Programme double

Les problèmes de sommeil et d'anxiété: les approches naturelles

Eric Simard, Dr en biologie
chercheur en longévité cellulaire
www.esimard.com

Usages thérapeutiques des oméga-3: où en est rendu la science

Eric Simard, docteur en biologie et chercheur (www.esimard.com).

1

Usages thérapeutiques des oméga-3: où en est rendu la science

Eric Simard, docteur en biologie et chercheur (www.esimard.com).

2

Divulgation et conflits d'intérêts

- Je suis président de Idunn Technologies qui commercialise des suppléments.
- Je suis un administrateur du Centre Axis.
- Je ne parlerai pas de produits de prescription puisque l'industrie pharmaceutique le fait très bien.
- Toutes les informations présentées sont supportées par des données probantes de la littérature scientifique, rapportées en références à la fin.

3

Présentation / déclaration

Eric Simard, Ph.D. est Dr en biologie, chercheur dans le domaine du vieillissement.

- Auteur de 4 livres avec 11 autres professionnels.
- Président de l'Association Professionnelle pour la Santé Intégrative (APSI).
- A été président du Comité consultatif du Conseil de Recherche en Science et en Génie du Canada, bureau du Québec, pendant plus de 10 ans.
- Membre nommé de la Commission de l'éthique en science et technologie du Conseil des Ministres.
- Président de Idunn Technologies.

N.B. A été VP Science et développement pour une entreprise d'oméga-3, responsable du développement de produits pour les deux filiales pharmaceutiques.

4

Contenu

5

Objectifs

ES1

- Rappeler les fonctions biologiques des oméga-3.
- Connaître les principaux usages thérapeutiques supportés par les données probantes.
- Discuter des méta-analyses et recommandations publiées par des organismes reconnus.
- Définir les doses thérapeutiques et les applications propres à chaque molécule.

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Slide 6

ES1 Eric Simard, 2021-01-27

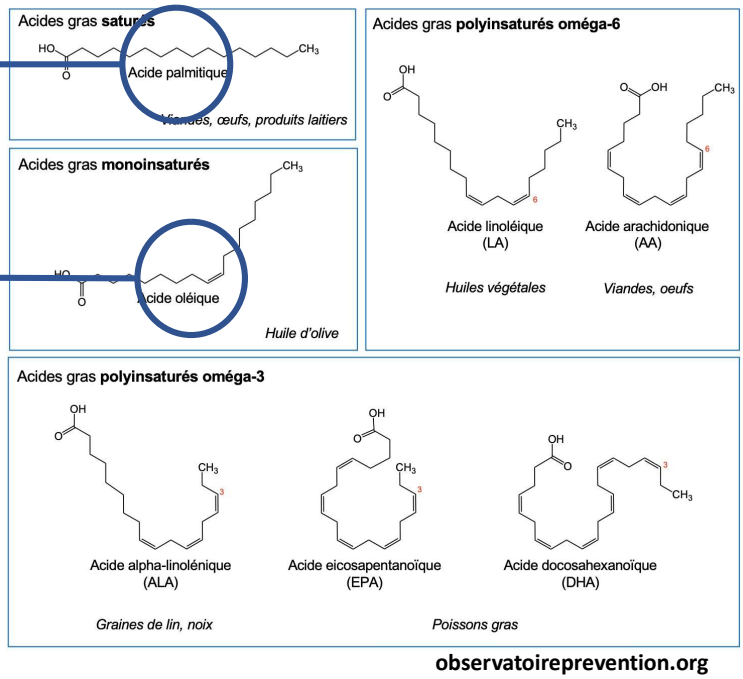
Contenu

7

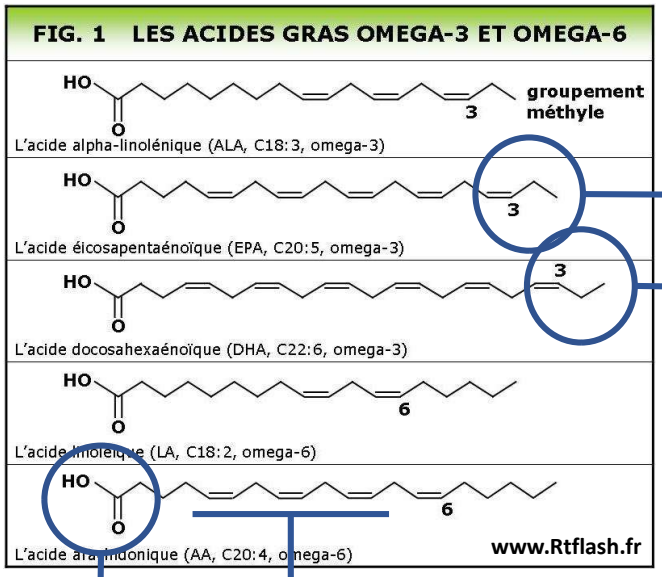
Saturé = non flexible

Insaturé = flexible

Un peu de chimie



8



ALA = source végétale (environ 5 à 10% de conversion en AEP/ADH)

AEP

ADH

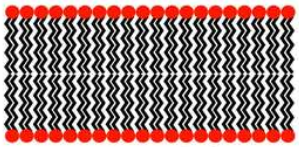
Les deux principaux oméga-3 sont essentiels et notre corps ne peut les synthétiser.

Un peu de chimie

Acide + Gras = un acide gras polyinsaturé

9

1- La fluidité membranaire



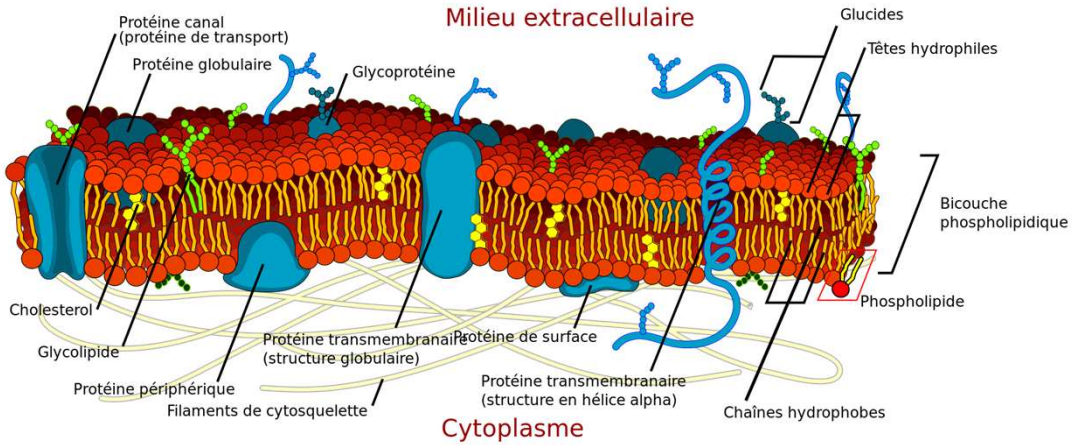
Membrane « figée »

Graisses saturées

Cela explique, par exemple, les effets bénéfiques des gras polyinsaturés sur la baisse du mauvais cholestérol sanguine par l'augmentation des récepteurs cellulaires au LDL (mauvais cholestérol; Kuo *et al*, 1990).

Powell *et al*, 2021.

10



Par LadyofHats Mariana Ruiz, traduction NicolasGrandjean — Traduction de File:Cell membrane detailed diagram en.svg. Image renamed from File:Diagrame détaillé membrane cellulaire.svg, Domaine public, https://commons.wikimedia.org/w/index.php?curid=6027270

La fluidité membranaire

Beaucoup de fonctions cellulaires qui peuvent être affectées par la fluidité des membranes: la disponibilité des récepteurs, l'influx nerveux, les échanges gazeux, l'apport en nutriment, la communication cellulaire, etc.

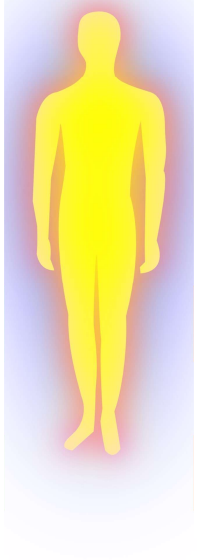
11

2- Le contrôle de l'inflammation

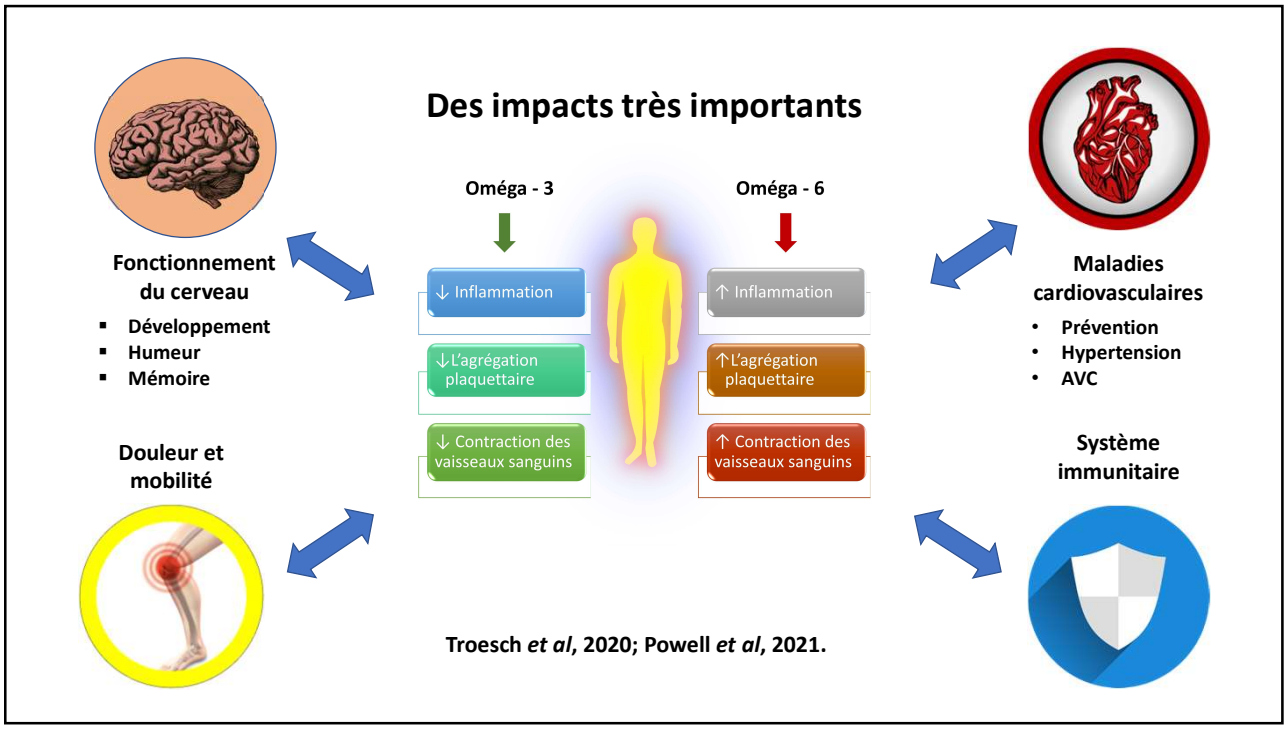
Dans le corps humain, les oméga-3 et les oméga-6 sont utilisés pour le contrôle de l'inflammation

Oméga - 3

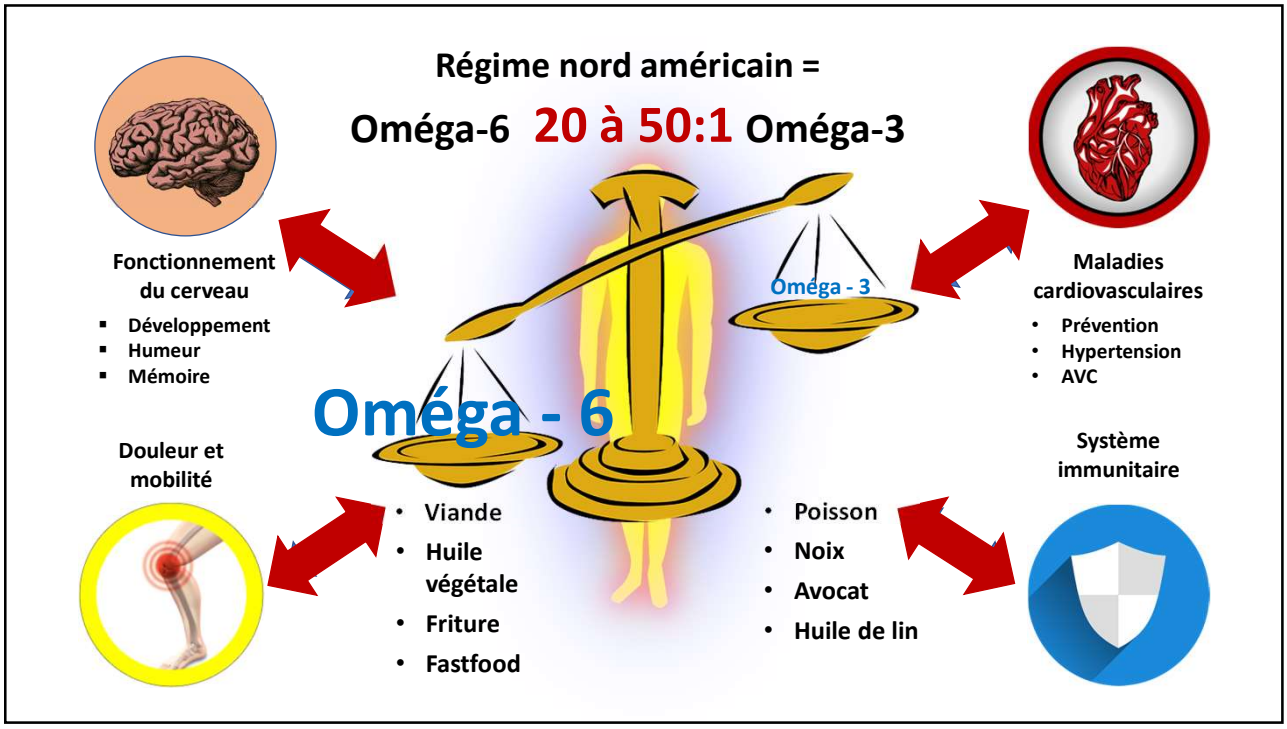
Oméga - 6



12


Des impacts très importants
Oméga - 3
Oméga - 6
↓ Inflammation
↓L'agrégation plaquettaire
↓ Contraction des vaisseaux sanguins
↑ Inflammation
↑L'agrégation plaquettaire
↑ Contraction des vaisseaux sanguins
Fonctionnement du cerveau
Développement
Humeur
Mémoire
Douleur et mobilité
Maladies cardiovasculaires
Prévention
Hypertension
AVC
Système immunitaire
Troesch et al, 2020; Powell et al, 2021.

13


Régime nord américain =
Oméga-6 20 à 50:1 Oméga-3
Fonctionnement du cerveau
Développement
Humeur
Mémoire
Douleur et mobilité
Maladies cardiovasculaires
Prévention
Hypertension
AVC
Système immunitaire
Oméga - 3
Oméga - 6
Viande
Huile végétale
Friture
Fastfood
Poisson
Noix
Avocat
Huile de lin

14

Oméga - 3 et santé humaine

- Plusieurs études sont négatives:

  N.B. ce n'est pas parce que ça ne peut pas complètement prévenir une condition ou une maladie qu'il n'y a pas un effet positif, significatif sur la santé.

  - Pour quelle population ?
  - Quelle dosage ?
  - Quelle application ?
  - Combien d'études ?
- Qu'en est-il de leur impact possible sur la longévité ?

15

LES TÉLOMÈRES

Des indicateurs très fiables de la durée de vie utile des cellules = plus tu es en santé, plus tes cellules peuvent durer longtemps, plus ils sont longs (Starkweather, et *al*. 2014).

- L'activité physique les rallonge.
- Le stress les raccourcis.
- La mauvaise alimentation les raccourcis.
- Ils raccourcissent en vieillissant.
- Les cellules meurent s'ils sont trop courts.
- La prise de suppléments d'oméga-3 les rallonge (amélioration de la santé des cellules: Sawan Ali *et al*, 2022).

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LES TÉLOMÈRES

- Supplément pour 6 à 12 mois.
- Personnes en santé ou non.
- La consommation d'**antioxydants** et la **réduction de l'inflammation** réduisent le raccourcissement des télomères.
- Ces mécanismes pourraient aussi expliquer les effets des oméga-3.

Research Article

Sawan Ali, Giovanni Scapagnini, and Sergio Davinelli*

Effect of omega-3 fatty acids on the telomere length: A mini meta-analysis of clinical trials

https://doi.org/10.1515/bmc-2021-0024
received December 17, 2021; accepted January 24, 2022

Abstract: Telomeres are protective caps at the end of eukaryotic chromosomes, whose length is correlated with health and lifespan. Telomere attrition is a common feature of the aging process and can be accelerated by oxidative stress and chronic inflammation. Various nutrients influence the telomere length, partially due to their antioxidant and anti-inflammatory properties. The aim of this review was to meta-analytically assess the effect of omega-3 fatty acids on the telomere length. We searched four databases (PubMed, Web of Sciences, Scopus, and the Cochrane Library) from inception until November 2021. Of 573 records, a total of 5 clinical trials were included for the quantitative meta-analysis, comprising a total of 337 participants. The results revealed an overall beneficial effect of omega-3 fatty acids on the telomere length (mean difference = 0.16; 95% CI, 0.02, 0.30; p = 0.02). Despite a limited number of studies, the available evidence suggests that omega-3 fatty acids may positively affect the telomere length. However, larger clinical trials are needed to confirm our findings, along with studies aimed to clarify the underlying molecular mechanisms.

Keywords: telomere, omega-3, PUFA, diet, meta-analysis

formed by proteins and repeated sequences of DNA (5′-TAGGG-3′) at the end of eukaryotic chromosomes. Together, telomeric DNA and telomeric proteins maintain the structural integrity of chromosomes, thus keeping genomic stability [4].

Telomeres are subject to shortening at each cycle of cell division, losing approximately 50-to 100 base pairs per mitotic division in human cells [5]. However, the rate of telomere loss is affected by numerous factors other than the mitotic replication rate. Oxidative stress and chronic low-grade inflammation (also known as inflammaging) are thought to be the major contributors to telomere shortening. Due to the high guanine-cytosine content, telomeres are extremely prone to oxidative damage compared to nontelomeric sequences. Likewise, the proinflammatory phenotype that accompanies aging in mammals is also linked to the onset of age-associated diseases and telomere shortening [6,7]. Additionally, extensive evidence supports that the telomere length (TL) is a dynamic trait sensitive to environmental factors. An accelerated telomere shortening has been associated with smoking, air pollution, excessive food intake, and psychological stress. Exposure to these factors may promote telomere attrition by increasing oxidative stress and inflammation [8–10].

Although the association between diet and telomere maintenance is currently under investigation, recent

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International Journal of Environmental Research and Public Health

MDPI

Article

Relationships among Environment, Climate, and Longevity in China

Yi Huang [1,2,*], Mark Rosenberg [2], Lingli Hou [1] and Mengjin Hu [1]

[1] School of Geographic Science, Nantong University, Nantong 226007, China; ntugeo@sina.com (L.H.); tinyyellowfish@sina.com (M.H.)
[2] Department of Geography and Planning, Queen's University, Kingston, ON K7L 3N6, Canada; rosenber@queensu.ca
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Received: 2 September 2017; Accepted: 6 October 2017; Published: 8 October 2017

Abstract: Human longevity is influenced by environment and nutrition. We considered environmental and nutritional factors relating to longevity in Chinese cities. We found higher 85+/65+ distribution ratios, indicating enhanced longevity, in the coastal and southern regions of China. These areas also featured higher humidity, low standard deviation of monthly temperature, higher levels of selenium (Se) distribution in soil, and greater sea fish consumption. Moderate climate is more conducive to longevity, however, there is no significant difference in longevity between different sub-climatic types within moderate climate; the relation between humidity and longevity is not always positive, the relation between altitude and longevity is not always negative. Nutritional factors like Se and omega-3 fatty acids contained in sea fish were crucial to longevity. In contrast, the consumption of meat and freshwater fish were less related to longevity. Taken together, humidity, altitude, and per capita sea fish consumption, when evaluated via geographically weighted regression, explained 66% and 68% of longevity among Chinese individuals in 2000 and 2010, respectively. Other factors require further discussion.

Keywords: longevity; selenium; omega-3; sea fish; altitude; climate

Longévité en Chine

- Corrélation avec l'altitude, l'humidité, la consommation de sélénium (sol) et la consommation d'oméga-3 (poissons de la mer).
- 3 à 10 consommations par mois vs 1 consommation ou moins pour les personnes éloignées du bord de la mer.

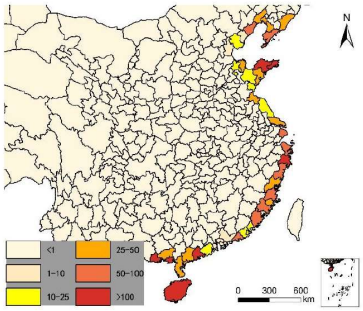

Figure 11. Per capita sea fishing of each city in China in 2016 (kg).

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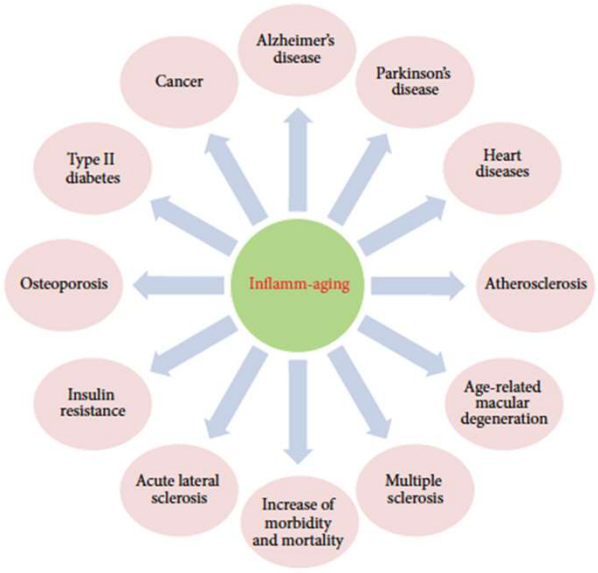

FIGURE 1: The relationship between inflamm-aging and diseases.

VIEILLISSEMENT

L'inflammation est impliquée dans l'incidence ou le développement d'un grand nombre de maladies.

Xia et al. *J Immunol Res*. 2016.

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VIEILLISSEMENT

La consommation d'oméga-3 réduirait certains impacts du vieillissement, mais aussi, certains processus par la modification de l'expression des gènes. La composition du microbiote influencerait cet effet bénéfique.

genes

MDPI

Article

Multi-Omics Interpretation of Anti-Aging Mechanisms for ω-3 Fatty Acids

Shu-Hui Xie [1,†], Hui Li [1,†], Jing-Jing Jiang [1], Yuan Quan [2,*] and Hong-Yu Zhang [2]

[1] College of Informatics, Huazhong Agricultural University, Wuhan 430070, China; xieshuhui@webmail.hzau.edu.cn (S.-H.X.); lihui2611@webmail.hzau.edu.cn (H.L.); jiangjj@webmail.hzau.edu.cn (J.-J.J.)
[2] Hubei Key Laboratory of Agricultural Bioinformatics, College of Informatics, Huazhong Agricultural University, Wuhan 430070, China; zhy630@mail.hzau.edu.cn
* Correspondence: quanyuan@mail.hzau.edu.cn; Tel.: +86-180-6242-5336
† These authors contributed equally.

Abstract: Aging is one of the hottest topics in biomedicine. Previous research suggested that ω-3 fatty acids have preventive effects on aging. However, most of previous studies on the anti-aging effects of ω-3 fatty acids are focused on clinical observations, and the anti-aging mechanisms of ω-3 fatty acids have not been fully elucidated. This stimulated our interest to use multi-omics data related to ω-3 fatty acids in order to interpret the anti-aging mechanisms of ω-3 fatty acids. First, we found that ω-3 fatty acids can affect methylation levels and expression levels of genes associated with age-related diseases or pathways in humans. Then, a Mendelian randomization analysis was conducted to determine whether there is a causal relationship between the effect of ω-3 fatty acids on blood lipid levels and variation in the gut microbiome. Our results indicate that the impact of ω-3 fatty acids on aging is partially mediated by the gut microbiome (including *Actinobacteria*, *Bifidobacteria* and *Streptococcus*). In conclusion, this study provides deeper insights into the anti-aging mechanisms of ω-3 fatty acids and supports the dietary supplementation of ω-3 fatty acids in aging prevention.

Keywords: ω-3 fatty acids; aging; methylation; Mendelian randomization; gut microbiome

check for updates

Citation: Xie, S.-H.; Li, H.; Jiang, J.-J.; Quan, Y.; Zhang, H.-Y. Multi-Omics Interpretation of Anti-Aging Mechanisms for ω-3 Fatty Acids. *Genes* **2021**, *12*, 1691. https://doi.org/10.3390/genes12111691

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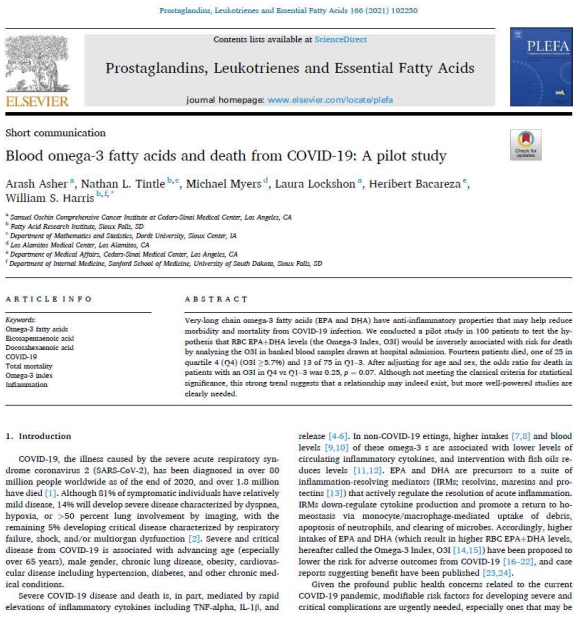
Covid-19 ?

Impacts sur les risques d'infection

Effets des niveaux d'oméga-3 chez les gens atteints de la Covid: le risque relatif de décès (OR) est **4 fois plus élevé** chez les personnes ayant un index omega-3 faible.



Prostaglandins, Leukotrienes and Essential Fatty Acids 166 (2021) 102250

Contents lists available at ScienceDirect

Prostaglandins, Leukotrienes and Essential Fatty Acids

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

Short communication

Blood omega-3 fatty acids and death from COVID-19: A pilot study

Arash Asher [a], Nathan L. Tintle [b,c], Michael Myers [d], Laura Lockshon [a], Heribert Bacareza [e], William S. Harris [b,f,*]

[a] Samuel Oschin Comprehensive Cancer Institute at Cedars-Sinai Medical Center, Los Angeles, CA
[b] Fatty Acid Research Institute, Sioux Falls, SD
[c] Department of Mathematics and Statistics, Dordt University, Sioux Center, IA
[d] Los Alamitos Medical Center, Los Alamitos, CA
[e] Department of Medical Affairs, Cedars-Sinai Medical Center, Los Angeles, CA
[f] Department of Internal Medicine, Sanford School of Medicine, University of South Dakota, Sioux Falls, SD

ARTICLE INFO

Keywords:
Omega-3 fatty acids
Eicosapentaenoic acid
Docosahexaenoic acid
COVID-19
Total mortality
Omega-3 index
Inflammation

ABSTRACT

Very-long chain omega-3 fatty acids (EPA and DHA) have anti-inflammatory properties that may help reduce morbidity and mortality from COVID-19 infection. We conducted a pilot study in 100 patients to test the hypothesis that RBC EPA+DHA levels (the Omega-3 Index, O3I) would be inversely associated with risk for death by analyzing the O3I in banked blood samples drawn at hospital admission. Fourteen patients died, one of 25 in quartile 4 (Q4) (O3I ≥5.7%) and 13 of 75 in Q1–3. After adjusting for age and sex, the odds ratio for death in patients with an O3I in Q4 vs Q1–3 was 0.25, $p = 0.07$. Although not meeting the classical criteria for statistical significance, this strong trend suggests that a relationship may indeed exist, but more well-powered studies are clearly needed.

1. Introduction

COVID-19, the illness caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has been diagnosed in over 80 million people worldwide as of the end of 2020, and over 1.8 million have died [1]. Although 81% of symptomatic individuals have relatively mild disease, 14% will develop severe disease characterized by dyspnea, hypoxia, or >50 percent lung involvement by imaging, with the remaining 5% developing critical disease characterized by respiratory failure, shock, and/or multiorgan dysfunction [2]. Severe and critical disease from COVID-19 is associated with advancing age (especially over 65 years), male gender, chronic lung disease, obesity, cardiovascular disease including hypertension, diabetes, and other chronic medical conditions.

Severe COVID-19 disease and death is, in part, mediated by rapid elevations of inflammatory cytokines including TNF-alpha, IL-1β, and release [4-6]. In non-COVID-19 ettings, higher intakes [7,8] and blood levels [9,10] of these omega-3 s are associated with lower levels of circulating inflammatory cytokines, and intervention with fish oils reduces levels [11,12]. EPA and DHA are precursors to a suite of inflammation-resolving mediators (IRMs; resolvins, maresins and protectins [13]) that actively regulate the resolution of acute inflammation. IRMs down-regulate cytokine production and promote a return to homeostasis via monocyte/macrophage-mediated uptake of debris, apoptosis of neutrophils, and clearing of microbes. Accordingly, higher intakes of EPA and DHA (which result in higher RBC EPA+DHA levels, hereafter called the Omega-3 Index, O3I [14,15]) have been proposed to lower the risk for adverse outcomes from COVID-19 [16–22], and case reports suggesting benefit have been published [23,24].

Given the profound public health concerns related to the current COVID-19 pandemic, modifiable risk factors for developing severe and critical complications are urgently needed, especially ones that may be

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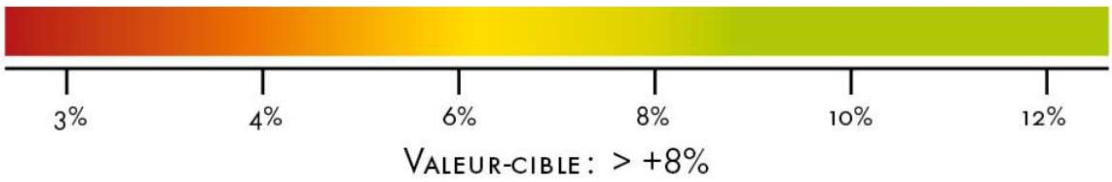
L' **index omega-3**

% des omega-3 à chaine longue dans les membranes des érythrocytes



- ≥ 8 à 12 % donne le plus de protection (cardiovasculaire).
- ≤ 4% donne le moins de protection (Harris et Von Schacky, 2004. Harris, 2010. Harris *et al*, 2017.)

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L'index omega-3

- Taux moyen: 4,5% (Canada)
- 2,6% des canadiens ≥ 8% (protecteur)
- 43% des canadiens ≤ 4% (risque élevé)

N.B. Manger du poisson gras ≥ 3 portions par semaine **+ des suppléments** = index ≥ 8%

Prévention ou dosage thérapeutique ?

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Dosages thérapeutiques* : ≥ 1800 mg/j

*Institut de cardiologie de Montréal.

- Oméga-3 : **1000mg ou plus d'huile par capsule**
  - 18/12: 180mg AEP / 120mg ADH = 30% d'oméga-3
  - 30/20: 300mg AEP / 200mg ADH = 50% d'oméga-3
  - 40/20: 400mg AEP / 200mg ADH = 60% d'oméga-3
  - 90% : 600mg AEP / 300mg ADH = 90% d'oméga-3
- Purifés dissociés
  - 5/1: 665mg AEP / 133mg ADH (AEP et ADH)
  - 7/1 : 350mg AEP / 50mg ADH = OM3
  - 20/1: 500mg AEP / 25mg ADH = JOY
- ↑ EPA = inflammation, cardio, articulation, dépression.
- ↑ ADH = santé cognitive, grossesse, focus et capacités mentales.

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Contenu

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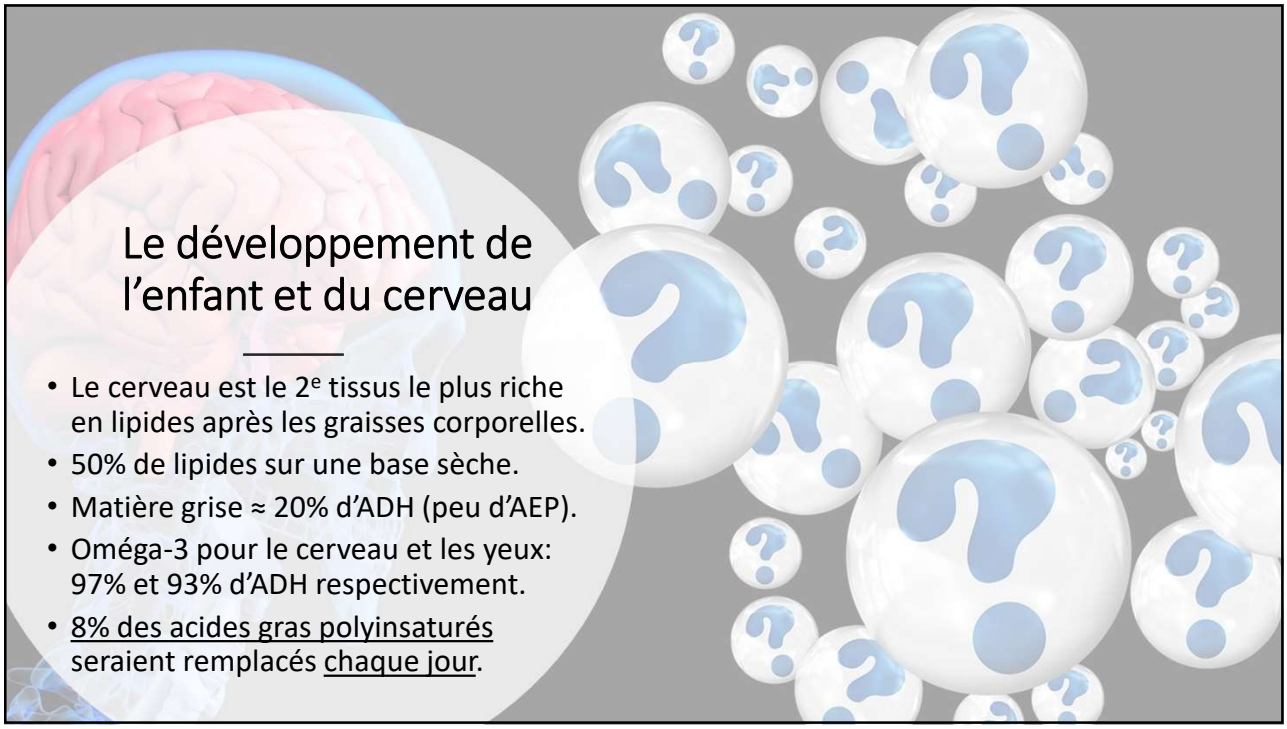

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LE DÉVELOPPEMENT DU CERVEAU

- Les oméga-3 sont essentiels au développement du cerveau.
- La consommation des parents, durant le développement du fœtus et durant l'enfance, influence l'épigénétique du vieillissement.

Current Nutrition Reports
https://doi.org/10.1007/s13668-022-00402-7

MATERNAL AND CHILDHOOD NUTRITION (AC WOOD, SECTION EDITOR)

Epigenetic Aging in Early Life: Role of Maternal and Early Childhood Nutrition

Nicholas A. Koemel[1,2] · Michael R. Skilton[1,2,3]

Accepted: 5 February 2022

Abstract
Purpose of Review Early life presents a pivotal period during which nutritional exposures are more likely to cause epigenetic modifications, which may impact an individual's health during adulthood. This article reviews the current evidence regarding maternal and early childhood nutritional exposures and their role in epigenetic aging.
Recent Findings Maternal and early life consumption of diets higher in fiber, antioxidants, polyphenols, B vitamins, vitamin D, and ω-3 fatty acids is associated with slower epigenetic aging. Conversely, diets higher in glycemic load, fat, saturated fat, and ω-6 fatty acids demonstrate a positive association with epigenetic aging.
Summary Maternal and early life nutrition directly and indirectly influences epigenetic aging via changes in one-carbon metabolism, cardiometabolic health, and the microbiome. Clinical trials are warranted to determine the specific foods, dietary patterns, and dietary supplements that will normalize or lower epigenetic aging across the life course.

Keywords Maternal diet · Epigenetics · Early life · Childhood nutrition · Aging · Developmental Origins of Health and Disease (DOHaD)

Introduction

The Barker hypothesis, now more frequently referred to as the Developmental Origins of Health and Disease (DOHaD), originated from epidemiological evidence published in the long-term effects of early life exposures, including the role of maternal diet in fetal development and health and disease in later life [2]. Fetal epigenetic modifications may play an important role as a mechanism that links maternal nutrition with both fetal development and long-term health outcomes

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ELSEVIER
Pharmacological Research
Volume 177, March 2022, 106100

Review

The effects of omega-3 polyunsaturated fatty acids supplementation in pregnancy, lactation, and infancy: An umbrella review of meta-analyses of randomized trials

Fatemeh Dehghani Firouzabadi, Sakineh Shab-Bidar, Ahmad Jayedi

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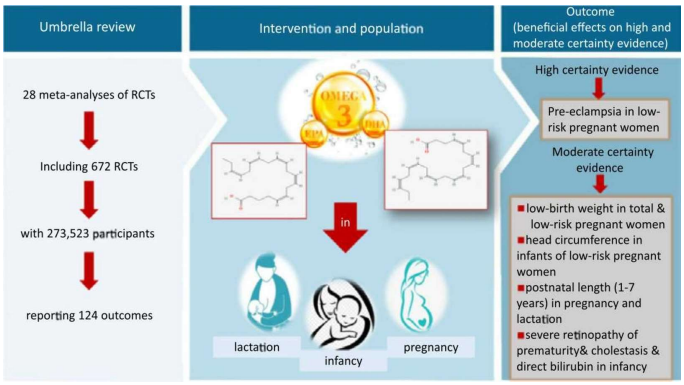
https://doi.org/10.1016/j.phrs.2022.106100 Get rights and content

Abstract

We aimed to perform an umbrella review of systematic reviews and meta-analyses (SRMAs) of randomized clinical trials (RCT) of the effects of long-chain omega-3 fatty acid supplementation in pregnancy, lactation, and infancy. We searched PubMed, Scopus, and Web of Science to November 2020. Two independent investigators extracted the information, evaluated the methodological quality of SRMAs using A Measurement Tool to Assess Systematic Reviews-2 (AMSTAR2), and rated the certainty of evidence using the Grades of Recommendation, Assessment, Development and Evaluation (GRADE) approach. Either a fixed-effects or a random-effects model was used to recalculate the effect sizes and 95%CIs, depending on the number of trials. Overall, 28 SRMAs of RCTs, reporting 124 outcomes from 672 RCTs with 273,523 participants were considered eligible for the present umbrella review. Our results demonstrated evidence of moderate to high certainty that

Oméga-3 et développement: revue globale.

- Analyses systématiques et méta-analyses.
- 28 méta-analyses; 672 études cliniques.
- 273 523 participants.



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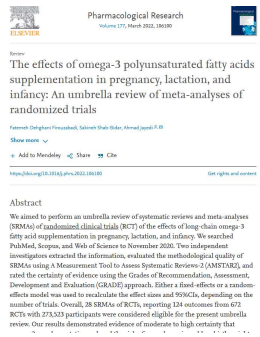
Oméga-3 et développement: revue globale.

- Évidences modérées à élevées:
  - ↓ les risques de prééclampsie ,
  - ↓ les risques d'une naissance à faible poids,
  - ↑ de la circonférence de la tête (lorsque pris durant la grossesse).
  - ↓ rétinopathie sévère du prématuré,
  - ↓ cholestase (bile) (lorsqu'il est utilisé dans la petite enfance).

Haute pression durant la grossesse = ↑ risques complications, fausses couches et accouchement prématurée (3 à 7%).


Pharmacological Research

The effects of omega-3 polyunsaturated fatty acids supplementation in pregnancy, lactation, and infancy: An umbrella review of meta-analyses of randomized trials

Abstract

We aimed to perform an umbrella review of systematic reviews and meta-analyses (SRMAs) of randomized clinical trials (RCT) of the effects of long-chain omega-3 fatty acid supplementation in pregnancy, lactation, and infancy. We searched PubMed, Scopus, and Web of Science to November 2020. Two independent investigators extracted the information, evaluated the methodological quality of SRMAs using A Measurement Tool to Assess Systematic Reviews-2 (AMSTAR2), and rated the certainty of evidence using the Grades of Recommendation, Assessment, Development and Evaluation (GRADE) approach. Either a fixed-effects or a random-effects model was used to recalculate the effect sizes and 95%CIs, depending on the number of trials. Overall, 28 SRMAs of RCTs, reporting 124 outcomes from 672 RCTs with 273,323 participants were considered eligible for the present umbrella review. Our results demonstrated evidence of moderate to high certainty that

Firouzabadi *et al*, 2022.

- Effets favorables sur:
  - risques de naissance prématurée (1000 mg AEP/ADH /jour à partir de 20 semaines de grossesse; Best *et al*, 2022),
  - dépression durant ou après la grossesse,
  - contrôle de la glycémie et de l'inflammation pour la femme enceinte,
  - le système immunitaire (allergies) et la capacité visuelle chez l'enfant.

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LA VISION

- Le rôle de l'ADH dans la réduction de l'oxydation et la protection de la vision a été étudié dans différents types de modèles, particulièrement pour la rétinopathie diabétique proliférative, pour la dégénérescence maculaire et le glaucome.
- Des doses élevées d'ADH sont nécessaires pour permettre des bénéfices (≥**1050 mg/j**).


antioxidants

MDPI

Review

Antioxidant Activity and Neuroprotective Role of Docosahexaenoic Acid (DHA) Supplementation in Eye Diseases That Can Lead to Blindness: A Narrative Review

María Lafuente [1,*], María Elena Rodríguez González-Herrero [1], Stéphanie Romeo Villadóniga [2] and Joan Carles Domingo [3]

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Abstract: The objective of this narrative review is to provide updated evidence, based on data from experimental and clinical studies, of the prominent role of omega-3 polyunsaturated fatty acids (n-3 PUFAs) for a number of crucial mechanisms involved in counteracting cell damage induced by oxidative stress in eye diseases. This article is focused on the antioxidant and neuroprotective effects of docosahexaenoic acid (DHA), which have been assessed in different experimental models and clinical studies, particularly in proliferative diabetic retinopathy, age-related macular degeneration and glaucoma that are the most common eye diseases leading to severe vision loss. The mechanisms involved in the role of DHA in protecting human retinal pigment epithelial cells from oxidative stress as well as the interaction with glutathione (GSH) are also described. The review is intended to provide novel and salient findings supporting the rationale of the use of dietary supplementation with high-dose DHA (1050 mg/day) in the form of triglyceride as a potent antioxidant compound for improving the eye health. However, the overall clinical evidence for the use of dietary strategies based on supplementation with n-3 PUFAs in eye diseases linked to oxidative stress other than high-dose DHA triglyceride is both limited and inconsistent.

Keywords: omega-3 fatty acids; docosahexaenoic acid; glutathione; diabetic macular edema; glaucoma; oxidative stress; eye health

check for updates

Citation: Lafuente, M.; Rodríguez González-Herrero, M.E.; Romeo Villadóniga, S.; Domingo, J.C. Antioxidant Activity and Neuroprotective Role of Docosahexaenoic Acid (DHA) Supplementation in Eye Diseases That Can Lead to Blindness: A Narrative Review. *Antioxidants* **2021**, *10*, 386. https://doi.org/10.3390/antiox10030386

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Published: 5 March 2021

1. Introduction

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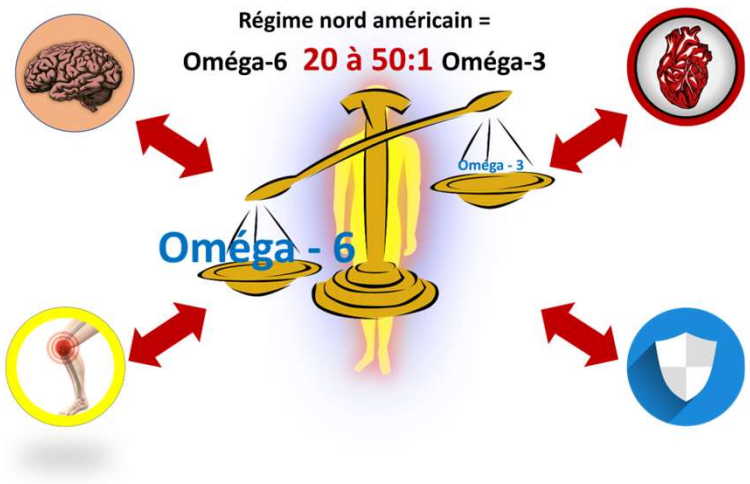
LE DÉVELOPPEMENT: LES ALLERGIES

- Les allergies sont une réaction inflammatoire.
- Les oméga-3 pourraient protéger du développement des allergies, mais aussi réduire l'intensité des réactions.
- La consommation durant la grossesse réduirait les allergies.

Miles et Calder, 2017.



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Contenu

1. Les fonctions biologiques des oméga-3 (17)
2. Le développement de l'enfant et du cerveau (6)
3. **L'inflammation** **(4)**
4. La santé cardiovasculaire (8)
5. L'état d'esprit et la santé cognitive (3)
6. Les contre-indications (2)

32

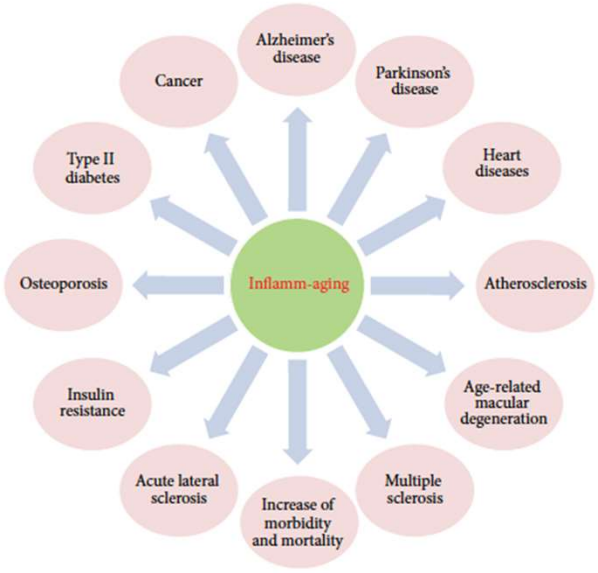
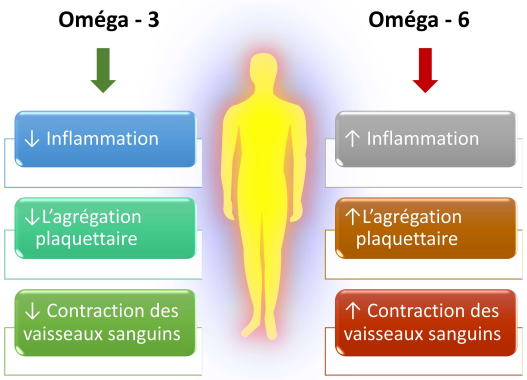


FIGURE 1: The relationship between inflamm-aging and diseases.

Xia et al. *J Immunol Res.* 2016.



L'inflammation joue un rôle central dans l'incidence et/ou le développement d'un grand nombre de maladies. L'équilibre oméga-6/oméga-3 est essentiel à la gestion de l'inflammation.

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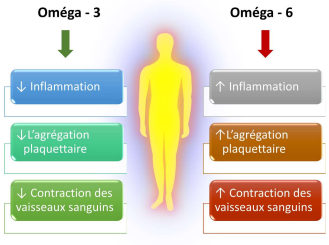
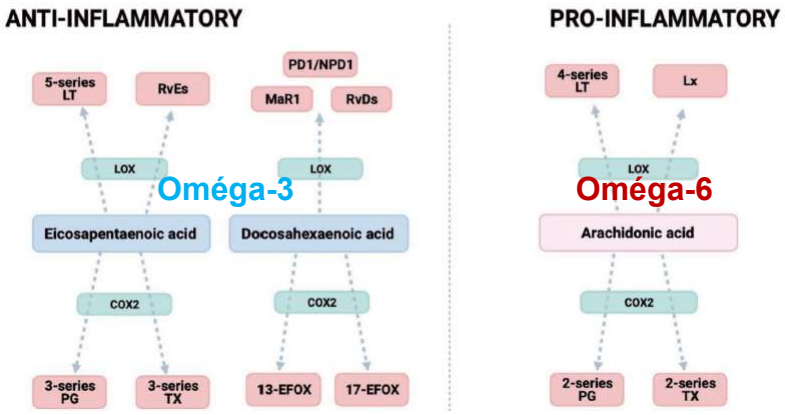


''Proresolving mediator'': lipoxins (oméga-6), resolvins, protectins, and maresins (omega-3).



Tung et al, 2021; Molfino et al, 2017.

Les oméga-3 servent à produire les molécules anti-inflammatoires et les oméga-6, les molécules pro-inflammatoires. <u>Un sain équilibre assure une meilleure gestion</u>.

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Sigaux et al. Arthritis Research & Therapy (2022) 24:100
https://doi.org/10.1186/s13075-022-02781-2

Arthritis Research & Therapy

RESEARCH ARTICLE Open Access

Impact of type and dose of oral polyunsaturated fatty acid supplementation on disease activity in inflammatory rheumatic diseases: a systematic literature review and meta-analysis

Johanna Sigaux[†*], Sylvain Mathieu[†], Yann Nguyen[1], Pauline Sanchez[2], Jean-Guillaume Letarouilly[2], Martin Soubrier[3], Sébastien Czernichow[4,7], René-Marc Flipo[5], Jérémie Sellam[6] and Claire Dalen[4]

Abstract

Background: Polyunsaturated fatty acid (PUFA) supplementation has been reported to improve disease activity in inflammatory rheumatic diseases (IRDs). However, data are often conflicting and studies insufficiently large to draw conclusions. This systematic literature review and meta-analysis aimed to better estimate the effect of oral supplementation with omega (n)-3 and n-6 PUFA on IRD activity in terms of duration, dose, type, and source.

Methods: The literature was searched in PubMed, EMBASE, and Cochrane Library databases up to October 2020. Studies were reviewed in accordance with PRISMA guidelines. The effect of PUFA supplementation on disease activity was expressed as the standardized mean difference (95% CI). Metaregression and subgroup analyses involved type of IRD, Jadad score, PUFA source (animal or vegetable), and doses.

Results: We obtained 42 references; 30 randomized controlled studies were included comparing the effects of PUFA versus control on disease activity (710 IRD patients receiving PUFA supplementation and 710 controls, most with rheumatoid arthritis). We found a significant improvement in pain, swollen and tender joint count, Disease Activity Score in 28 joints, and Health Assessment Questionnaire score in IRD patients receiving PUFA supplementation as compared with controls, with a significant decrease in erythrocyte sedimentation rate but not C-reactive protein level. Although meta-regression revealed no difference by IRD type or source or dose of PUFA supplementation, subgroup analysis revealed more parameters significantly improved with animal- than vegetable-derived PUFAs and 3- to 6-month supplementation. Most studies examined high-dose supplementation (>2 g/day).

Conclusion: PUFA consumption, especially omega-3 from animal source >2 g/day, may improve IRD activity and might be an adjuvant therapy in rheumatoid arthritis.

Trial registration: The protocol was registered at PROSPERO (CRD42021253685).

† Johanna Sigaux and Sylvain Mathieu contributed equally to this work.
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Full list of author information is available at the end of the article

Oméga-3 et maladies rhumatoïdes inflammatoires.

- Analyses systématiques et méta-analyses.
- 30 études cliniques, 1420 participants.
- 3 à 6 mois.
- **Dose thérapeutique ≥ 2000 mg/j.**
- Effets significatifs comparés au placébo sur:
  - le nombre d'articulations douloureuses, enflées et sensibles,
  - le niveau d'activité de la maladie (évaluation pour 28 articulations) et
  - les résultats du questionnaire d'évaluation de la santé.
- Meilleur impact des oméga-3 de poisson.

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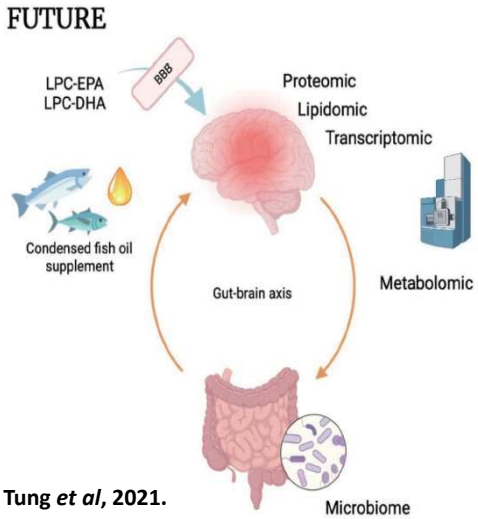

Tung *et al*, 2021.

nutrients

MDPI

Review

The Potential Effects of Probiotics and ω-3 Fatty Acids on Chronic Low-Grade Inflammation

Ashley N. Hutchinson [1,*,†], Lina Tingö [1,2,†] and Robert Jan Brummer [1]

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Abstract: Chronic low-grade inflammation negatively impacts health and is associated with aging and obesity, among other health outcomes. A large number of immune mediators are present in the digestive tract and interact with gut bacteria to impact immune function. The gut microbiota itself is also an important initiator of inflammation, for example by releasing compounds such as lipopolysaccharides (LPS) that may influence cytokine production and immune cell function. Certain nutrients (e.g., probiotics, ω-3 fatty acids [FA]) may increase gut microbiota diversity and reduce inflammation. *Lactobacilli* and *Bifidobacteria*, among others, prevent gut hyperpermeability and lower LPS-dependent chronic low-grade inflammation. Furthermore, ω-3 FA generate positive effects on inflammation-related conditions (e.g., hypertriglyceridemia, diabetes) by interacting with immune, metabolic, and inflammatory pathways. Ω-3 FA also increase LPS-suppressing bacteria (i.e., *Bifidobacteria*) and decrease LPS-producing bacteria (i.e., *Enterobacteria*). Additionally, ω-3 FA appear to promote short-chain FA production. Therefore, combining probiotics with ω-3 FA presents a promising strategy to promote beneficial immune regulation via the gut microbiota, with potential beneficial effects on conditions of inflammatory origin, as commonly experienced by aged and obese individuals, as well as improvements in gut-brain-axis communication.

Keywords: probiotics; omega-3 (ω-3) fatty acids; inflammation; gut microbiota; gut-brain axis; dysbiosis

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Contenu

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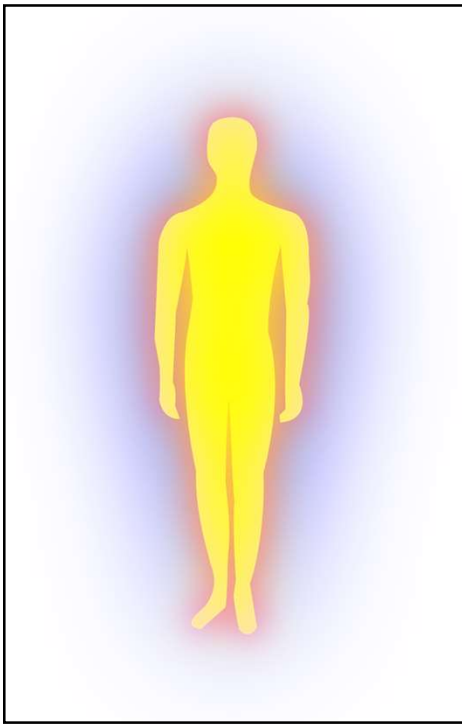

Oméga - 3 et santé cardiovasculaire

- Plusieurs études sont négatives ?
  - Quels dosages ont été testés ?
  - Durant combien de temps ?
  - N.B. La vaste majorité de la population nord-américaine est en mauvaise santé métabolique (88%: Araújo *et al*, 2019.). Est-ce que juste la prise d'oméga-3 peut empêcher un décès ? **NON**
  - Est-ce que la prise d'oméga-3 peut aider à la santé cardiovasculaire ? **OUI**

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Oméga - 3 et santé cardiovasculaire: 3 études éloquentes

- Burr et al, 1989 - 2033 hommes victimes d'un infarctus récent:
  - 2 ans de suivi,
  - **↓ 29% de la mortalité** comparativement au groupe placébo.
- Anon, 1999 - 11 324 patients victimes d'un infarctus récent :
  - 1 gr/j d'oméga-3 en suppléments
  - 3 ½ de suivi = mort, infarctus ou accident vasculaire cérébral.
  - Après 1 an en comparant avec le groupe placébo:
    - **↓ 15 %** de l'ensemble des incidents suivis,
    - **↓ 45% de la mortalité** cardiaque subite.
- Yokohama et al, 2007 – 18 645 patients en hypercholestérolémie:
  - EPA + statines ou juste statines
  - Après en moyenne 4,6 ans = **↓ 19% des événements** cardiovasculaires majeurs.

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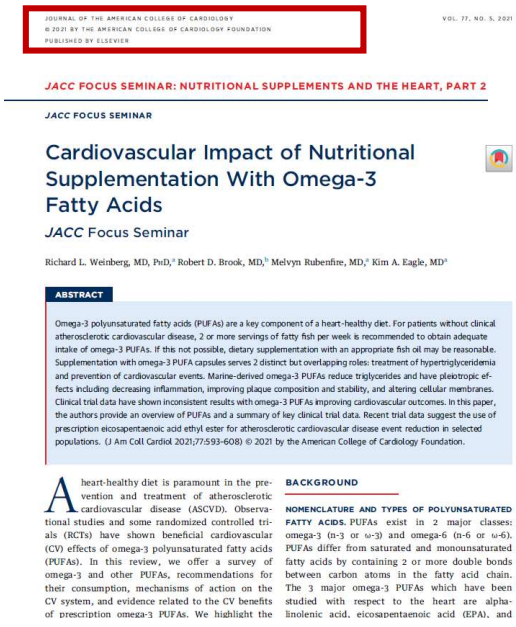
Omega-3 et santé cardiovasculaire

Journal du collège américain de cardiologie



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VOL. 77, NO. 5, 2021

JACC FOCUS SEMINAR: NUTRITIONAL SUPPLEMENTS AND THE HEART, PART 2

JACC FOCUS SEMINAR

Cardiovascular Impact of Nutritional Supplementation With Omega-3 Fatty Acids

JACC Focus Seminar

Richard L. Weinberg, MD, PhD,[a] Robert D. Brook, MD,[b] Melvyn Rubenfire, MD,[c] Kim A. Eagle, MD[a]

ABSTRACT

Omega-3 polyunsaturated fatty acids (PUFAs) are a key component of a heart-healthy diet. For patients without clinical atherosclerotic cardiovascular disease, 2 or more servings of fatty fish per week is recommended to obtain adequate intake of omega-3 PUFAs. If this not possible, dietary supplementation with an appropriate fish oil may be reasonable. Supplementation with omega-3 PUFA capsules serves 2 distinct but overlapping roles: treatment of hypertriglyceridemia and prevention of cardiovascular events. Marine-derived omega-3 PUFAs reduce triglycerides and have pleiotropic effects including decreasing inflammation, improving plaque composition and stability, and altering cellular membranes. Clinical trial data have shown inconsistent results with omega-3 PUFAs improving cardiovascular outcomes. In this paper, the authors provide an overview of PUFAs and a summary of key clinical trial data. Recent trial data suggest the use of prescription eicosapentaenoic acid ethyl ester for atherosclerotic cardiovascular disease event reduction in selected populations. (J Am Coll Cardiol 2021;77:593-608) © 2021 by the American College of Cardiology Foundation.

BACKGROUND

A heart-healthy diet is paramount in the prevention and treatment of atherosclerotic cardiovascular disease (ASCVD). Observational studies and some randomized controlled trials (RCTs) have shown beneficial cardiovascular (CV) effects of omega-3 polyunsaturated fatty acids (PUFAs). In this review, we offer a survey of omega-3 and other PUFAs, recommendations for their consumption, mechanisms of action on the CV system, and evidence related to the CV benefits of prescription omega-3 PUFAs. We highlight the

NOMENCLATURE AND TYPES OF POLYUNSATURATED FATTY ACIDS. PUFAs exist in 2 major classes: omega-3 (n-3 or ω-3) and omega-6 (n-6 or ω-6). PUFAs differ from saturated and monounsaturated fatty acids by containing 2 or more double bonds between carbon atoms in the fatty acid chain. The 3 major omega-3 PUFAs which have been studied with respect to the heart are alpha-linolenic acid, eicosapentaenoic acid (EPA), and

Points forts:

- La supplémentation en oméga-3 peut réduire le risque de maladie CV chez certains patients.
- Les oméga-3 à des doses de **2 à 4 g/j** ↓ les triglycérides sanguins de **25% à 40%.**
- Les effets des oméga-3, autres que la baisse des triglycérides, peuvent contribuer à leurs avantages cardiovasculaires.

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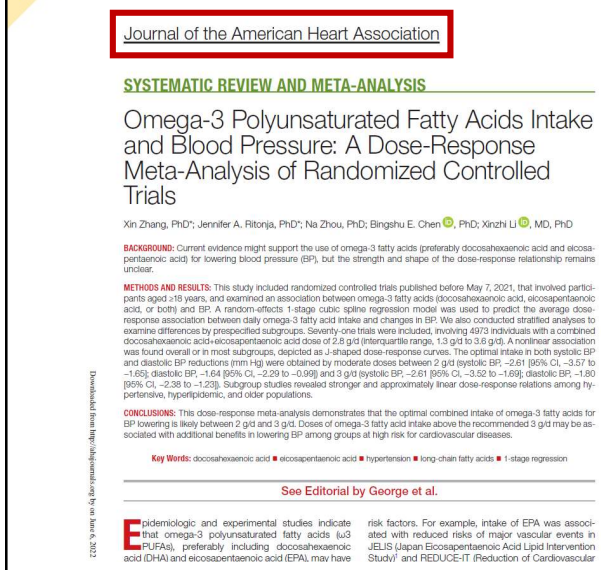

Journal of the American Heart Association

SYSTEMATIC REVIEW AND META-ANALYSIS

Omega-3 Polyunsaturated Fatty Acids Intake and Blood Pressure: A Dose-Response Meta-Analysis of Randomized Controlled Trials

Xin Zhang, PhD*; Jennifer A. Ritonja, PhD*; Na Zhou, PhD; Bingshu E. Chen, PhD; Xinzhi Li, MD, PhD

BACKGROUND: Current evidence might support the use of omega-3 fatty acids (preferably docosahexaenoic acid and eicosapentaenoic acid) for lowering blood pressure (BP), but the strength and shape of the dose-response relationship remains unclear.

METHODS AND RESULTS: This study included randomized controlled trials published before May 7, 2021, that involved participants aged ≥18 years, and examined an association between omega-3 fatty acids (docosahexaenoic acid, eicosapentaenoic acid, or both) and BP. A random-effects 1-stage cubic spline regression model was used to predict the average dose-response association between daily omega-3 fatty acid intake and changes in BP. We also conducted stratified analyses to examine differences by prespecified subgroups. Seventy-one trials were included, involving 4973 individuals with a combined docosahexaenoic acid+eicosapentaenoic acid dose of 2.8 g/d (interquartile range, 1.3 g/d to 3.6 g/d). A nonlinear association was found overall or in most subgroups, depicted as J-shaped dose-response curves. The optimal intake in both systolic BP and diastolic BP reductions (mm Hg) were obtained by moderate doses between 2 g/d (systolic BP, −2.61 [95% CI, −3.57 to −1.65]; diastolic BP, −1.64 [95% CI, −2.29 to −0.99]) and 3 g/d (systolic BP, −2.61 [95% CI, −3.52 to −1.69]; diastolic BP, −1.80 [95% CI, −2.38 to −1.23]). Subgroup studies revealed stronger and approximately linear dose-response relations among hypertensive, hyperlipidemic, and older populations.

CONCLUSIONS: This dose-response meta-analysis demonstrates that the optimal combined intake of omega-3 fatty acids for BP lowering is likely between 2 g/d and 3 g/d. Doses of omega-3 fatty acid intake above the recommended 3 g/d may be associated with additional benefits in lowering BP among groups at high risk for cardiovascular diseases.

Key Words: docosahexaenoic acid ■ eicosapentaenoic acid ■ hypertension ■ long-chain fatty acids ■ 1-stage regression

See Editorial by George et al.

Epidemiologic and experimental studies indicate that omega-3 polyunsaturated fatty acids (ω3 PUFAs), preferably including docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA), may have risk factors. For example, intake of EPA was associated with reduced risks of major vascular events in JELIS (Japan Eicosapentaenoic Acid Lipid Intervention Study)[1] and REDUCE-IT (Reduction of Cardiovascular

Omega-3 et santé cardiovasculaire

Hypertension

- Méta-analyse de 71 essais cliniques
- Près de 5000 personnes
- Bénéfices significatifs entre 2000 à 3000 mg/j
- Bénéfices supérieurs à plus de 3000 mg/j
- Les bénéfices ne sont pas plus élevés à 5000 mg/j
- **Pris par l'alimentation ou en supplément**

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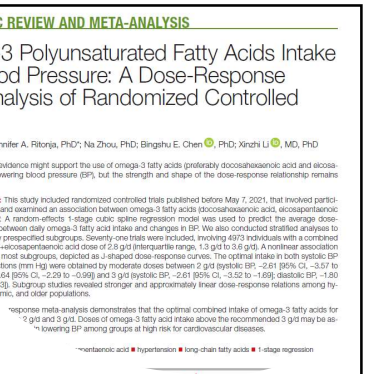
La dose quotidienne par l'alimentation ?

≥ 1000 à 2000 mg/jour = l'équilibre de base

≥ 2000 mg/jour = dosage thérapeutique

- 120 à 150 gr de saumon = 1500 mg
- Œufs oméga-3 (2) = 150 mg
- Suppléments concentrés (/gélule) = 613 à 864 mg



SYSTEMATIC REVIEW AND META-ANALYSIS

Omega-3 Polyunsaturated Fatty Acids Intake and Blood Pressure: A Dose-Response Meta-Analysis of Randomized Controlled Trials

Xin Zhang, PhD*; Jennifer A. Ritonja, PhD*; Na Zhou, PhD; Bingshu E. Chen, PhD; Xinzhi Li, MD, PhD

	Lundi	Mardi	Mercredi	Jeudi	Vendredi	Samedi	Dimanche
Déjeuner	Œufs (2)	75 gr de saumon	-	-	-	Œufs (2)	-
Diner	-	-	-	120 gr de saumon	-	-	120 gr de maquereau
Souper	-	-	-	-	-	Sardine (canne)	-
Suppléments (gélules)	4	3	4	2	4	0	2

≈ 1100 mg/jour

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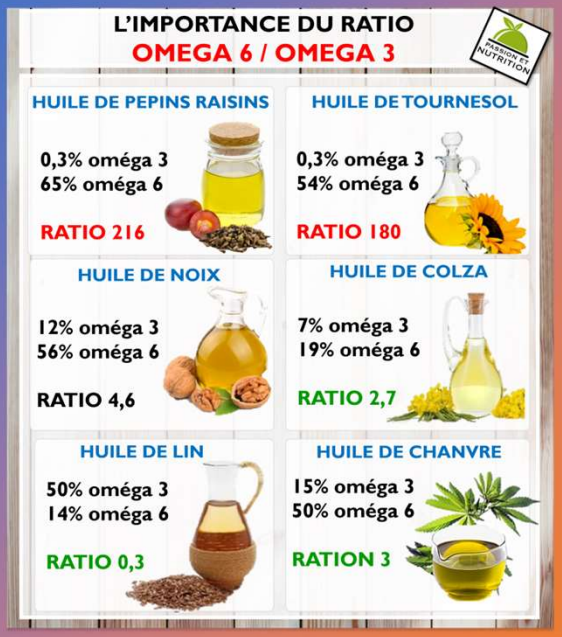

- Globalement, il faut améliorer le ratio Oméga-6/Oméga-3 pour s'approcher de **4:1** au lien de **20 à 50:1**.

Huiles et graisses végétales contenant des oméga-6	Teneur en oméga-6 : acide linoléique mg/100 g	Teneur en oméga-6 : acide arachidonique mg/100g
Huile de soja	52850	7700
Huile de tournesol	50176	178
Margarine	17100	2600

Viande et charcuterie contenant des oméga-6	Teneur en oméga-6 : acide linoléique mg/100 g	Teneur en oméga-6 : acide arachidonique mg/100g
Soupe de poulet	4070	850
Poulet rôti	2020	226
Salam	308	29
Saucis	932	68
Dinde	2091	179
Porc	854	191
Bœuf	237	39

Une fois du poulet pour une fois du poisson gras ≈ 4:1

www.norsan.fr

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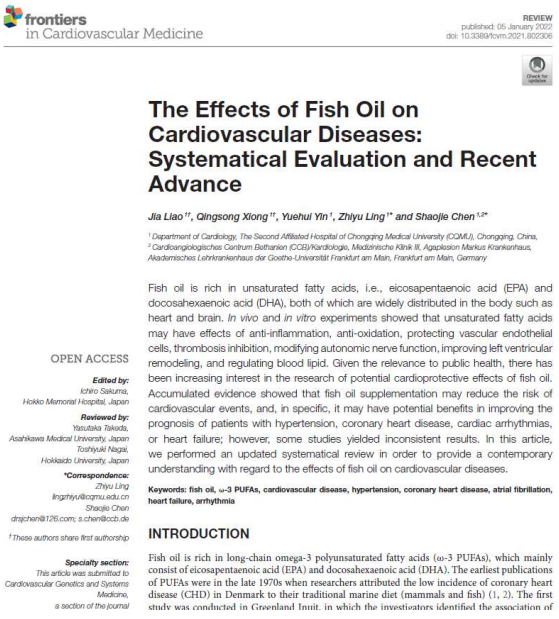
Omega-3 et santé cardiovasculaire

- Ils peuvent réduire le risque d'événement cardiovasculaire en prévention.
- Être bénéfiques dans les cas:
  - d'hypertension,
  - de maladies coronariennes,
  - d'arythmie ou
  - de crise cardiaque.



frontiers in Cardiovascular Medicine

REVIEW
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The Effects of Fish Oil on Cardiovascular Diseases: Systematical Evaluation and Recent Advance

Jia Liao[†], Qingsong Xiong[†], Yuehui Yin[†], Zhiyu Ling[*] and Shaojie Chen[1,2]*

[1] Department of Cardiology, The Second Affiliated Hospital of Chongqing Medical University (CQMU), Chongqing, China, [2] Cardioangiologisches Centrum Bethanien (CCB)/Kardiologie, Medizinische Klinik III, Agaplesion Markus Krankenhaus, Akademisches Lehrkrankenhaus der Goethe-Universität Frankfurt am Main, Frankfurt am Main, Germany

Fish oil is rich in unsaturated fatty acids, i.e., eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), both of which are widely distributed in the body such as heart and brain. *In vivo* and *in vitro* experiments showed that unsaturated fatty acids may have effects of anti-inflammation, anti-oxidation, protecting vascular endothelial cells, thrombosis inhibition, modifying autonomic nerve function, improving left ventricular remodeling, and regulating blood lipid. Given the relevance to public health, there has been increasing interest in the research of potential cardioprotective effects of fish oil. Accumulated evidence showed that fish oil supplementation may reduce the risk of cardiovascular events, and, in specific, it may have potential benefits in improving the prognosis of patients with hypertension, coronary heart disease, cardiac arrhythmias, or heart failure; however, some studies yielded inconsistent results. In this article, we performed an updated systematical review in order to provide a contemporary understanding with regard to the effects of fish oil on cardiovascular diseases.

Keywords: fish oil, ω-3 PUFAs, cardiovascular disease, hypertension, coronary heart disease, atrial fibrillation, heart failure, arrhythmia

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INTRODUCTION

Fish oil is rich in long-chain omega-3 polyunsaturated fatty acids (ω-3 PUFAs), which mainly consist of eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). The earliest publications of PUFAs were in the late 1970s when researchers attributed the low incidence of coronary heart disease (CHD) in Denmark to their traditional marine diet (mammals and fish) (1, 2). The first study was conducted in Greenland Inuit, in which the investigators identified the association of

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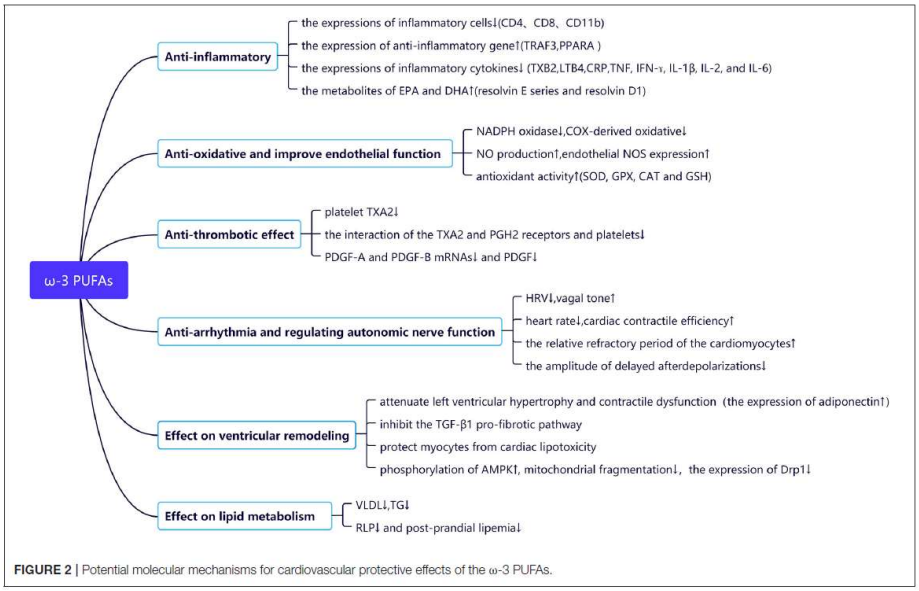
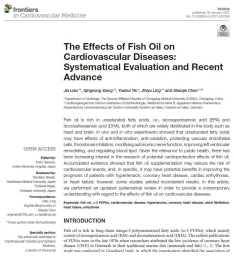


FIGURE 2 | Potential molecular mechanisms for cardiovascular protective effects of the ω-3 PUFAs.



The Effects of Fish Oil on Cardiovascular Diseases: Systematical Evaluation and Recent Advance

Liao *et al*, 2022; Yarizadeh *et al*, 2021; Siroma *et al*, 2022.

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Contenu

1. Les fonctions biologiques des oméga-3 (17)
2. Le développement de l'enfant et du cerveau (6)
3. L'inflammation (4)
4. La santé cardiovasculaire (8)
5. **L'état d'esprit et la santé cognitive** **(3)**
6. Les contre-indications (2)

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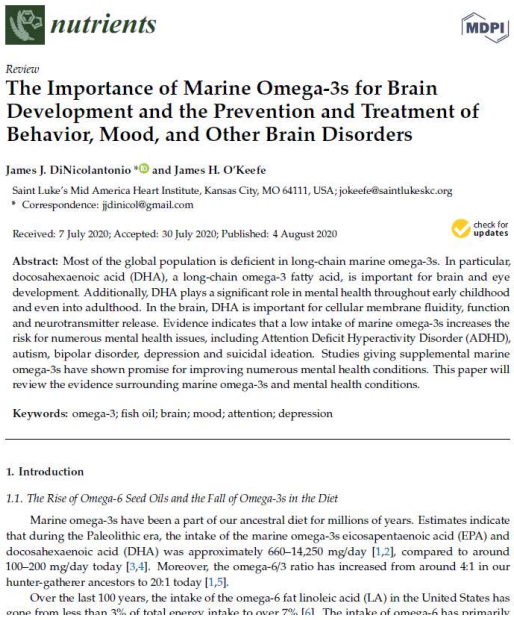
Oméga-3: état d'esprit et santé cognitive

- ADH pour le développement du cerveau et des yeux.
- ADH ↓ les risques de dépression reliés à la grosse et de TDAH chez l'enfant (enfant ≈ 500 mg d'ADH/j).
- ADH aide à réduire le déclin cognitif et ↑ santé oculaire (DMLA et sécheresse).
- L'EPA = la dépression.



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Review

The Importance of Marine Omega-3s for Brain Development and the Prevention and Treatment of Behavior, Mood, and Other Brain Disorders

James J. DiNicolantonio * and James H. O'Keefe

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Abstract: Most of the global population is deficient in long-chain marine omega-3s. In particular, docosahexaenoic acid (DHA), a long-chain omega-3 fatty acid, is important for brain and eye development. Additionally, DHA plays a significant role in mental health throughout early childhood and even into adulthood. In the brain, DHA is important for cellular membrane fluidity, function and neurotransmitter release. Evidence indicates that a low intake of marine omega-3s increases the risk for numerous mental health issues, including Attention Deficit Hyperactivity Disorder (ADHD), autism, bipolar disorder, depression and suicidal ideation. Studies giving supplemental marine omega-3s have shown promise for improving numerous mental health conditions. This paper will review the evidence surrounding marine omega-3s and mental health conditions.

Keywords: omega-3; fish oil; brain; mood; attention; depression

1. Introduction

1.1. The Rise of Omega-6 Seed Oils and the Fall of Omega-3s in the Diet

Marine omega-3s have been a part of our ancestral diet for millions of years. Estimates indicate that during the Paleolithic era, the intake of the marine omega-3s eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) was approximately 660–14,250 mg/day [1,2], compared to around 100–200 mg/day today [3,4]. Moreover, the omega-6/3 ratio has increased from around 4:1 in our hunter-gatherer ancestors to 20:1 today [1,5].

Over the last 100 years, the intake of the omega-6 fat linoleic acid (LA) in the United States has gone from less than 3% of total energy intake to over 7% [6]. The intake of omega-6 has primarily

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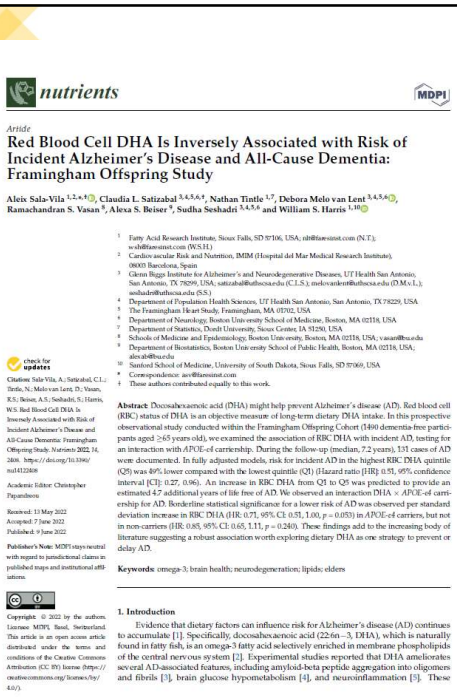

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Article

Red Blood Cell DHA Is Inversely Associated with Risk of Incident Alzheimer's Disease and All-Cause Dementia: Framingham Offspring Study

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Abstract: Docosahexaenoic acid (DHA) might help prevent Alzheimer's disease (AD). Red blood cell (RBC) status of DHA is an objective measure of long-term dietary DHA intake. In this prospective observational study conducted within the Framingham Offspring Cohort (1840 dementia-free participants aged ≥65 years old), we examined the association of RBC DHA with incident AD, testing for an interaction with *APOE-ε4* carriership. During the follow-up (median, 7.2 years), 131 cases of AD were documented. In fully adjusted models, risk for incident AD in the highest RBC DHA quintile (Q5) was 49% lower compared with the lowest quintile (Q1) (Hazard ratio [HR] 0.51, 95% confidence interval [CI]: 0.27, 0.96). An increase in RBC DHA from Q1 to Q5 was predicted to provide an estimated 4.7 additional years of life free of AD. We observed an interaction DHA × *APOE-ε4* carriership for AD. Borderline statistical significance for a lower risk of AD was observed per standard deviation increase in RBC DHA (HR: 0.71, 95% CI: 0.51, 1.00, $p = 0.053$) in *APOE-ε4* carriers, but not in non-carriers (HR: 0.85, 95% CI: 0.65, 1.11, $p = 0.240$). These findings add to the increasing body of literature suggesting a robust association worth exploring dietary DHA as one strategy to prevent or delay AD.

Keywords: omega-3; brain health; neurodegeneration; lipids; elders

1. Introduction

Evidence that dietary factors can influence risk for Alzheimer's disease (AD) continues to accumulate [1]. Specifically, docosahexaenoic acid (22:6n−3, DHA), which is naturally found in fatty fish, is an omega-3 fatty acid selectively enriched in membrane phospholipids of the central nervous system [2]. Experimental studies reported that DHA ameliorates several AD-associated features, including amyloid-beta peptide aggregation into oligomers and fibrils [3], brain glucose hypometabolism [4], and neuroinflammation [5]. These

Oméga-3: état d'esprit et santé cognitive

Alzheimer

- Les personnes ayant un taux sanguin élevé d'ADH encourent **un risque réduit de 49%**.
- Une augmentation de l'ADH (du 1er au 5è quintile) pourrait permettre de « gagner » **4,7 années de vie supplémentaires sans maladie d'Alzheimer**.
- Une consommation accrue d'ADH pourrait réduire le risque de développer la maladie d'Alzheimer.

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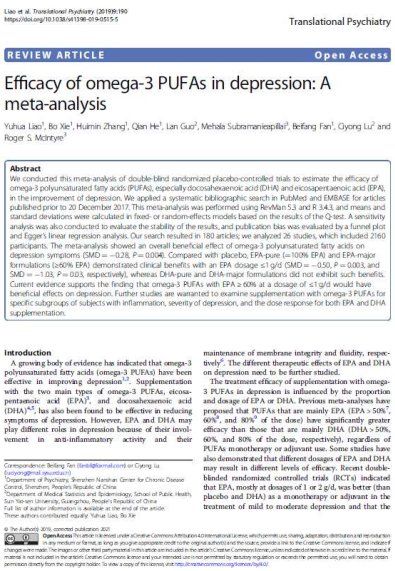

Liao et al. *Translational Psychiatry* (2019)9:190
https://doi.org/10.1038/s41398-019-0515-5

Translational Psychiatry

REVIEW ARTICLE Open Access

Efficacy of omega-3 PUFAs in depression: A meta-analysis

Yuhua Liao[1], Bo Xie[1], Huimin Zhang[1], Qian He[1], Lan Guo[2], Mehala Subramaniapillai[3], Beifang Fan[1], Gyong Lu[2] and Roger S. McIntyre[3]

Abstract

We conducted this meta-analysis of double-blind randomized placebo-controlled trials to estimate the efficacy of omega-3 polyunsaturated fatty acids (PUFAs), especially docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA), in the improvement of depression. We applied a systematic bibliographic search in PubMed and EMBASE for articles published prior to 20 December 2017. This meta-analysis was performed using RevMan 5.3 and R 3.4.3, and means and standard deviations were calculated in fixed- or random-effects models based on the results of the Q-test. A sensitivity analysis was also conducted to evaluate the stability of the results, and publication bias was evaluated by a funnel plot and Egger's linear regression analysis. Our search resulted in 180 articles; we analyzed 26 studies, which included 2160 participants. The meta-analysis showed an overall beneficial effect of omega-3 polyunsaturated fatty acids on depression symptoms (SMD = −0.28, $P = 0.004$). Compared with placebo, EPA-pure (≈100% EPA) and EPA-major formulations (≥60% EPA) demonstrated clinical benefits with an EPA dosage ≤1 g/d (SMD = −0.50, $P = 0.003$, and SMD = −1.03, $P = 0.03$, respectively), whereas DHA-pure and DHA-major formulations did not exhibit such benefits. Current evidence supports the finding that omega-3 PUFAs with EPA ≥ 60% at a dosage of ≤1 g/d would have beneficial effects on depression. Further studies are warranted to examine supplementation with omega-3 PUFAs for specific subgroups of subjects with inflammation, severity of depression, and the dose response for both EPA and DHA supplementation.

Introduction

A growing body of evidence has indicated that omega-3 polyunsaturated fatty acids (omega-3 PUFAs) have been effective in improving depression[1–5]. Supplementation with the two main types of omega-3 PUFAs, eicosapentaenoic acid (EPA)[6], and docosahexaenoic acid (DHA)[6,7], has also been found to be effective in reducing symptoms of depression. However, EPA and DHA may play different roles in depression because of their involvement in anti-inflammatory activity and their maintenance of membrane integrity and fluidity, respectively[8]. The different therapeutic effects of EPA and DHA on depression need to be further studied.

The treatment efficacy of supplementation with omega-3 PUFAs in depression is influenced by the proportion and dosage of EPA or DHA. Previous meta-analyses have proposed that PUFAs that are mainly EPA (EPA > 50%[7], 60%[9], and 80%[5] of the dose) have significantly greater efficacy than those that are mainly DHA (DHA > 50%, 60%, and 80% of the dose, respectively), regardless of PUFAs monotherapy or adjuvant use. Some studies have also demonstrated that different dosages of EPA and DHA may result in different levels of efficacy. Recent double-blinded randomized controlled trials (RCTs) indicated that EPA, mostly at dosages of 1 or 2 g/d, was better than placebo and DHA) as a monotherapy or adjuvant in the treatment of mild to moderate depression and that the

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Full list of author information is available at the end of the article.
These authors contributed equally: Yuhua Liao, Bo Xie

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Oméga-3 et dépression : Méta-analyse.

- 26 études cliniques, 2160 participants: effet thérapeutique sur l'amélioration de la dépression.
- Effets significatifs sur les symptômes de dépression vs placébo (P = 0.004):
  - ≥ 60% d'AEP:
    - N.B. équilibre naturel = 67%,
  - ≥ 1000 mg d'AEP/j.
- Aucun effet significatif de l'ADH.

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Contenu

1. Les fonctions biologiques des oméga-3 (17)
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4. La santé cardiovasculaire (8)
5. L'état d'esprit et la santé cognitive (3)
6. **Les contre-indications** **(2)**

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Les contre-indications

- Arrêter la prise une semaine avant toutes interventions chirurgicales
- Femmes enceintes: arrêter la prise au moins une semaine avant l'accouchement.
- Attention aux allergies (poisson).
- Anticoagulants (faibles risques): entre 3000 et 4000 mg/jour d'oméga-3 = surveillance, demander un IRN.
- Léger effet antihypertenseur: surveillance pour les médicaments pour la pression.
- Arythmie: serait bénéfique jusqu'à 4000 mg/jour, mais au-delà de 4000 pourraient augmenter.
- Cyclosporine (Neoral, Sandimmune): pourrait causer une augmentation des effets secondaires.

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Conclusions

- Les oméga-3 sont essentiels au bon fonctionnement des cellules
- La diète nord-américaine est fortement déséquilibrée pour le ratio oméga-6/3 (de 20 à 50:1 et devrait être aux environ de 4:1).
- La consommation alimentaire de poisson devrait être élevée pour juste maintenir un indice d'oméga-3 sain.
- Les dosages thérapeutiques requirent ≥ 1800 mg/jour d'AEP/ADH
- Certaines applications ont beaucoup de support scientifique:
  - Développement du cerveau.
  - Santé cardiovasculaire.
  - L'inflammation.
  - La santé cognitive/dépression.

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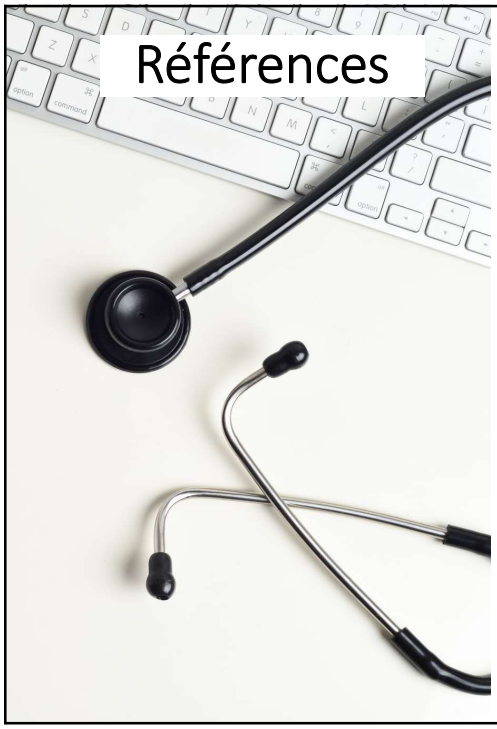

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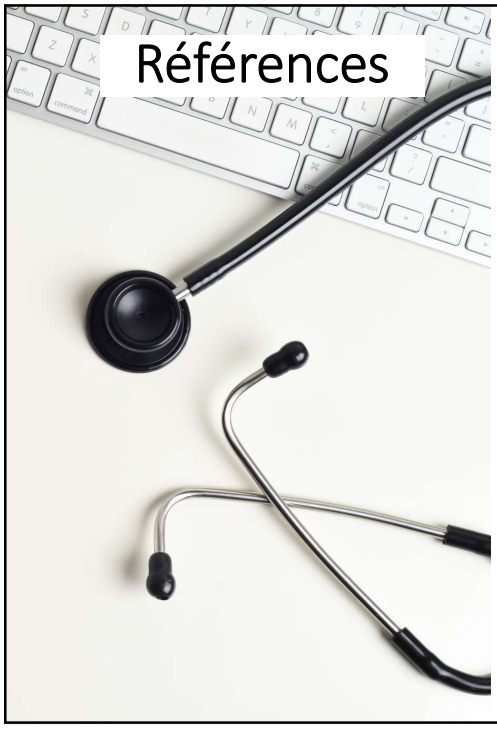

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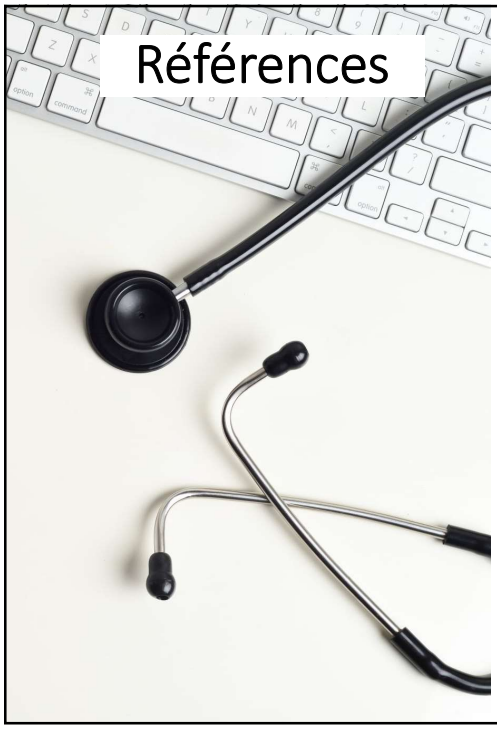

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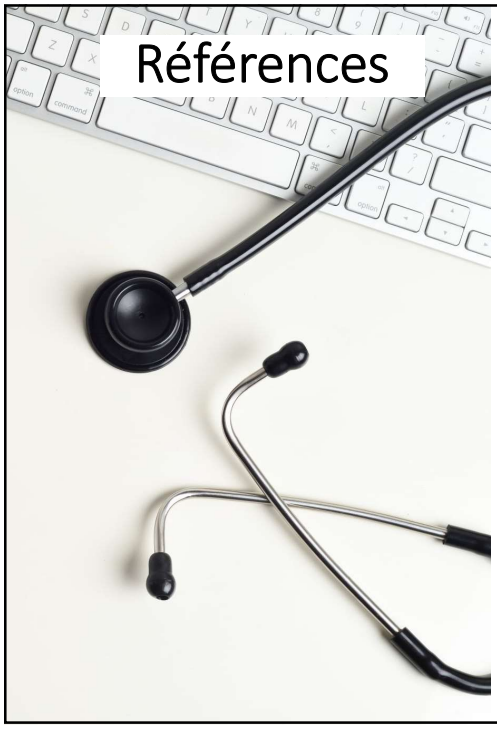

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Eric Simard, Priorité bien vieillir

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Merci!

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Les problèmes de sommeil et d'anxiété: les approches naturelles

Eric Simard, Dr en biologie
chercheur en longévité cellulaire
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Présentation / déclaration

Eric Simard, Ph.D. est Dr en biologie, chercheur dans le domaine du vieillissement.

- Président de l'Association Professionnelle pour la Santé Intégrative (APSI).
- Auteur de 4 livres avec 11 autres professionnels de la santé.
- A été président du Comité consultatif du Conseil de Recherche en Science et en Génie du Canada, bureau du Québec, pendant plus de 10 ans.
- Membre nommé de la Commission de l'éthique en science et technologie du Conseil des Ministres.
- Président de Idunn Technologies (Vitoli).

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Contenu de la présentation

1. Micronutriments qui peuvent faire l'objet de carence et/ou améliorer la gestions des problèmes de sommeil ou de stress.
2. Les ingrédients/produits pour le sommeil
3. Les ingrédient/produits pour le stress et l'anxiété
4. Dans la pratique

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Objectifs

- Connaître les PSN pour les problèmes de stress et de sommeil.
- Retenir la signification des ratios d'extraction vs la standardisation pour les extraits de plantes.
- Réviser les considérations en lien avec votre pratique.

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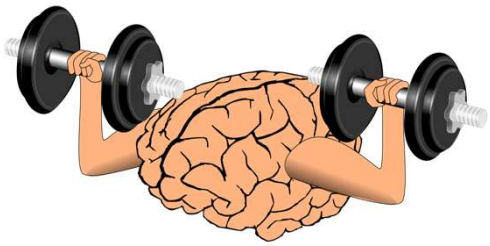
Contenu de la présentation

1. **Micronutriments qui peuvent faire l'objet de carence et/ou améliorer la gestions des problèmes de sommeil ou de stress.**
2. Les ingrédients/produits pour le sommeil
3. Les ingrédient/produits pour le stress et l'anxiété
4. Dans la pratique

62

PSN pour le sommeil et le stress

Micronutriments qui peuvent améliorer la gestions des problèmes de sommeil ou de stress.



Une revue systématique (Ji *et al*, 2017) :

- À partir de 26 études scientifiques (19 observationnelles et 7 cliniques) retenues (vitamines/minéraux et le sommeil),
- Il y aurait un rôle des micronutriment dans le développement des phases du sommeil autant chez l'enfant que chez les gens vieillissant.
- Corrélation positive (enfants et adultes) avec le **Fe, le Mg et le Zn**.
- Certaines vitamines et minéraux pourraient avoir l'effet contraire (K, Cu, multivitamine **?**).

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Contenu de la présentation

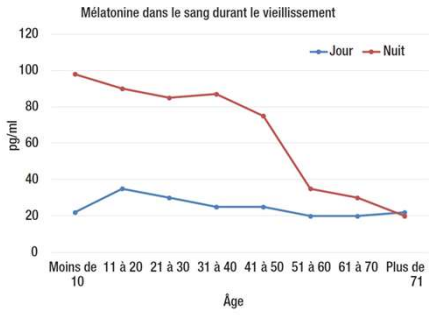
1. Micronutriments qui peuvent faire l'objet de carence et/ou améliorer la gestions des problèmes de sommeil ou de stress.
2. **Les ingrédients/produits pour le sommeil**
3. **Les ingrédient/produits pour le stress et l'anxiété**
4. Dans la pratique

64

PSN pour le sommeil et le stress

Les ingrédients/produits pour le sommeil

1. **Mélatonine: <u>induction du sommeil</u>**
   (sans altération des phases).
   - Posologie = 3 à 5 mg habituellement,
   - Dose maximale de 10 mg,
   - 30 minutes avant de dormir.



Eric Simard, 2016. Vivre jeune plus longtemps.

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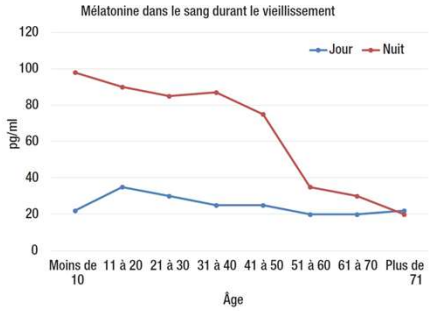
PSN pour le sommeil et le stress

Les ingrédients/produits pour le sommeil



Eric Simard, 2016. Vivre jeune plus longtemps.

N.B. Deux médicaments à surveiller:

- interaction spécifique avec la FLUVOXAMINE (=LUVOX nom commercial- augmentation des concentrations plasmatiques de FLUVOXAMINE et la Fluvoxamine augmenterait l'effet de la mélatonine) et
- avec NIFÉDIPINE (=ADALAT nom commercial- diminution de l'effet de la NIFEDIPINE).

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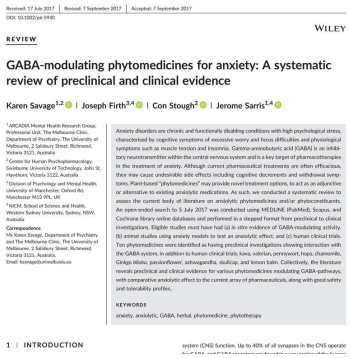
PSN pour le sommeil et le stress

Les ingrédients/produits pour le stress - MOA



Received: 17 July 2017 | Revised: 7 September 2017 | Accepted: 7 September 2017
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WILEY

REVIEW

GABA-modulating phytomedicines for anxiety: A systematic review of preclinical and clinical evidence

Karen Savage[1,2] | Joseph Firth[3,4] | Con Stough[2] | Jerome Sarris[1,4]

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Anxiety disorders are chronic and functionally disabling conditions with high psychological stress, characterised by cognitive symptoms of excessive worry and focus difficulties and physiological symptoms such as muscle tension and insomnia. Gamma-aminobutyric acid (GABA) is an inhibitory neurotransmitter within the central nervous system and is a key target of pharmacotherapies in the treatment of anxiety. Although current pharmaceutical treatments are often efficacious, they may cause undesirable side effects including cognitive decrements and withdrawal symptoms. Plant-based "phytomedicines" may provide novel treatment options, to act as an adjunctive or alternative to existing anxiolytic medications. As such, we conducted a systematic review to assess the current body of literature on anxiolytic phytomedicines and/or phytoconstituents. An open-ended search to 5 July 2017 was conducted using MEDLINE (PubMed), Scopus, and Cochrane library online databases and performed in a stepped format from preclinical to clinical investigations. Eligible studies must have had (a) in vitro evidence of GABA-modulating activity, (b) animal studies using anxiety models to test an anxiolytic effect, and (c) human clinical trials. Ten phytomedicines were identified as having preclinical investigations showing interaction with the GABA system, in addition to human clinical trials: kava, valerian, pennywort, hops, chamomile, Ginkgo biloba, passionflower, ashwagandha, skullcap, and lemon balm. Collectively, the literature reveals preclinical and clinical evidence for various phytomedicines modulating GABA-pathways, with comparative anxiolytic effect to the current array of pharmaceuticals, along with good safety and tolerability profiles.

KEYWORDS
anxiety, anxiolytic, GABA, herbal, phytomedicine, phytotherapy

1 | INTRODUCTION

system (CNS) function. Up to 40% of all synapses in the CNS operate

Par le mécanisme d'action:

«Collectivement, la littérature révèle des données probantes précliniques et cliniques pour diverses ''phytomédicines'' (phytomédicaments) modulant les circuits du GABA, avec un effet anxiolytique comparable à la gamme actuelle de produits pharmaceutiques, ainsi que de bons profils d'innocuité et de tolérabilité" », concluent les chercheurs.

N.B. L'efficacité est bien sûr moins élevée.

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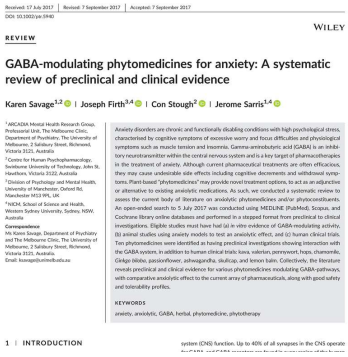
PSN pour le sommeil et le stress

Les ingrédients/produits pour le stress - MOA

Études précliniques sur le système GABA et essais cliniques chez l'humain :

le kava ;
la valériane ;
Le gotu-kola;
le houblon ;
la camomille ;
le ginkgo biloba ;
la passiflore ;
L'ashwagandha ;
la scutellaire (scutellaire américaine);
la mélisse.



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REVIEW

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KEYWORDS
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1 | INTRODUCTION

system (CNS) function. Up to 40% of all synapses in the CNS operate

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PSN pour le sommeil et le stress

Les ingrédients/produits pour le stress

N.B. les produits naturels habituellement utilisés pour le stress sont souvent utilisés aussi pour le sommeil.

- Valériane; grand nombre d'études, très sécuritaire.
- Passiflore; grand nombre d'études, différentes applications.
- Kava; grand nombre d'études, doutes sur les risques hépatiques.
- Millepertuis; problème de nombreuses interactions.
- L'Ashwagandha et la rhodiole sont des plantes reconnues pour aider à la gestion du stress chronique durant le jour (pas d'effet significatif sur le sommeil).
- Des molécules spécifiques: la L-Théanine (molécule qui tient son nom du thé vert) et le **GABA** (neurotransmetteur naturellement présent dans les plantes).

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PSN pour le sommeil et le stress

Les ingrédients/produits pour le stress

Risque de dépendance ou d'accoutumance des PSN ?
L'exemple de la valériane

- Les extraits de valériane augmentent la production de GABA et réduisent sa recapture synaptique (similaire au diazepam; Alramadhan *et al*, 2012).
- Certaines molécules se lieraient aussi à d'autres récepteurs anxiolytiques (Kennedy et Wightam, 2011; Gooneratne, 2008).
- La valériane n'a pas d'interaction significative connue (Kelber *et al*, 2014).

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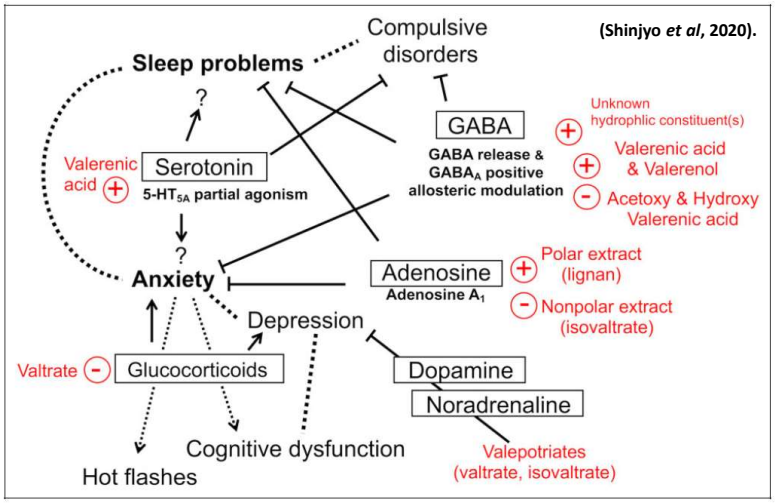
PSN pour le sommeil et le stress

Risque de dépendance ou d'accoutumance des PSN ?

L'exemple de la valériane



(Shinjyo *et al*, 2020).

Pour les extraits de plante, l'absence de dépendance ou d'accoutumance serait reliée aux multiples mécanismes d'action qui sont nécessaires pour rendent l'effet significatif.

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PSN pour le sommeil et le stress

Les ingrédients/produits pour le stress

Valériane (*Valeriana officinalis*):

- Le plus de support clinique.
- Le jour ou la nuit (quelqu'un qui dort bien, elle ne devrait pas causer de somnolence).
- Guadagna *et al*, 2020: 100 à 600 mg/jour d'extraits de la racine (0,8% d'acide valérénique).
- European Medicine Agency (EMA): 400 à 600 mg d'extrait ou 0.3 - 3 g jusqu'à 3 fois par jour (racine).
- Très sécuritaire, aucune contre-indication ou interaction importante.

Valerian Root in Treating Sleep Problems and Associated Disorders—A Systematic Review and Meta-Analysis

Noriko Shinjyo[1,2], Guy Waddell[3], and Julia Green[4]

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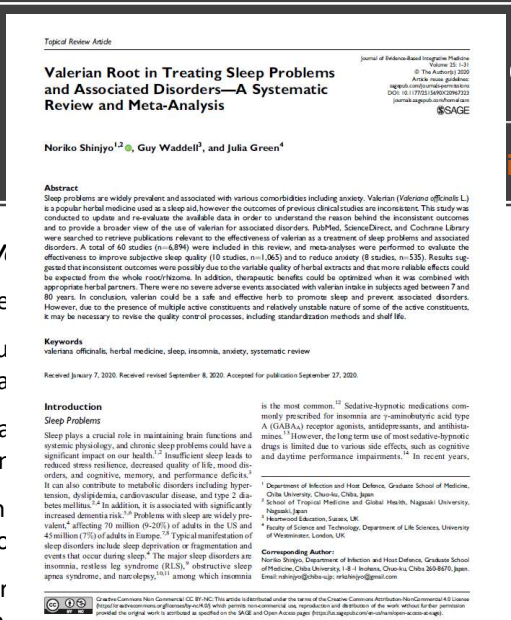
eil et le stress

its pour le stress

Valériane (*V*

- Le plus de
- Le jour ou devrait pa
- Guadagna de la racir
- European d'extrait c
- Très sécur interactio



Topical Review Article

Valerian Root in Treating Sleep Problems and Associated Disorders—A Systematic Review and Meta-Analysis

Journal of Evidence-Based Integrative Medicine
Volume 25: 1–31
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Noriko Shinjyo[1,2], Guy Waddell[3], and Julia Green[4]

Abstract

Sleep problems are widely prevalent and associated with various comorbidities including anxiety. Valerian (*Valeriana officinalis* L.) is a popular herbal medicine used as a sleep aid, however the outcomes of previous clinical studies are inconsistent. This study was conducted to update and re-evaluate the available data in order to understand the reason behind the inconsistent outcomes and to provide a broader view of the use of valerian for associated disorders. PubMed, ScienceDirect, and Cochrane Library were searched to retrieve publications relevant to the effectiveness of valerian as a treatment of sleep problems and associated disorders. A total of 60 studies (n=6,894) were included in this review, and meta-analyses were performed to evaluate the effectiveness to improve subjective sleep quality (10 studies, n=1,065) and to reduce anxiety (8 studies, n=535). Results suggested that inconsistent outcomes were possibly due to the variable quality of herbal extracts and that more reliable effects could be expected from the whole root/rhizome. In addition, therapeutic benefits could be optimized when it was combined with appropriate herbal partners. There were no severe adverse events associated with valerian intake in subjects aged between 7 and 80 years. In conclusion, valerian could be a safe and effective herb to promote sleep and prevent associated disorders. However, due to the presence of multiple active constituents and relatively unstable nature of some of the active constituents, it may be necessary to revise the quality control processes, including standardization methods and shelf life.

Keywords

valeriana officinalis, herbal medicine, sleep, insomnia, anxiety, systematic review

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Introduction

Sleep Problems

Sleep plays a crucial role in maintaining brain functions and systemic physiology, and chronic sleep problems could have a significant impact on our health.[1,2] Insufficient sleep leads to reduced stress resilience, decreased quality of life, mood disorders, and cognitive, memory, and performance deficits.[3] It can also contribute to metabolic disorders including hypertension, dyslipidemia, cardiovascular disease, and type 2 diabetes mellitus.[3,4] In addition, it is associated with significantly increased dementia risk.[5,6] Problems with sleep are widely prevalent,[4] affecting 70 million (9-20%) of adults in the US and 45 million (7%) of adults in Europe.[7,8] Typical manifestation of sleep disorders include sleep deprivation or fragmentation and events that occur during sleep.[9] The major sleep disorders are insomnia, restless leg syndrome (RLS),[9] obstructive sleep apnea syndrome, and narcolepsy,[10,11] among which insomnia is the most common.[12] Sedative-hypnotic medications commonly prescribed for insomnia are γ-aminobutyric acid type A ($GABA_A$) receptor agonists, antidepressants, and antihistamines.[13] However, the long-term use of most sedative-hypnotic drugs is limited due to various side effects, such as cognitive and daytime performance impairments.[14] In recent years,

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Shinjyo *et al*, 2020. Valerian Root in Treating Sleep Problems and associated disorders - a systematic review and meta-analysis.

- 60 études cliniques (N=6894).
- Méta-analyse positive pour l'anxiété le jour et le sommeil la nuit.
- Les effets peuvent être optimisés lorsque combinés à une autre plante (Houblon et Passiflore donneraient les meilleurs résultats (Borras *et al*, 2021).

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PSN pour le sommeil et le stress

Les ingrédients/produits pour le stress

Passiflore (*Passiflora incarnata*)

- Le jour ou la nuit.
- Aide à réduire les dépendances; ''…the BZF co-treatments with diazepam also prevented the incurrence of diazepam-dependence, which might be because of the aromatase enzyme inhibiting properties associated with the BZF moiety'' (BZF = ''benzoflavone'' extrait de passiflore: Dhawan *et al*, 2003).
- Améliorait la durée total du sommeil par la modulation de plusieurs gènes reliés au cycle circadien.
- Extrait de la fleure standardisé en vitexine (1,5 à 3,5% selon la qualité de l'extrait); 150 à 1000 mg / jour.
- Très sécuritaire, aucune contre-indication ou interaction importante.

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PSN pour le sommeil et le stress

Les ingrédients/produits pour le stress

Kava kava (*Piper methysticum*)

- Cochrane review (7 études cliniques considérées); efficacité significativement plus importante que le placébo pour l'anxiété (Pittler et Erns, 2003).
- 250 à 400 mg d'un extrait standardisé.
- Avait été retiré par Santé Canada dû aux risques de toxicité hépatique.
- N.B. Ne pas prendre avec de l'alcool et certains de ses polyphénols seraient des inhibiteurs potentiels de plusieurs enzyme du CYP 450 system (CYP1A2, 2C9, 2C19, 2D6, 3A4 and 4A9/11).

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PSN pour le sommeil et le stress

Les ingrédients/produits pour le stress

Millepertuis (*Hypericum perforatum*).

- Support clinique pour la dépression et l'anxiété.
- Pourrait avoir d'autres bénéfices dans le domaine de la douleur et des problèmes cognitifs.
- Interactions avec : antidépresseurs, antipsychotiques, anticoagulants, analgésiques, bloqueurs des canaux calciques, IPP, statines, oestrogènes (donc contraceptifs notamment), etc.
- '' Products that had a daily dose of <1 mg hyperforin were less likely to be associated with major interaction for drugs that were CYP3A4 or p-glycoprotein substrates.'' (Chrubasik-Hausmann *et al*, 2019).
- Extraits standardisés à 0,3% hypericine et/ou 3 à 5% d'hyperforine) : 300 mg, 3 fois par jour.
- N.B. Effet sur le cytochrome p450 3A4.

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PSN pour le sommeil et le stress

Les ingrédients/produits pour le stress

Des molécules spécifiques: la L-Théanine et le GABA.

- **La L-théanine:**
  - franchit la barrière hémato-encéphalique en 30 minutes, avec une concentration sanguine maximale de 5 heures (Janet Bryan, 2008).
  - Elle augmente la production de GABA et de dopamine, avec une action comparable à certaines benzodiazépines (Alramadhan et al, 2012).
  - Anxiolytique pour le jour ou la nuit (pas d'effet somnifère): 100 à 400 mg par jour.
  - Une possible réduction de la tension artérielle et une diminution de l'effet des produits stimulants du système nerveux central sont aussi possibles, réduisant de ce fait leur efficacité (surveillance).

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PSN pour le sommeil et le stress

Les ingrédients/produits pour le stress

Des molécules spécifiques: la L-Théanine et le GABA.

- **Le GABA** (acide gamma-aminobutyrique; le plus important neurotransmetteur inhibiteur du cerveau)
  - Mécanismes d'action sur le corps humain encore inconnus.
  - Incertitude sur sa capacité à passer la barrière hémato-encéphalique.
  - Présence dans les aliments: les épinards sont relativement riches (?); 2,34 kg crus = 100 mg de GABA.
  - Revue systématique; 14 études cliniques (Hepsomali *et al*, 2020):
    - Évidences modérées pour le stress
    - Évidences faibles pour le sommeil
  - 20 à 200 mg, dose habituelle de 100 mg (2,34 kg d'épinards ?).
  - Interaction ?

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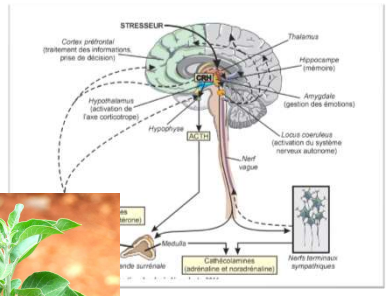
PSN pour le sommeil et le stress

Les ingrédients/produits pour le stress

- **L'Ashwagandha (*Withania somnifera*) et la rhodiole (*Rhodiola rosea*)**
  - Une autre approche pour le stress et l'anxiété.
  - Gestion du stress par un effet modulateur de l'axe '' hypothalamo-hypophyso-surrénalien''.



- **Aswagandha** = analyse systématique, 5 études cliniques positive (Pratte *et al*, 2014):
  - 125 à 1000 mg d'un extrait par jour (concentration ?).
  - Lopresti *et al*, 240 mg/jour.

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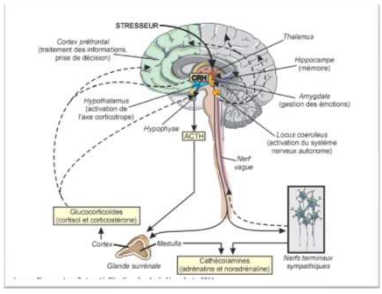
PSN pour le sommeil et le stress

Les ingrédients/produits pour le stress



100 à 600 mg d'extraits (concentrations ?) par jour (**N.B. contre-indiqué pour les troubles bi-polaires**).

L'Ashwagandha (*Withania somnifera*) et la rhodiole (*Rhodiola rosea*)

- **Rhodiole** = stress et dépression
  - Effets cliniques positifs sur la performance physique, mentale et la capacité de concentration.
  - Réduit/prévient les effets et les symptômes du stress chronique.
  - Étude d'équivalence à la sertraline, avec placebo (Maho *et al*, 2015); Rhodiole légèrement moins efficace, mais un taux de moins de la moitié des effets secondaires rapportés (30 vs 63%).
  - Étude d'effets aditifs avec la sertraline permettant de réduire la dose (Gao *et al*, 2020).

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PSN pour le sommeil et le stress

Les ingrédients/produits pour le stress

Quelques trucs avec les extraits:

1. La signification du ratio d'extraction.

Les mentions 4:1 ou 8:1 signifient 4 ou 8 fois plus concentré, respectivement, que la plante originale, mais en quoi, on en a aucune idée.

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PSN pour le sommeil et le stress

Les ingrédients/produits pour le stress

Quelques trucs avec les extraits:

2. Les standardisations, comme l'acide valérinique pour la valériane ou la vitexine pour la passiflore, permettent de confirmer la provenance, réduire les risques d'adultération et confirmer le niveau de concentration en éléments actifs.

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PSN pour le sommeil et le stress

Les ingrédients/produits pour le stress

Quelques trucs avec les extraits:

3. La réglementation canadienne accepte des niveaux relativement faibles d'éléments actifs par rapport aux moyennes des études cliniques publiées, mais les niveaux maximaux respects les risques d'usage usuels. Ainsi, un produit 2 fois plus concentré risque d'être plus près des doses cliniques significatives même si vous ne les connaissez pas par cœur.

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Contenu de la présentation

1. Micronutriments qui peuvent faire l'objet de carence et/ou améliorer la gestions des problèmes de sommeil ou de stress.
2. Les ingrédients/produits pour le sommeil
3. Les ingrédient/produits pour le stress et l'anxiété
4. **Dans la pratique**

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PSN pour le sommeil et le stress

En pratique: 3 types de cas

1. **Doivent prendre des somnifères (7 à 10 jours ?).**
2. **Des situations de réduction ou cessation de traitement par un hypnotique conventionnel suite à la demande du patient lui-même.**
3. **Une situation où vous, comme pharmacien, jugiez qu'il y aurait un indicateur de risque pour le patient à continuer l'utilisation d'un somnifère conventionnel.**

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PSN pour le sommeil et le stress

En pratique

2. Des situations de réduction ou cessation de traitement par un hypnotique conventionnel, *suite à la demande du patient lui-même* :

- Il a perdu l'effet thérapeutique avec le temps (tolérance)
- Il a des effets secondaires (anticholinergiques, sédation diurne, trouble de mémoire, etc.)
- Il est indisposé ou soucieux de son addiction ou dépendance à plus ou moins long terme à son somnifère
- Il est inquiet pour les risques de démence et d'Alzheimer qui pourraient augmenter
- Il a fait une chute
- Il utiliser aussi de l'alcool, du cannabis, et désire cesser son somnifère
- Ses causes d'insomnie (ex : dépression, anxiété, autre trouble de l'humeur) ont été réglées et il pense ne plus avoir besoin de somnifère. Etc.

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PSN pour le sommeil et le stress

En pratique

3. Une situation où *vous, comme pharmacien, jugiez qu'il y aurait un indicateur de risque pour le patient à continuer l'utilisation d'un somnifère* conventionnel :

- Il prend une benzodiazépine depuis longtemps, et les recommandations officielles sont un usage pour 7 à 10 jours
- Il a débuté récemment des opioïdes pour douleurs chroniques et l'interaction potentielle vous inquiète
- Toute co-prescription avec un nouveau médicament qui peut causer une interaction significative
- De nouvelles co-morbidités se sont développées chez le patient (ex : rétention urinaire, constipation, etc.) et son somnifère peut aggraver sa situation
- Votre patient semble commencer à avoir des troubles cognitifs et déclin de sa mémoire

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PSN pour le sommeil et le stress

Exemples de cas

4. Recommandations

- Dans toutes les situations, toujours informer sur l'hygiène de sommeil; un horaire de sommeil régulier tous les jours, ↑exposition à lumière pendant la journée, pas d'usage d'écrans le soir, éteindre au moins 30 minutes avant coucher, réduire excitation avant coucher, température, bruit, etc.
- Rassurer le patient qu'une ↓ ou cessation de leur somnifère est possible, mais sera un processus qui exigera une implication et de la patience de leur part.
- Fixer ensemble des attentes réalistes : la réduction graduelle peut s'étendre sur plusieurs mois.
- Responsabiliser le patient et l'impliquer dans la démarche. Par exemple, il a le doit de cesser le sevrage et faire des pauses s'il ressent des symptômes de sevrage, encouragez-le à vous en aviser si c'est le cas.

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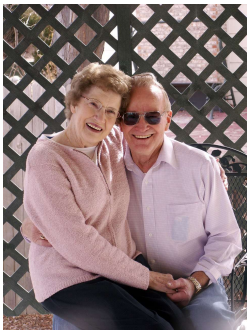
PSN pour le sommeil et le stress

Exemples de cas



4. Recommandations (suite)

- Personnalisez la stratégie de réduction graduelle; un calendrier de sevrage, soyez flexible, avisez-le du risque d'insomnie rebond...
- Nous pensons que l'addition d'un bon PSN est potentiellement un outil additionnel à ne pas négliger dans le plan de sevrage:
  - effet pharmacologique réel,
  - Indépendamment de l'efficacité, même un placébo a un effet indéniable,
  - débuter le PSN une semaine avant le sevrage,
  - peuvent aussi être utilisés pour l'anxiété le jour.
- Considérez:
  - OPQ, guide d'exercice, 3.2 et 3.2.2 (Modification pour assurer la sécurité du patient)
  - Rémunération selon la règle 10 (21,25$ médicament couvert) ou la règle 38 (effets indésirables…).

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Conclusion

- Un grand nombre d'extraits de plantes sont utilisés pour la gestion du stress et les problèmes de sommeil. Considérez celles qui ont le plus de données probantes.
- Deux grandes approches existes: les produits/ingrédients agissant sur la recapture du GABA et les produits/ingrédient qui agissent sur l'axe ''hypothalamo-hypophyso-surrénalien''.
- Étant donnée la pluralité des mécanismes d'actions, une personne pourrait ne pas répondre à un produit, mais répondre à un autre.

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Conclusion

Considérations pour les sevrages de somnifères

- Réviser les recommandations de suivi.
- Les extraits de plantes peuvent être donnés en concomitance pour aider à retrouver un sommeil naturel plus rapidement.
- La passiflore aiderait à réduire les dépendances.
- Les PSN ayant des propriétés anxiolytiques devraient être recommandés durant le jour afin de contrer l'effet anxiogène du sevrage des somnifères (qui mène souvent à l'abandon de la démarche).

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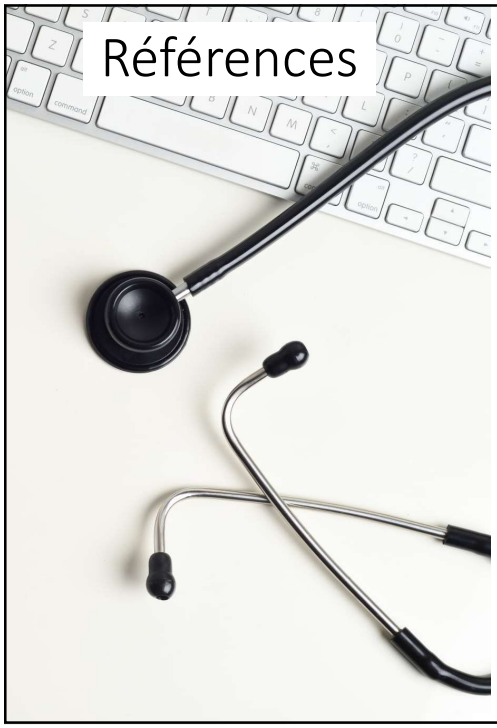

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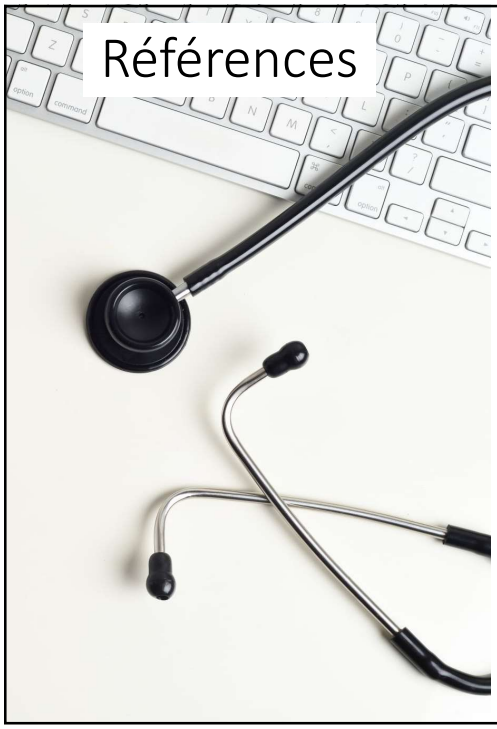

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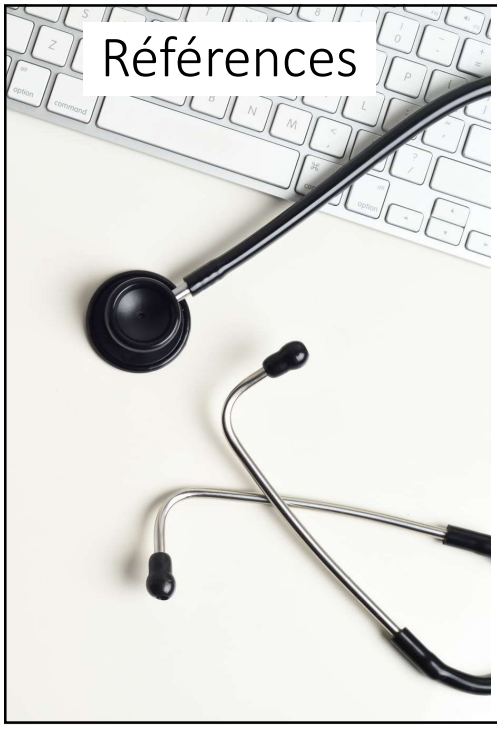

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