Uluslararası Türk Dünyası
Multipl Skleroz Kongresi
14 - 17 Şubat 2019
Gülhane Halil Akçiçek Konferans Salonu, Ankara

MS'TE BESLENME VE EGZERSİZ

Dr. Özlem Taşkapılıoğlu

«Besinler ilacınız, ilacınız besininiz olsun.»

- MS’te beslenme hakkında mitler-gerçekler

«Daha fazla fiziksel aktivite ve egzersiz, daha az oturma süresi!»

- MS’te egzersiz hakkında öneriler

WESTERN DIETS & LIFE STYLE

Animal fat, red meat, fried food, sweetened drinks and sugar, high salt, low in fiber, alcohol, sedentary lifestyle, processed food

↓

DYSBIOTIC GUT MICROBIOTA

[high ratio W-diet bacteria / V-diet bacteria; low biodiversity]

↓

INTESTINAL INFLAMMATION

- Inflammation, and alteration of intestinal immunity;
- Low Treg/Th17 ratio in the intestinal mucosa;
- Increase of LPS. Disruption of the intestinal barrier

↓

SYSTEMIC INFLAMMATION

- Translocation of LPS, peptides, proteins, activated T-cells, gut bacteria into circulation.
- Low-grade endotoxemia (>200pg/ml LPS)

↓

NEUROINFLAMMATION

- Increase of BBB permeability. Passage of pro-inflammatory molecules and cells. Activation of microglia and astrocytes. Damage to myelin and/or neurons.

Neurotherapeutics (2018) 15:75–91

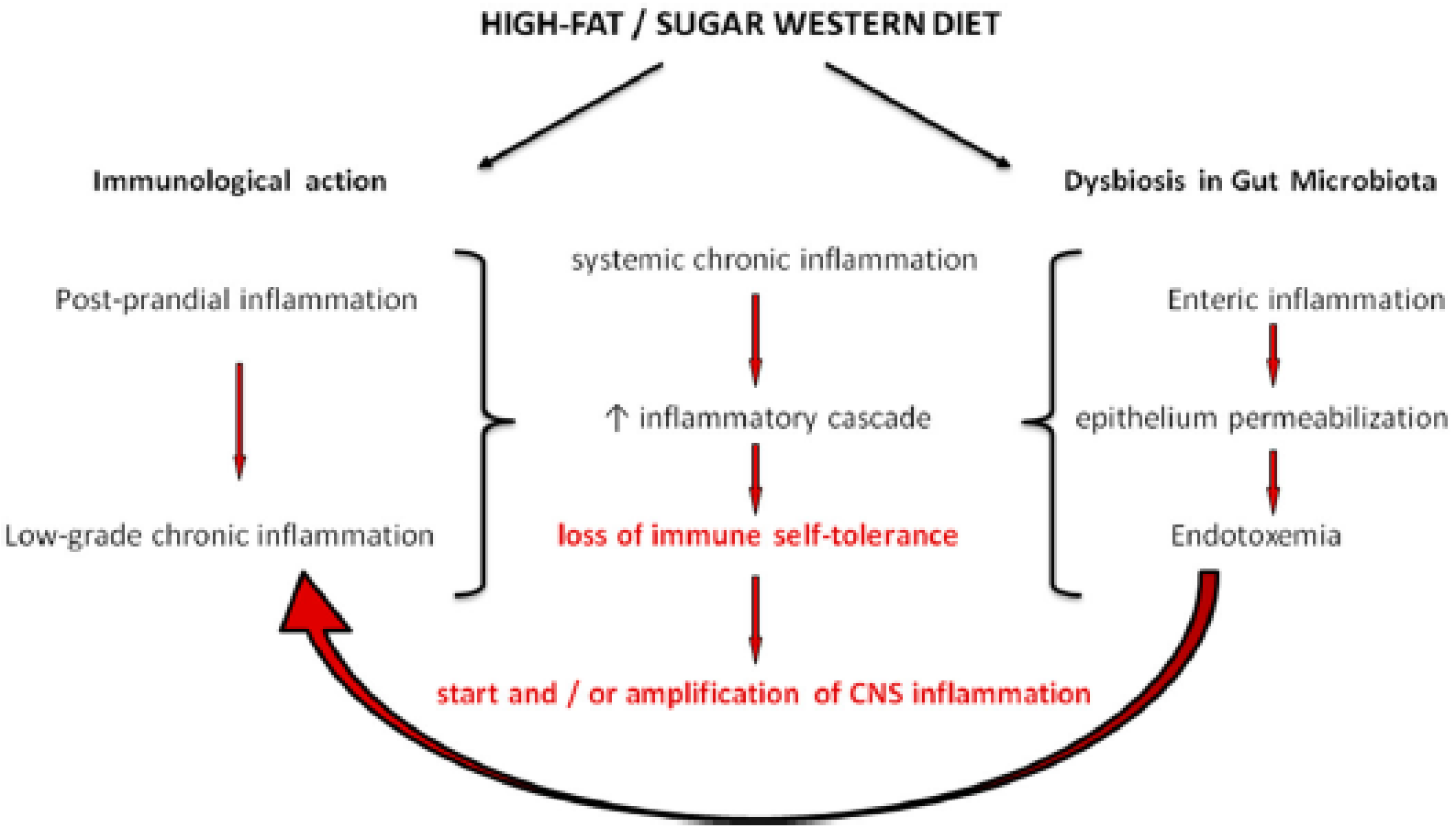
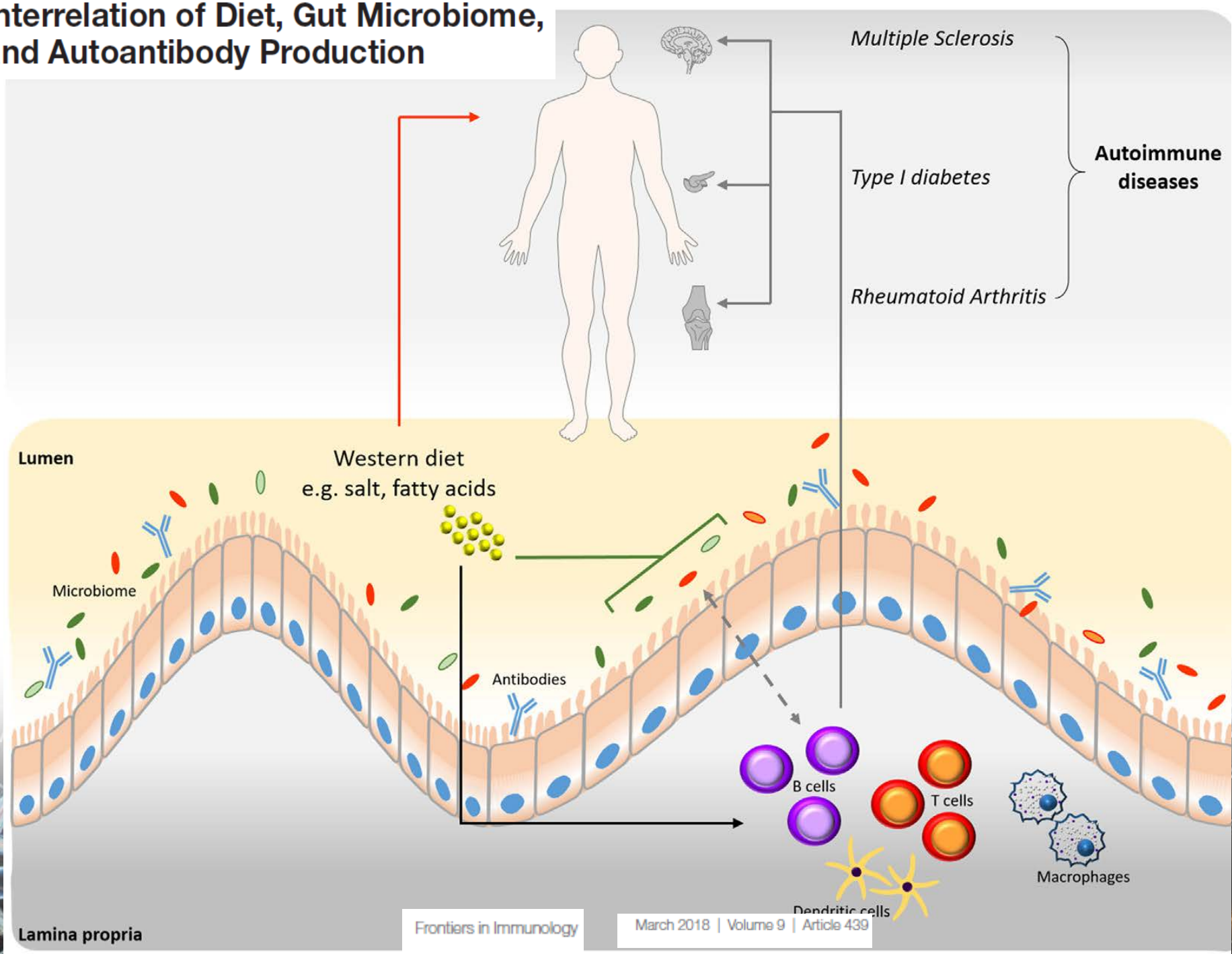


Figure 2 Putative mechanisms connecting diet, local, and systemic inflammation and autoimmunity processes.

Interrelation of Diet, Gut Microbiome, and Autoantibody Production



Frontiers in Immunology
March 2018 | Volume 9 | Article 439

Gastrointestinal influences in multiple sclerosis: Focus on the role of the microbiome

Anna Francis and Cris S. Constantinescu

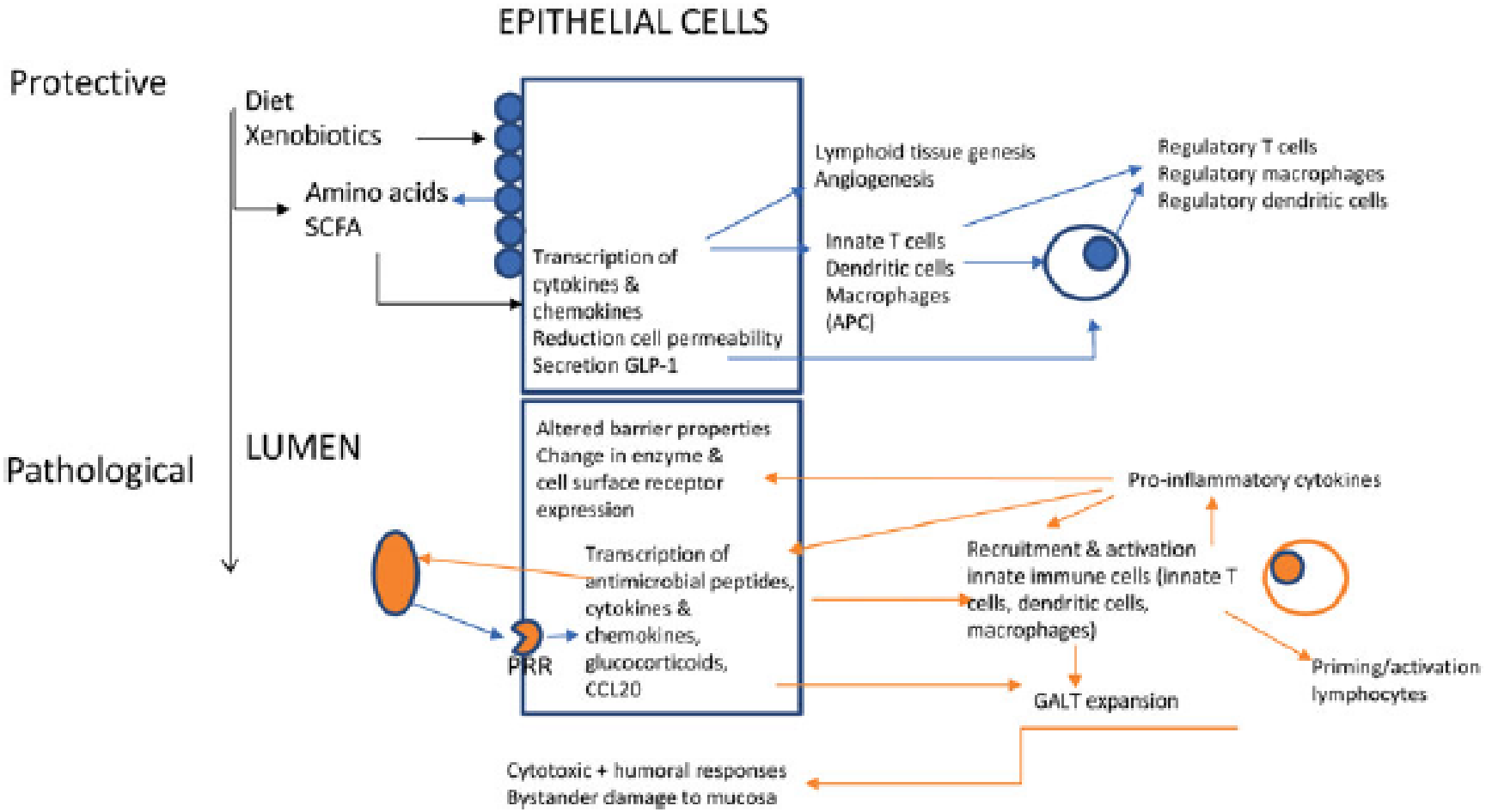


Figure 1 The gut microbiota can induce protective or harmful local immune responses depending on the patterns of receptor activation. APC, antigen-presenting cells; CL20 chemokine ligand 20; GALT gut associated lymphoid tissue; GLP-1 glucagon-like peptide-1; SCFA, short-chain fatty acids; PRR- pathogen recognition receptor.

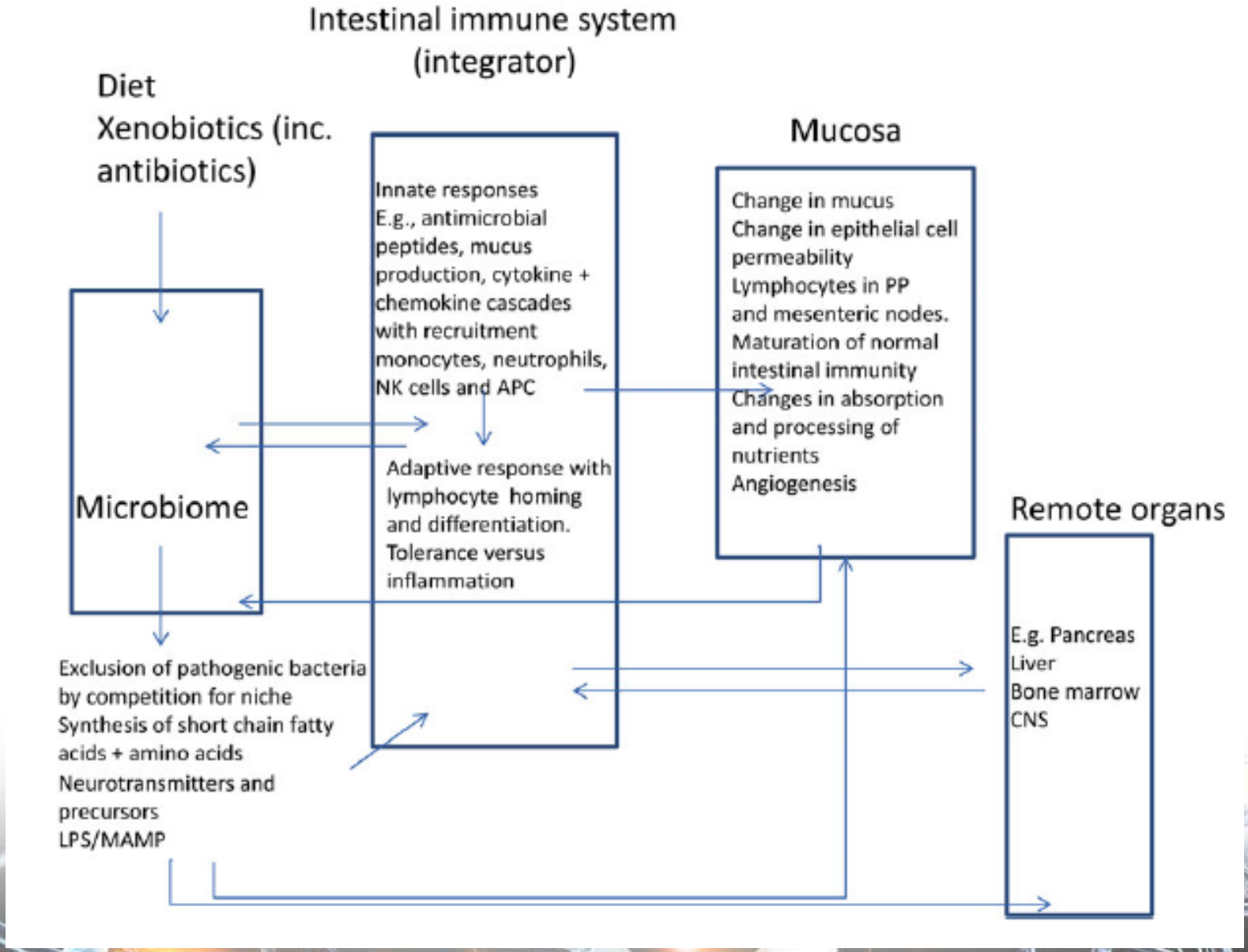


Figure 2 The intestinal immune system acts as an interface between the microbiome and the intestinal mucosa and distant tissues. APC, antigen-presenting cells; CNS, central nervous system; LPS, lipopolysaccharides; MAMP Microbe Associated Molecular Pattern; NK, natural killer; PP, Peyer's patches.

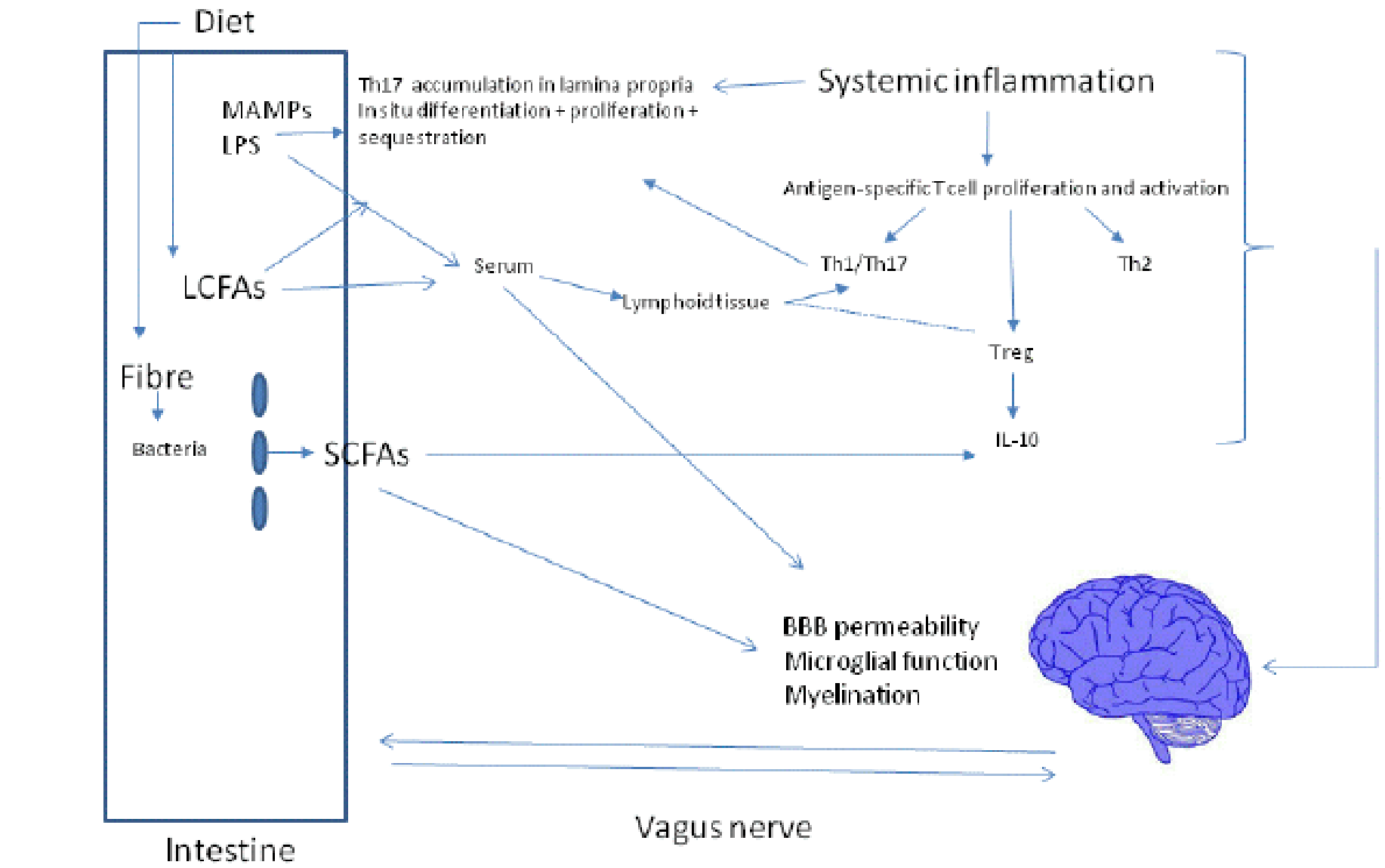
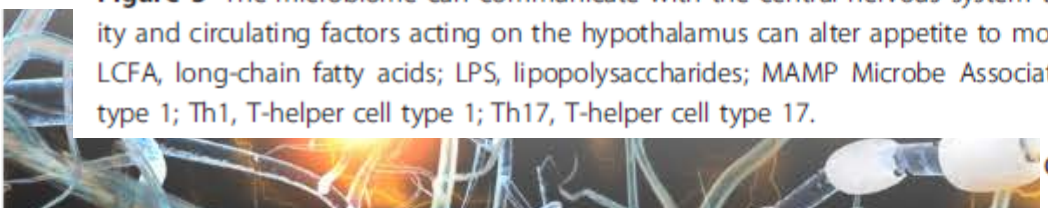


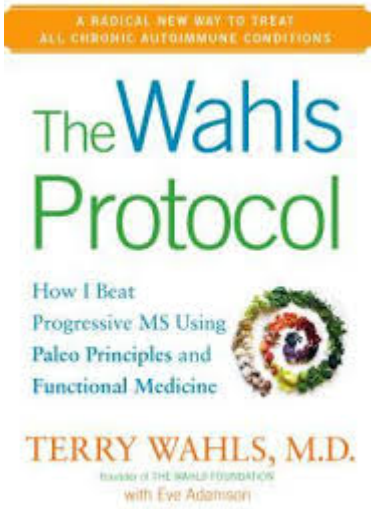
Figure 3 The microbiome can communicate with the central nervous system through various pathways. The vagus nerve allows reciprocal connectivity and circulating factors acting on the hypothalamus can alter appetite to modulate the microbiome.[20] BBB, blood–brain barrier; IL-10, interleukin-10; LCFA, long-chain fatty acids; LPS, lipopolysaccharides; MAMP Microbe Associated Molecular Pattern; SCFA, short-chain fatty acids; Th1, T-helper cell type 1; Th1, T-helper cell type 1; Th17, T-helper cell type 17.

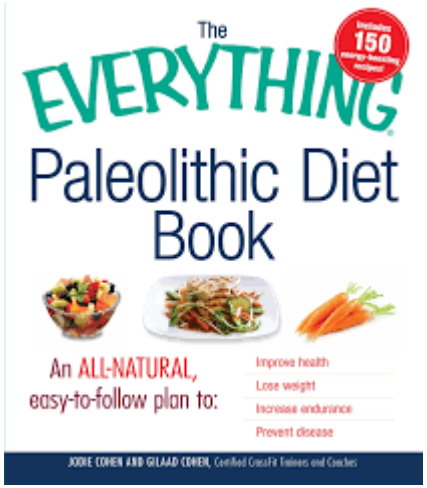


Swank

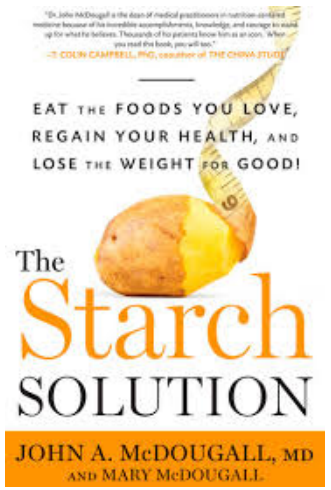
Kousmine

Paleolitik

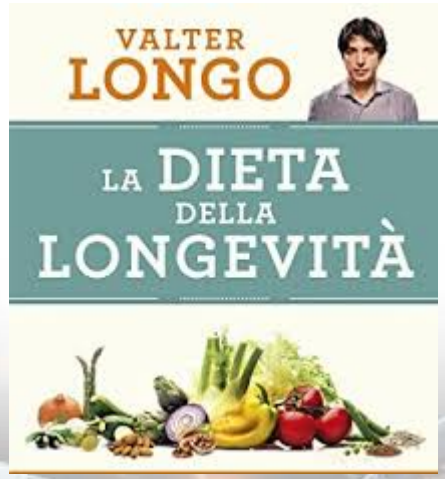




McDougall



Oruca benzeyen Longo diyeti



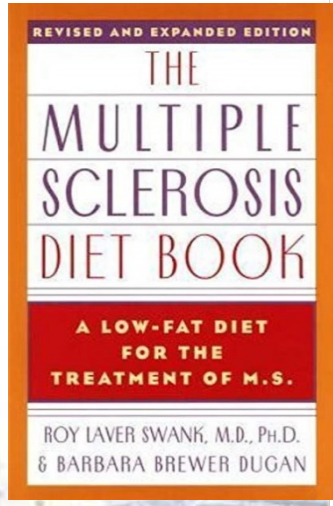
Akdeniz diyeti

Glutensiz

Antienflamatuvar

Dr. Roy Swank: Gözlemsel çalışma

- 1953, 1970 ve 2003
- Swank'ın diyet kitabı son baskı 1987
- 1990: 144 MSli 34 yıllık takip çalışması
- Total ve doymuş yağ oranı düşük diyet
- Düşük hastalık aktivitesi ve progresyonu
- Nişastalı sebze ağırlıklı
- %10 yağ, %14 protein, %75 karbonhidrat



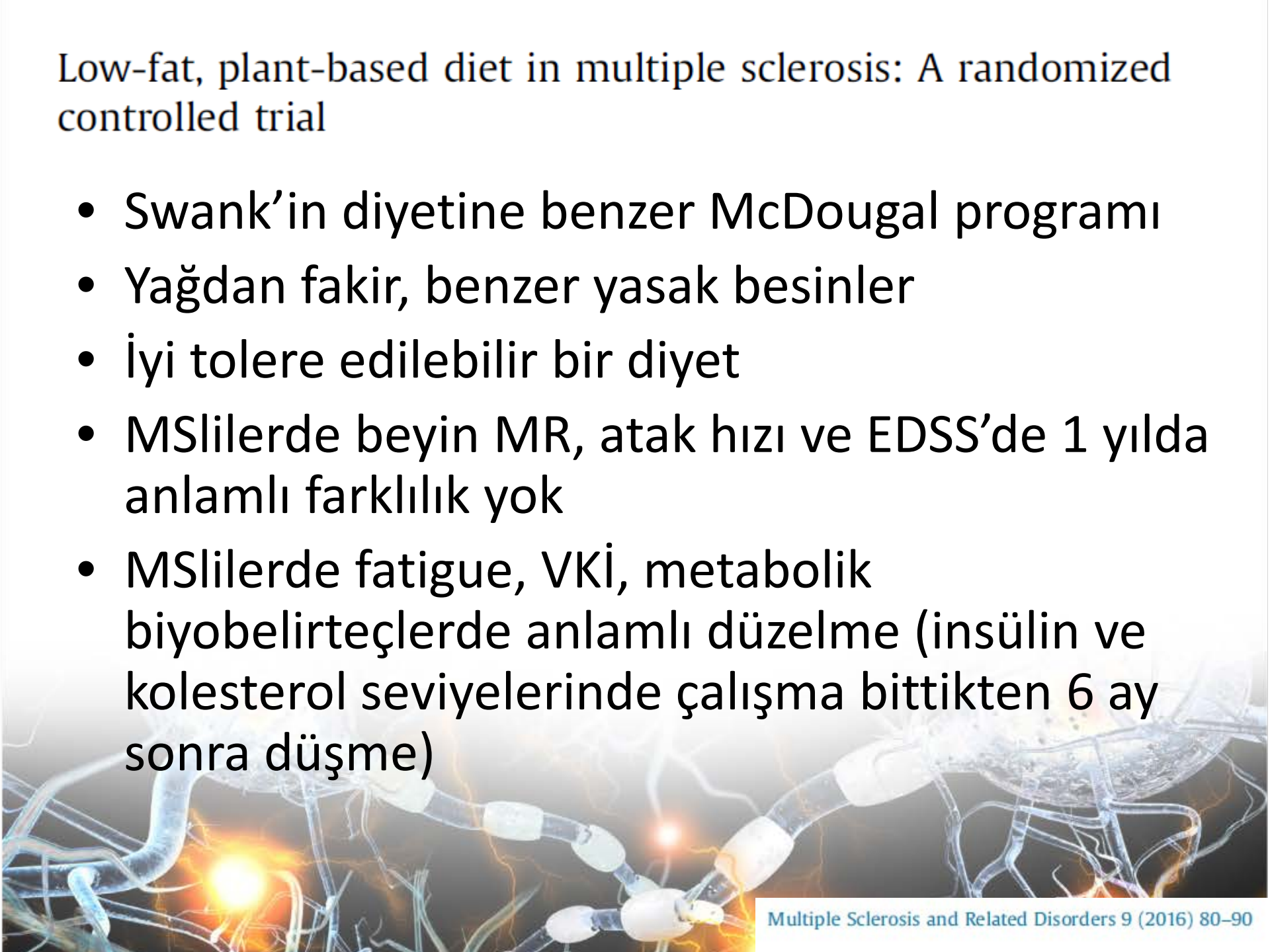
ET, BALIK, YUMURTA, SÜT ÜRÜNLERİ,
BİTKİSEL YAĞLAR (MISIR VE ZEYTİNYAĞI)

SWANK MS FOUNDATION

Multiple Sclerosis and Related Disorders 9 (2016) 80–90

Low-fat, plant-based diet in multiple sclerosis: A randomized controlled trial

- Swank'in diyetine benzer McDougal programı
- Yağdan fakir, benzer yasak besinler
- İyi tolere edilebilir bir diyet
- MSlilerde beyin MR, atak hızı ve EDSS'de 1 yılda anlamlı farklılık yok
- MSlilerde fatigue, VKİ, metabolik biyobelirteçlerde anlamlı düzelme (insülin ve kolesterol seviyelerinde çalışma bittikten 6 ay sonra düşme)



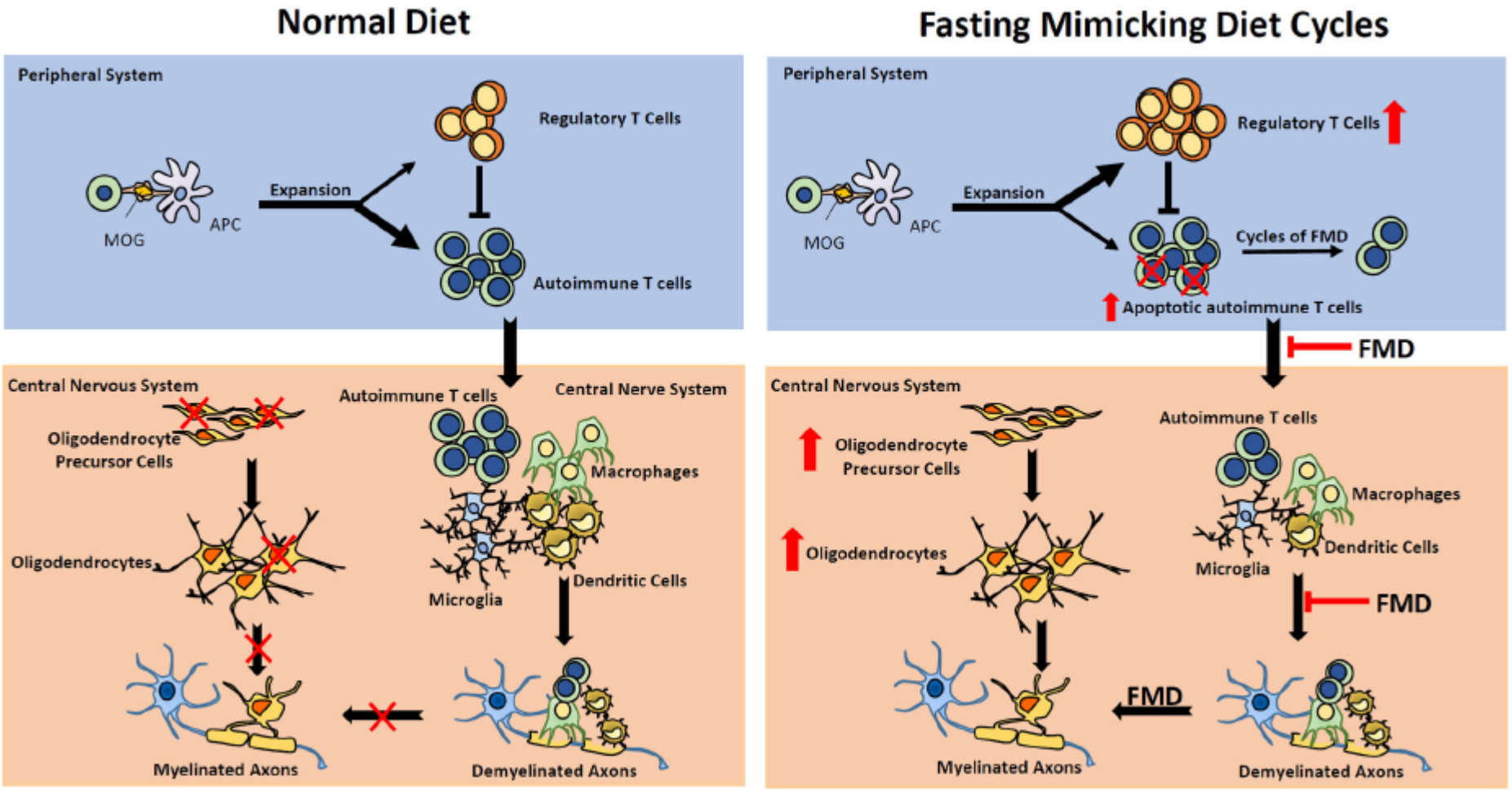
Multiple Sclerosis and Related Disorders 9 (2016) 80–90

Table 1 Proinflammatory dietary factors

Food components	Effects
1) Saturated fatty acids [prevalently of animal origin (butter, whole milk, cheese, meat, sausages); coconut oil and palm oil]	a) Binding to TLR-2 and TLR-4 and activation of the proinflammatory transcription factor, NF-κB b) Change of gut microbiota composition; gut dysbiosis c) ↑ IL-17A, ↓ PPAR-α, and β-fatty acid oxidation
2) *Trans* fatty acids (in margarine, meat, snacks, French fries, and other fried food)	a) Interference with natural "*cis*" unsaturated fatty acids b) Intestinal inflammation; upregulation of Th17 cells c) ↑ Cholesterol; ↑ abdominal fat; ↑ weight gain
3) Red meat	a) Iron is nitrosylated to nitroso compounds b) Abnormal iron deposits in MS c) GGT and hsCRP increase d) Heterocyclic amines during cooking e) Anti-Neu5Gc antibodies f) Arachidonic acid (eicosanoids) g) Activates the Th17 pathway
4) Sugar, refined cereals, sugar-sweetened beverages and low-fiber intake	a) Insulin increase—high calories b) Postprandial inflammation c) Biosynthetic pathways d) Feeding specific gut microbiota leading to dysbiosis
5) Increased dietary salt intake	a) Induce pathogenic Th17 cells and proinflammatory cytokines in EAE
6) Proteins of the MFGM: BTN, a major protein of the MFGM, is very similar to MOG, the MS candidate autoantigen.	a) MOG/BTN cross-reactive antibodies have been found in MS, in autism and in CHD b) BTN, as MOG, can induce EAE

MFGM = milk fat globule membrane; BTN = butyrophilin; MOG = myelin oligodendrocyte glycoprotein; MS = multiple sclerosis; TLR = Toll-like receptor; NF-κB = nuclear factor kappa B; IL= inteleukin; PPAR = peroxisome proliferator-activated receptor; Th = T helper; GGT = gamma-glutamyl transpeptidase; hsCRP = high-sensitivity C-reactive protein; Neu5Gc = *N*-glycolylneuraminic acid; EAE = experimental autoimmune encephalomyelitis; CHD = coronary heart disease

Diet mimicking fasting promotes regeneration and reduces autoimmunity and multiple sclerosis symptoms



Cell Rep. 2016 June 7; 15(10): 2136–2146.

- Oruca benzeyen beslenmenin EAE modelindeki etkileri
- Kronik ketojenik diyet
- Tüm sıçanlarda klinik hastalık şiddetini azalttı
- Sıçanların %20'sinde semptomları tamamen düzeltti
- Artmış kortikosteron seviyeleri ve Treg sayısı
- Düşük proinflamatuvar sitokinler, Th1 ve Th17 ve APCler
- Oligodendrosit öncü hücre rejenerasyonunda ve aksonal remiyelinizasyonda artış
- NCT01538355: RRMSli hastalarda kullanımının ilk verileri olumlu ve tolere edilebilir

Diet and Multiple Sclerosis: Scoping Review of Web-Based Recommendations

Table 2. Recommendations and rationale for the dietary patterns recommended by the websites.

Dietary pattern	Major characteristics	Rationale for this diet
Healthy balanced diet	Low-fat, high-fiber diet with whole grains and fish (similar to the diet recommended by the American Heart Association)	Increases the time between relapses and promotes overall health [24,25,34]; controls weight and fatigue, better bladder and bowel function [24,25]; reduces inflammation [47]; low vitamin & mineral intake can worsen multiple sclerosis (MS) symptoms [36]
Swank diet and its modifications including Overcoming MS and MS Recovery diet	Low-saturated fat, near-vegetarian diet with no red meat in the first year; dairy with <1% fat; no processed foods; saturated fat <15 g/day; unsaturated fat 20-50 g/day; cod liver oil and multivitamin every day	Low prevalence in population on low-saturated fat diets [32], low-saturated fat, near-vegetarian diet arrests or cures MS and slows progression [38]; fruits and vegetables reduce constipation and reduce weight [32]; lower frequency and severity of attacks [40]; better health outcomes; cow milk protein is similar to myelin and initiates autoimmune reaction in MS [18]; Swank diet reduces death rate [46]
Paleo diet and its modifications including Wahl's diet	Includes free-range meat and organic fruit and vegetables. Excludes grains, dairy, soy, legumes, and sugar	For optimum mitochondrial, myelin, and neurotransmitter functions [35,48]; to slow MS decline [35]; animal-based omega-3 to lessen progression and relapses [35]; seaweed for iodine, iron, calcium, and fiber helps increase alertness and mental clarity [35,48]; vitamins A, B, C, and K for myelin and brain health [27,48]; sulfur-rich vegetables for removing toxins and formation of neurotransmitters [27,48]; colorful fruits and vegetables for antioxidants [37]; grains are health destroying [37]; omega-3, creatine, and coenzyme Q10 help in mitochondrial function [48]
Best Bet diet	Includes vitamin, mineral, and herb supplements. Excludes dairy, refined sugar, eggs, yeast, gluten, and legumes	Remove proteins that resemble myelin [44] and act like allergens [45]

(Interact J Med Res 2018;8(1):e10050)

Anti-inflammatory nutritional intervention in patients with relapsing-remitting and primary-progressive multiple sclerosis: A pilot study

- McDougall diyeti ile MR'da değişiklik yok
- SPMS: Modifiye Paleo diyeti yorgunluk azalmış
- Omega-3 yağ asitleri, omega 3 ve 6 içeren karışımlar iyilik hali
- Vitamin desteği kullanmaya göre diyete uyum MSlilerde daha fazla

Experimental Biology and Medicine 2016; 241: 620–635

Ketogenic diets attenuate cyclooxygenase and lipoxygenase gene expression in multiple sclerosis

Enflamatuvar eikasanoidlerin biyosentezindeki anahtar enzimlerin (ALOX5, ALOX15, COX1,COX2) gen ekspresyon profili

Ketojenik diyet ekspresyonları düşürür

MS tedavisine destek amaçlı önerilebilir

EBioMedicine 36 (2018) 293–303

Diet, Gut Microbiota, and Vitamins D + A in Multiple Sclerosis

VEGETARIAN/VEGAN DIET (V-DIET)
anti-inflammatory

Complex carbohydrates (fibers), vegetables, fruit, fish, legumes, + [probiotics, vitamins D & A, lipoic acid, caloric restriction, physical exercise].

WESTERN DIET (W-DIET)
pro-inflammatory

Animal fat, trans fatty acids, red meat, sweetened drinks and sugar, high salt.

GUT EUBIOSIS – HEALTH, WELLNESS

Increase of:
V-diet bacteria , Microbial diversity, SCFA, Butyrate, Polysaccharide A (PSA), Microbial anti-inflammatory molecule (MAM); Histone deacetylase inhibitor; AHR receptor agonists, Treg/Th17 ratio.

GUT DYSBIOSIS - ENDOTOXEMIA

Increase of:
W-diet bacteria, Energy harvest, Bile acids, LPS, TNF, IL-6, IL-17, Gut barrier permeability, BBB permeability.

Decrease of:
Microbial diversity, VDR availability.

Neurotherapeutics (2018) 15:75–91

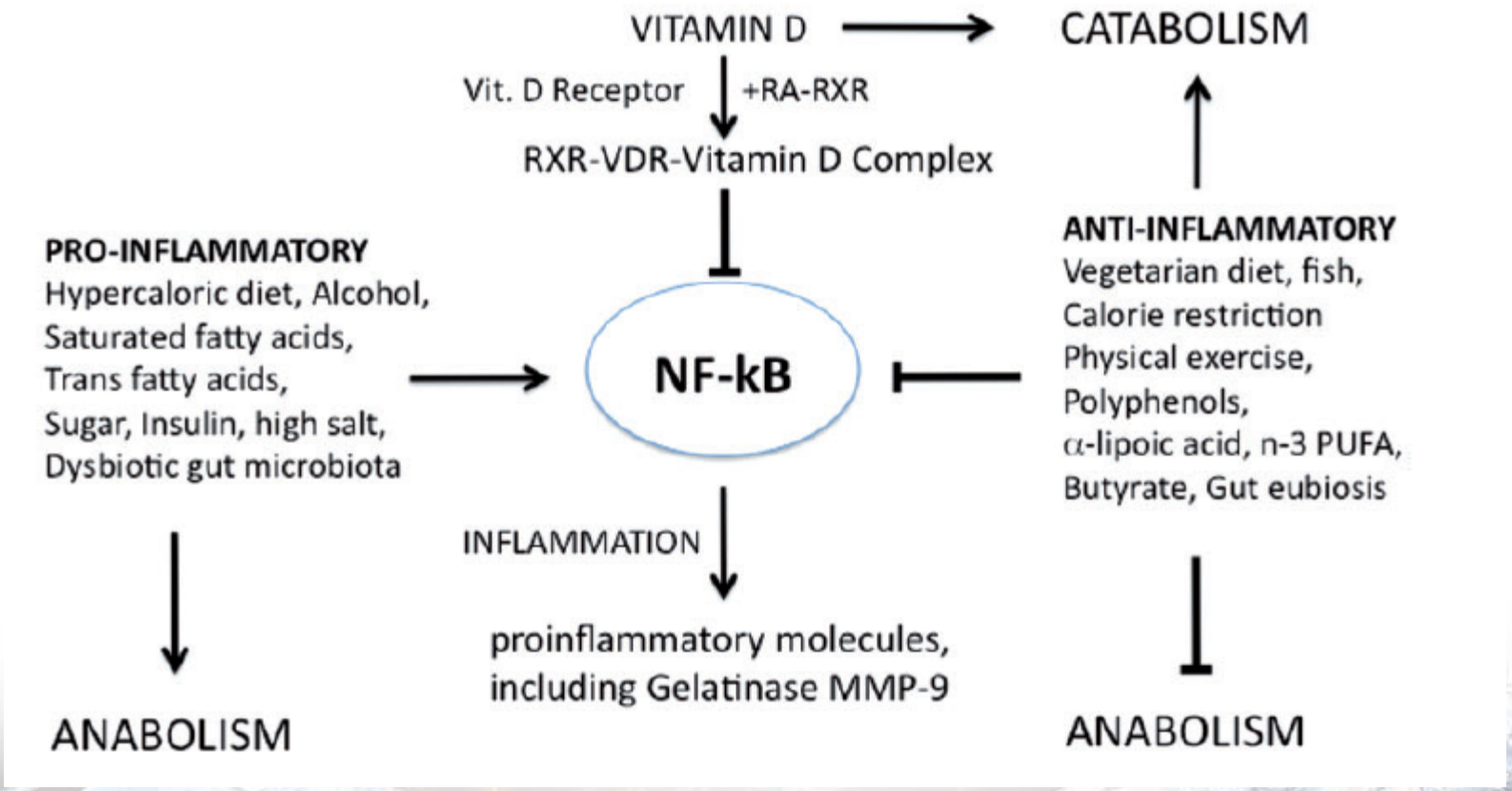


Figure 7 Schematic description of how nutritional intervention can influence the inflammatory status. VDR: vitamin D receptor; RXR: retinoid X-receptor; RA: 9 cis-retinoic acid; NF-kB: nuclear transcription factor-kB; MMP: metalloproteinase; n-3 PUFA: omega-3 polyunsaturated fatty acids

Influence of Diet in Multiple Sclerosis: A Systematic Review[1,2]

TABLE 2 Dose and duration of clinical trials with PUFA and vitamin D administration[1]

Study, year (ref)	Dose	Duration	Effect
PUFAs			
Weinstock-Guttman et al., 2005 (30)	3.30 g ω-3 FAs/d	12 mo	Decrease in relapse rates and reduced fatigue
Shinto et al., 2009 (29)	4.8 g ω-3 FAs/d	3 mo	Immunomodulatory efficacy for regulating MMP-9 concentrations in MS
Mauritz et al., 2013 (26)	200 mg antioxidants/d in a low-fat diet	1.5 mo	Decreased oxidative stress, C-reactive protein, and other inflammatory markers
Pantzaris et al., 2013 (27)	19.5 mL PUFAs + γ-tocopherol/d	30 mo	Decreased annual relapse rate and disability progression
Rezapour-Firouzi et al., 2013 (28)	18–21 g PUFAs/d	6 mo	Decrease in proinflammatory (IL-17) and increase in anti-inflammatory cytokines
Vitamin D			
Wingerchuk et al., 2005 (46)	1000 IU/d	48 wk	Decrease in exacerbation rate; improvement in brain lesions (MRI)
Kimball et al., 2007 (33)	4000–40,000 IU/d	28 wk	Decreased number of brain lesions (MRI)
Smolders et al., 2010 (40)	20,000 IU/d	12 wk	Immunomodulatory efficacy in MS
Steffensen et al., 2011 (43)	2800 IU/d	96 wk	No prevention of bone loss in MS population
Dörr et al., 2012 (31)	200–10,200 IU/d	72 wk	Immunomodulatory efficacy in MS
Kampman et al., 2012 (32)	2800 IU/d	96 wk	No effect
Soilu-Hänninen et al., 2012 (42)	2800 IU/d	12 wk	Reduced new lesions and improved timed tandem walk
Toghianifar et al., 2015 (44)	7000 IU/d	12 wk	Improved inflammatory response

Adv Nutr 2017;8:463–72.

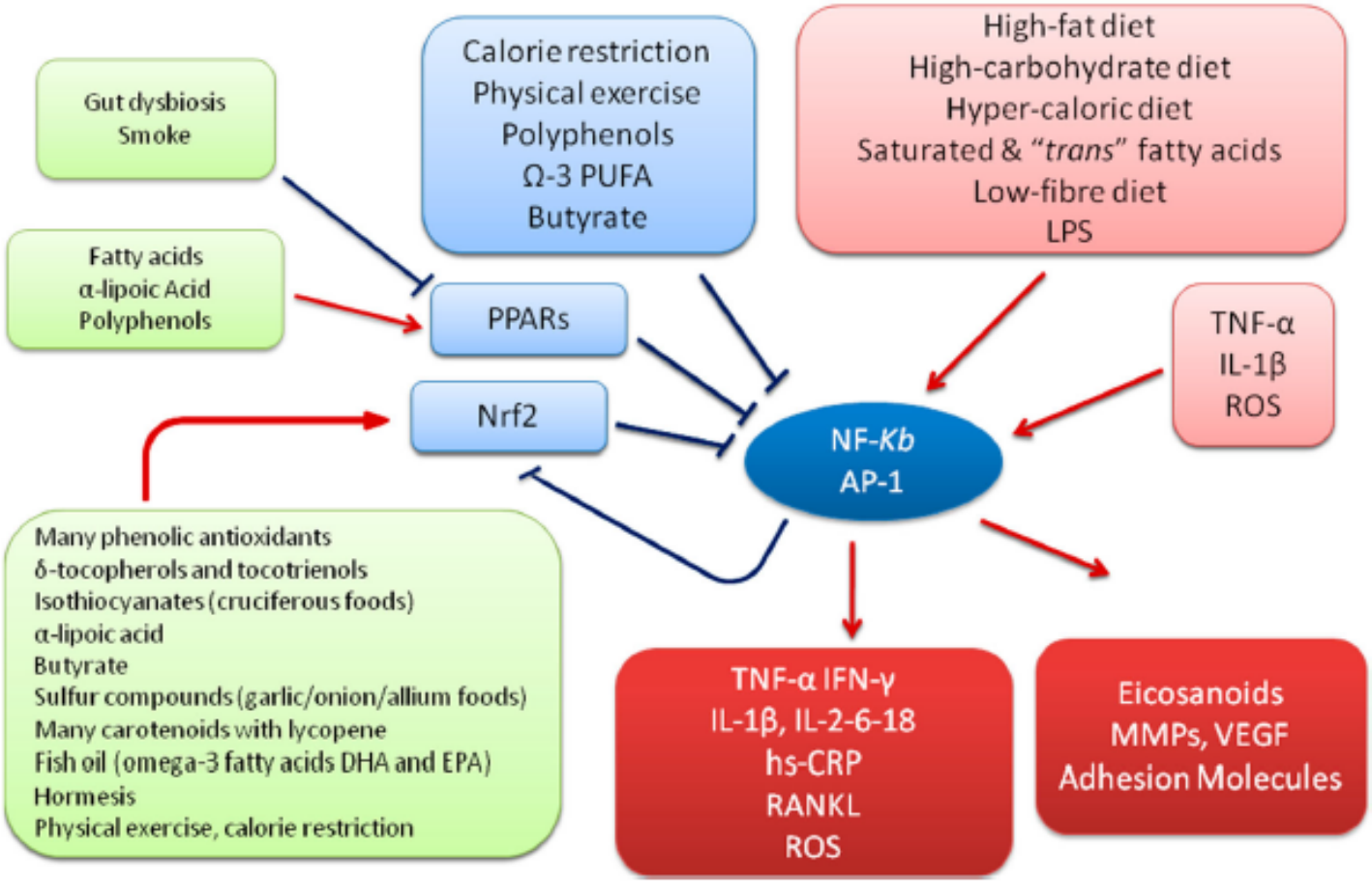
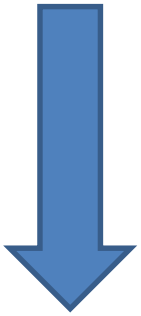


Figure 1 Outline of molecular interaction between dietary habits and immunologic regulatory system (Riccio P, Autoimmune Diseases 2010, modified).

ACTRIMS FORUM 2017

Genetik, çevresel ve
epigenetik faktörler



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MS yatkınlığı ve klinik seyir

Diet, Gut Microbiota, and Vitamins D + A in Multiple Sclerosis

VEGETARIAN/VEGAN DIET (V-DIET)
anti-inflammatory

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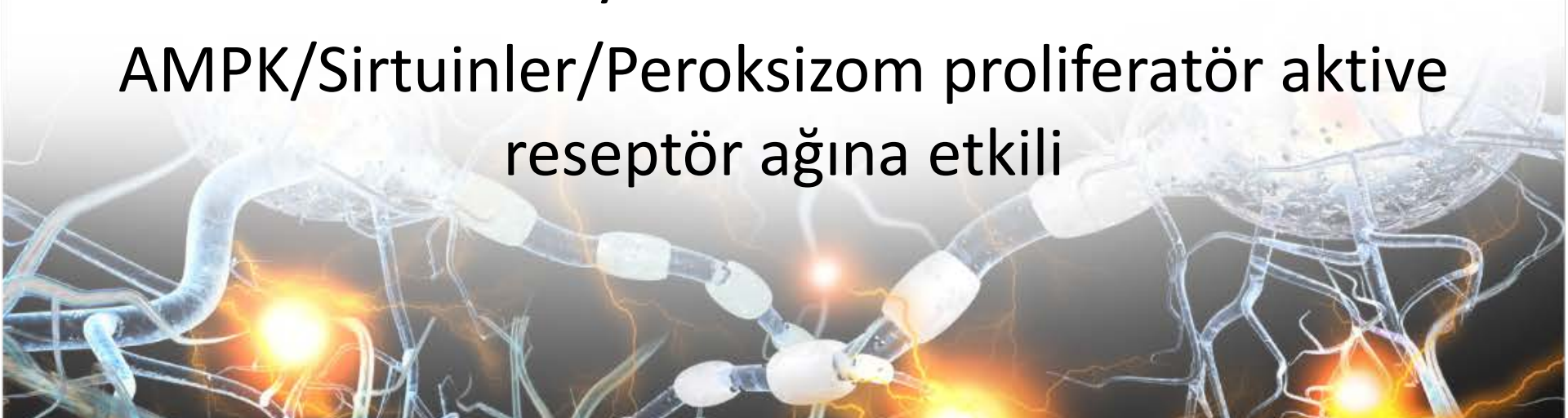
Decrease of:
Microbial diversity, VDR availability.

Neurotherapeutics (2018) 15:75–91

MS ve Egzersiz

- Kronik yorgunluğu azaltır
- Özürlülük ilerlemesini yavaşlatır
- Oksitadif metabolizayı upregüle eder
- Enflamasyonu downregüle eder
- Moleküler düzey:

AMPK/Sirtuinler/Peroksizom proliferatör aktive reseptör ağına etkili



MS ve Egzersiz

- Yaşam kalitesinde artış
- Antienflamatuvar sitokin sentezinde azalma
- Leptin seviyelerinde azalma
- Adiponektin seviyeleirnde artış
- Apiponektin reseptör aktivetesinde artış
- Sıçanlarda, egzersizinin bağırsak bakterilerinin bileşimini değiştirebildiği görülmüştür.

- Hastalık öncesi yüksek fiziksel aktivite düzeyine sahip bireyler fiziksel engelliliğe daha dirençli
- Günlük aktiviteler mümkün olduğunca artırılmalı
- Bireye özel olarak yapılandırılmış aerobik, kuvvetlendirme, germe ve denge gibi egzersiz programları
- Oturma zamanı mümkün olduğunca düşük

Fzt. Turhan Kahraman
MS Araştırmaları Derneği
Şubat 2019 Bülteni

- MS risk faktörleri **birbiri ile etkileşir**
  - Genetik
  - Beslenme/ Egzersiz/Güneş/Diğer
  - Beslenme ve mikrobiota ilişkisi
- Bazen **BEKLENMEDİK** ve **birbirinden bağımsız** olarak MS riskini etkiler:

  SNP- Vit D ve SNP- VKİ

- MS’te risk faktörleri duruma bağlı etki edebilir
- Ergenlik öncesi obezite, K’larda MS riskini
- Vit D desteğinin etkisi, yıllık daha fazla güneş alan yerlerde yaşayanlarda daha fazladır.
- Kısa zincirli yağ asitlerinin düzeltici etkisi liften zengin beslenenlerde daha belirgindir

BESLENME-MİKROBİYOTA

- Uzun zincirli yağ asitleri ile beslenme, otoimmüniteyi uyarır
- Kısa zincirli yağ asitlerinin ağızdan alımı ise hastalığa direnç gelişmesinde önemli
- Obezite+ Cinsel gelişim → Pediatrik MS'te hastalık başlangıç yaşını erkene çeker

Interactions between dietary inflammatory index, nutritional state and Multiple Sclerosis clinical condition

Background & aims: The Dietary Inflammatory Index (DII) consists of a tool that assesses dietary inflammatory potential based on the assignment of an inflammatory score to a variety of nutrients, seasonings and bioactive compounds. Pro-inflammatory diets are associated to weight and abdominal fat excess. High Body Mass Index (BMI) and Waist Circumference (WC) seem to contribute to a worse prognosis in Multiple Sclerosis (MS) patients. Therefore, this study seeks to investigate the relation between anthropometric indexes and body adiposity with the clinical condition and the Dietary Inflammatory Index of MS individuals.

Conclusions: The DII may interfere in the nutritional state of MS patients and the nutritional state may affect disability levels but it is necessary to establish which nutritional indicator can better predict the relation between DII and the clinical condition of MS patients.

Clinical Nutrition ESPEN 26 (2018) 35–41

Dietary and lifestyle factors in multiple sclerosis progression: results from a 5-year longitudinal MRI study

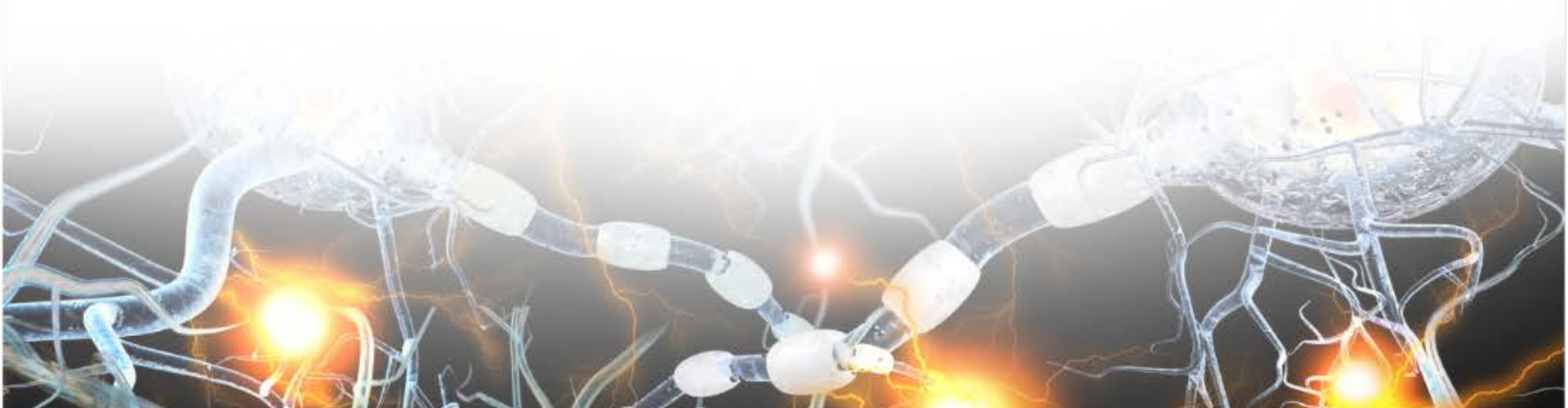
Dejan Jakimovski[1] · Bianca Weinstock-Guttman[2] · Sirin Gandhi[1] · Yi Guan[1] · Jesper Hagemeier[1] · Deepa P. Ramasamy[1] · Tom A. Fuchs[1] · Richard W. Browne[3] · Niels Bergsland[1] · Michael G. Dwyer[1,4] · Murali Ramanathan[5] · Robert Zivadinov[1,4]

Received: 14 August 2018 / Revised: 14 January 2019 / Accepted: 19 January 2019

Abstract

Background Evidence regarding the role, if any, of dietary and lifestyle factors in the pathogenesis of multiple sclerosis (MS) is poorly understood.

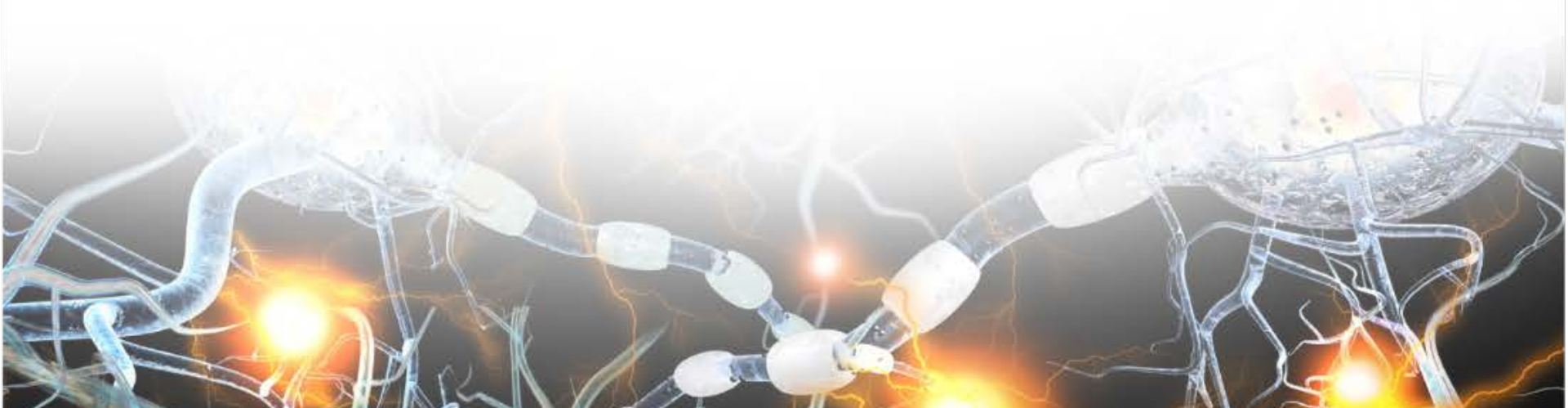
Objective To assess the effect of lifestyle-based risk factors linked to cardiovascular disease (CVD) on clinical and MRI-derived MS outcomes.



Demographic and clinical characteristics	CIS/MS (n= 175)	HCs (n= 42)	p value
Female, n (%)	128 (73.1)	30 (71.4)	0.85
Age at baseline, mean (SD)	46.9 (11.2)	46.8 (14.4)	0.92
Follow-up period, mean (SD)	5.4 (0.6)	5.5 (0.5)	0.52
BMI at baseline, mean (SD)	27.3 (5.6)	25.9 (5.8)	0.14
BMI at follow-up, mean (SD)	27.4 (5.8)	25.9 (5.8)	0.14
Diet score, mean (SD)	0.13 (0.3)	0.23 (0.3)	0.079
20 year CVD risk, mean (SD)	4.9 (7.1)	6.3 (8.8)	0.37
Framingham Risk Score, mean (SD)	2.4 (3.2)	–	–
Hypertension, n (%)	27 (15.4)	4 (9.5)	0.46
Hyperlipidemia, n (%)	26 (14.9)	7 (16.7)	0.81
Heart disease, n (%)	16 (9.1)	2 (4.8)	0.54
Disease duration, n (SD)	13.9 (10.2)	–	–
CIS/RRMS/PMS	24/106/45	–	–
EDSS at baseline, median (IQR)	2.5 (1.5–4.5)	–	–
EDSS at follow-up, median (IQR)	3.0 (2.0–5.6)	–	–
EDSS change, mean (SD)	0.4 (0.9)	–	–
Annualized relapse rate, mean (SD)	0.178 (0.37)	–	–
DMT use at baseline			
IFN-β, n (%)	72 (41.1)	–	–
Glatiramer acetate, n (%)	34 (19.4)	–	–
Natalizumab, n (%)	25 (14.3)	–	–
Other DMTs, n (%)	5 (2.9)	–	–
No DMT use, n (%)	39 (22.3)	–	–

Methods The study enrolled 175 MS or clinically isolated syndrome (CIS) patients and 42 age- and sex-matched healthy controls (HCs) who were longitudinally followed for 5.5 years. The 20-year CVD risk was calculated by Healthy Heart Score (HHS) prediction model which includes age, smoking, body mass index, dietary intake, exercise, and alcohol consumption. Baseline and follow-up MRI scans were obtained and cross-sectional and longitudinal changes of T2-lesion volume (LV), whole brain volume (WBV), white matter volume (WMV), gray matter volume (GMV), and lateral ventricular volume (LVV) were calculated.

Conclusion Lifestyle risk factors contribute to accelerated central brain atrophy in MS patients, whereas unhealthier diet is associated with MS lesion accrual. Despite the lower overall effect when compared to HCs, lifestyle-based modifications may still provide a beneficial effect on reducing brain atrophy in MS patients.



Teşekkür ederim.