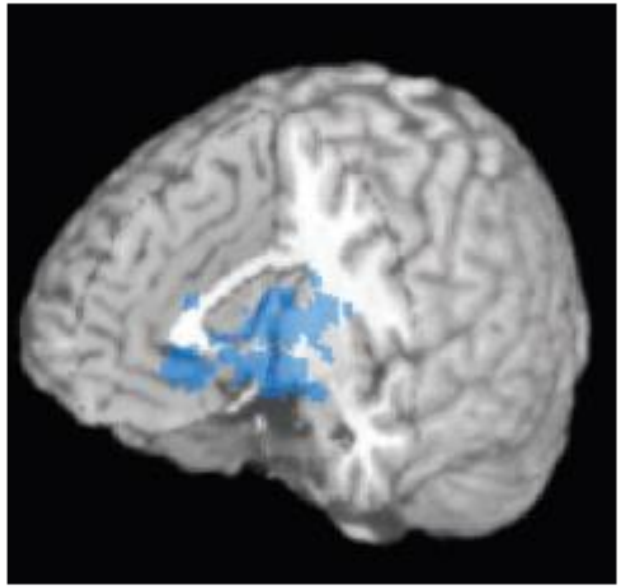


Figure 6.

Comparison of cerebral blood flow (CBF) among endurance Masters Athletes (MA, n=10), sedentary elderly adults (SE, n=10), and young control subjects (YC, n=9). (A) Brain regions showing greater CBF in MA compared with SE ($P<0.005$, cluster size=250). These voxels are located in the posterior cingulate cortex and precuneus. (B) Relative CBF (normalized against whole-brain value) in the cluster highlighted in (A). (C) Absolute CBF in the cluster highlighted in (A). CBF was measured by arterial spin labeling using MRI.





Unrewarding. Lonely people take less enjoyment from social interactions and exhibit less activity (blue) in the ventral striatum.

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Solidão:

Desconforto gerado devido a uma **discrepância** entre as **relações** sociais **existentes** e as **relações** sociais **desejadas.**

Fonte: Lam et al., Neuropsychopharmacology (2021) 46:1873–1887; https://doi.org/10.1038/s41386-021-01058-7


E se a solidão fosse encarada como a fome e a sede da alma?

Nat Neurosci. 2020 December ; 23(12): 1597–1605. doi:10.1038/s41593-020-00742-z.

Acute social isolation evokes midbrain craving responses similar to hunger

Livia Tomova[1,✉], **Kimberly L. Wang**[1], **Todd Thompson**[1], **Gillian A. Matthews**[2], **Atsushi Takahashi**[3], **Kay M. Tye**[2], **Rebecca Saxe**[1,3,4]

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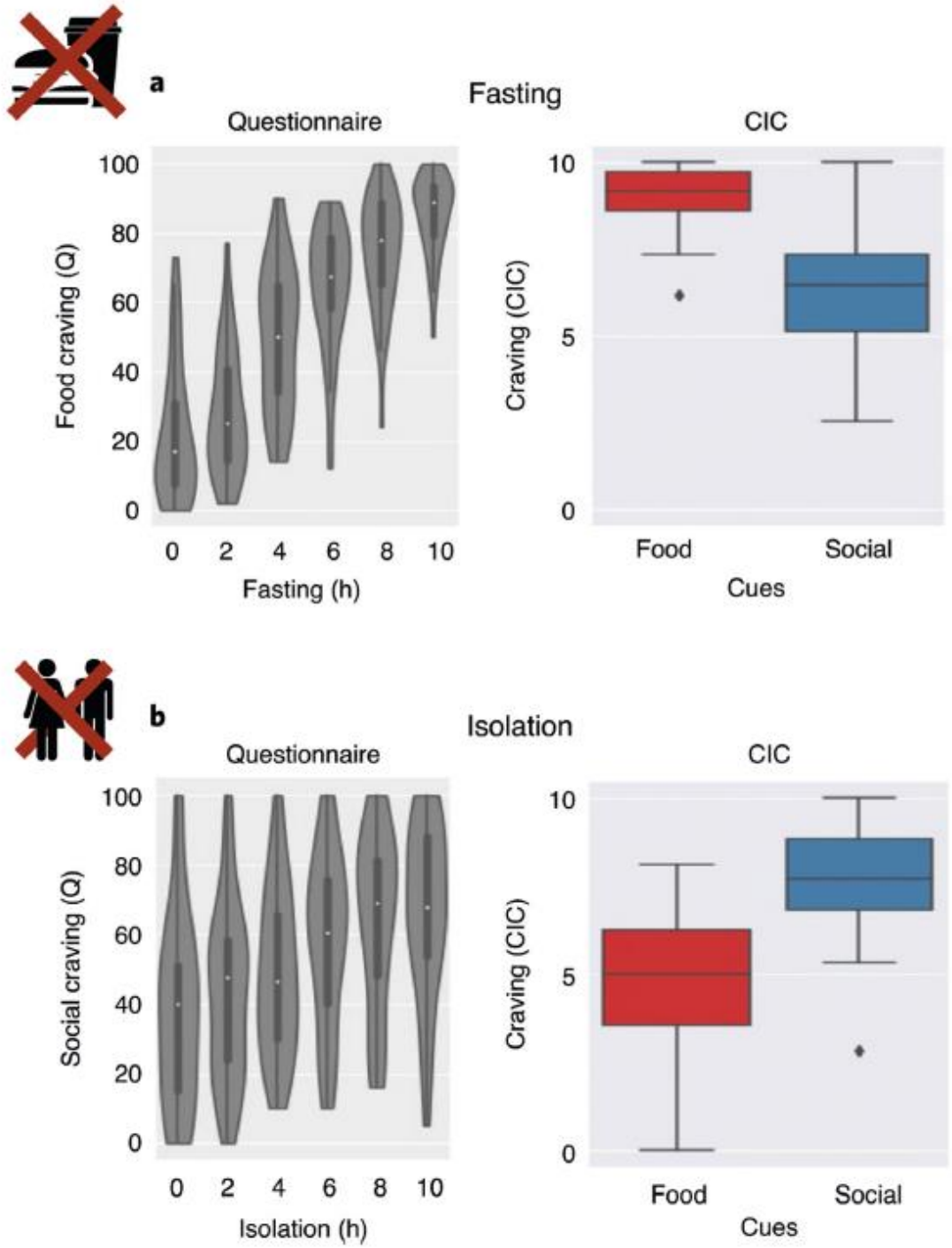

Fonte: Nat Neurosci. 2020 December ; 23(12): 1597–1605. doi:10.1038/s41593-020-00742-z.

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View Article

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10.1001/jamapsychiatry.2021.0113

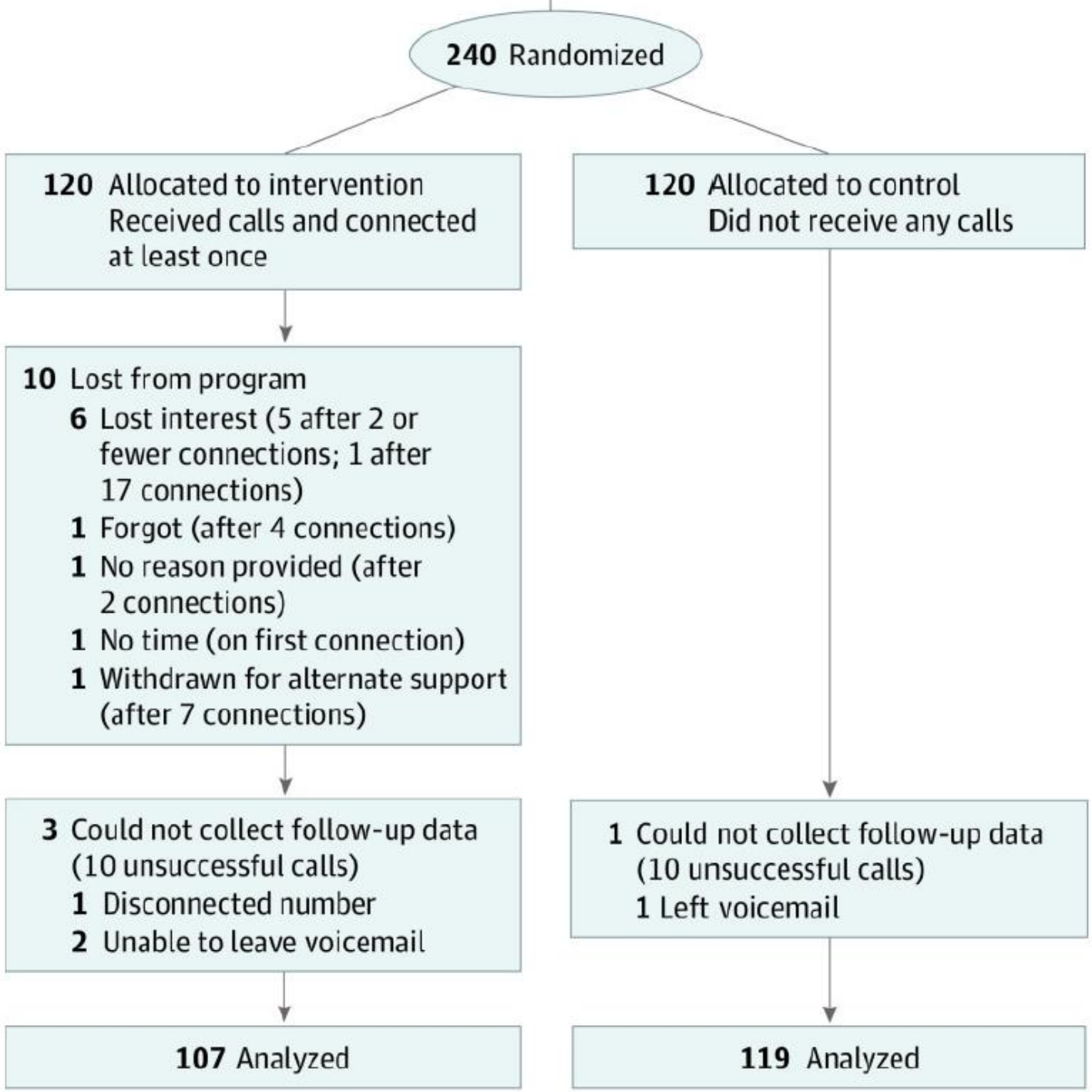
PMCID: PMC7903319
PMID: 33620417

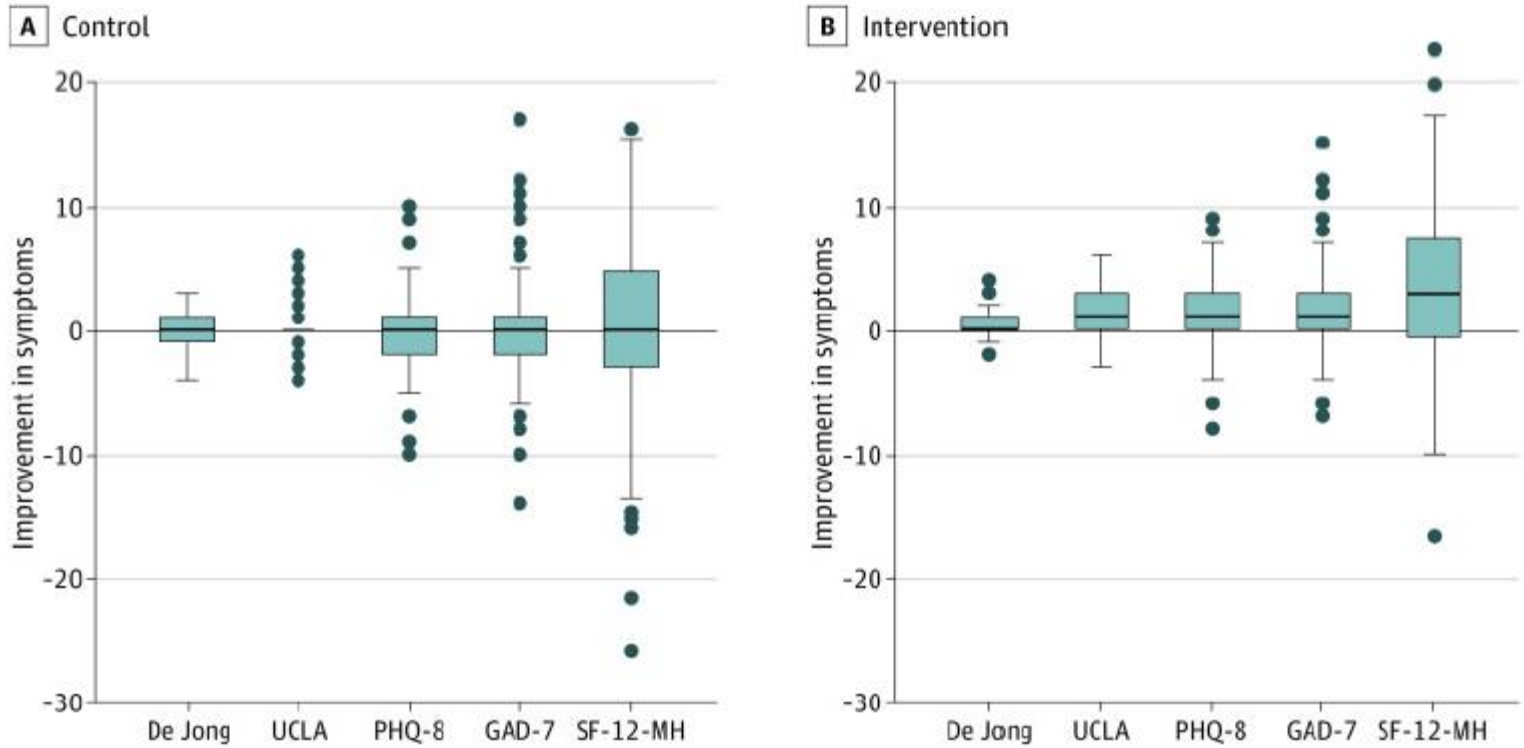
Effect of Layperson-Delivered, Empathy-Focused Program of Telephone Calls on Loneliness, Depression, and Anxiety Among Adults During the COVID-19 Pandemic

A Randomized Clinical Trial

Maninder K. Kahlon, PhD,[1] Nazan Aksan, PhD,[1] Rhonda Aubrey, MHI,[1] Nicole Clark, MBA,[1] Maria Cowley-Morillo,[1] Elizabeth A. Jacobs, MD, MAPP,[1,2] Rhonda Mundhenk, JD, MPH,[3] Katherine R. Sebastian, RN, MPH,[1] and Steven Tomlinson, PhD[4]

Sixteen callers, aged 17 to 23 years, were briefly trained in empathetic conversational techniques. Each called 6 to 9 participants over 4 weeks daily for the first 5 days, after which clients could choose to drop down to fewer calls but no less than 2 calls a week





Box Plots of Changes in Loneliness, Depression, Anxiety, and General Mental Health Over 4 Weeks in the Intervention and Control Arms

Em resumo...

Quando pensamos em saúde mental, estar ou pelo menos fazer-se presente, também é terapêutico.

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