



Congresso Internazionale di MEDICINA BIOINTEGRATA

La Malattia. Pre Post e Consecutio. L'Evoluzione Clinica del Paziente secondo la Visione Biointegrata

14-15-16 aprile 2023 ROMA

Disturbi cognitivi e disturbo d'ansia: oltre la siepe del farmaco



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Psychogeriatric, Psychology and Psychotherapy Clinic Celesia and Villa Scassi ASL3 Hospital Mental Health Department ASL3 - Health System Liguria Region - Genoa, Italy
European contact for cognitive primary prevention Liguria Region
TopMemory Center Director (Neuroscience & Psychotherapy)



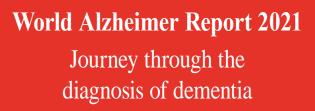


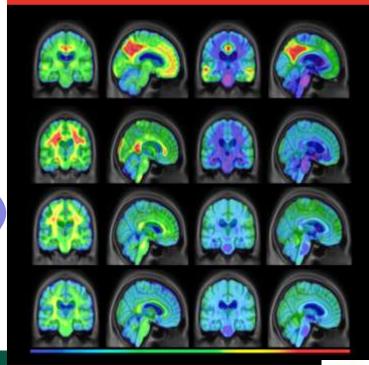






Over 55 million people live with dementia worldwide



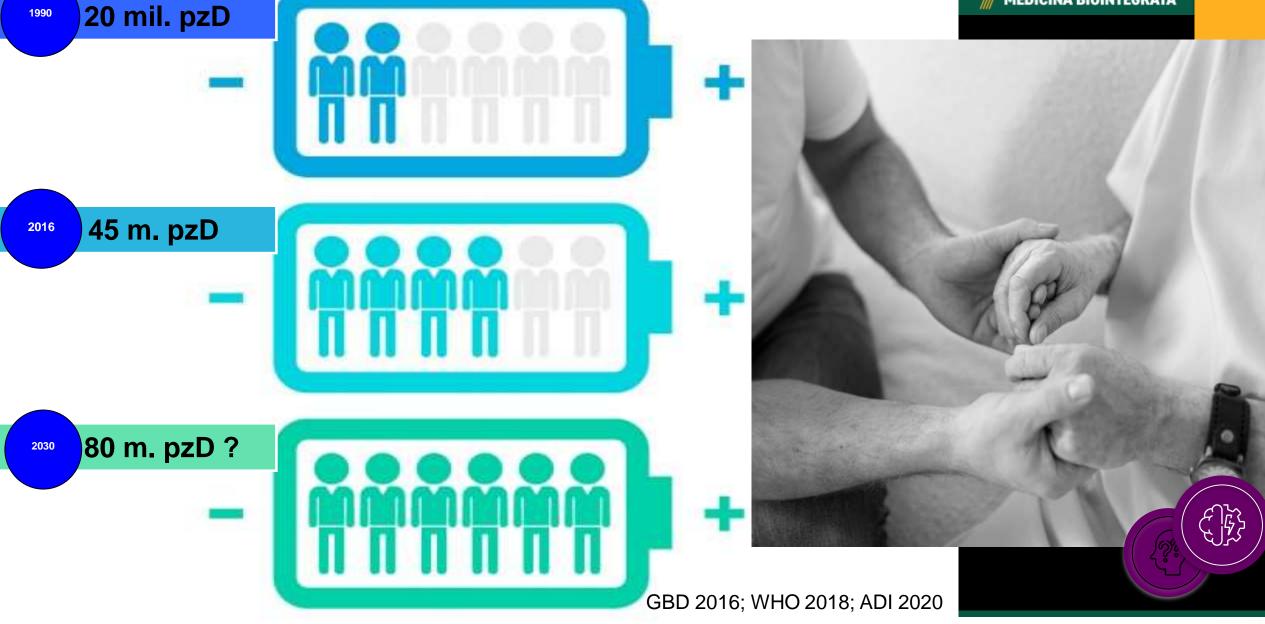


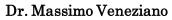




TOPMEMORY

Congresso Internazionale di MEDICINA BIOINTEGRATA









ALZHEIMER SYMPTONS •

MEMORY LOSS

DIFICULTY WITH

WORDS

CONFUSION WITH

TIME OR PLACE

1.2 milioni affetti da demenza (600 mila AD)

ISSN 2018; ISS 2022

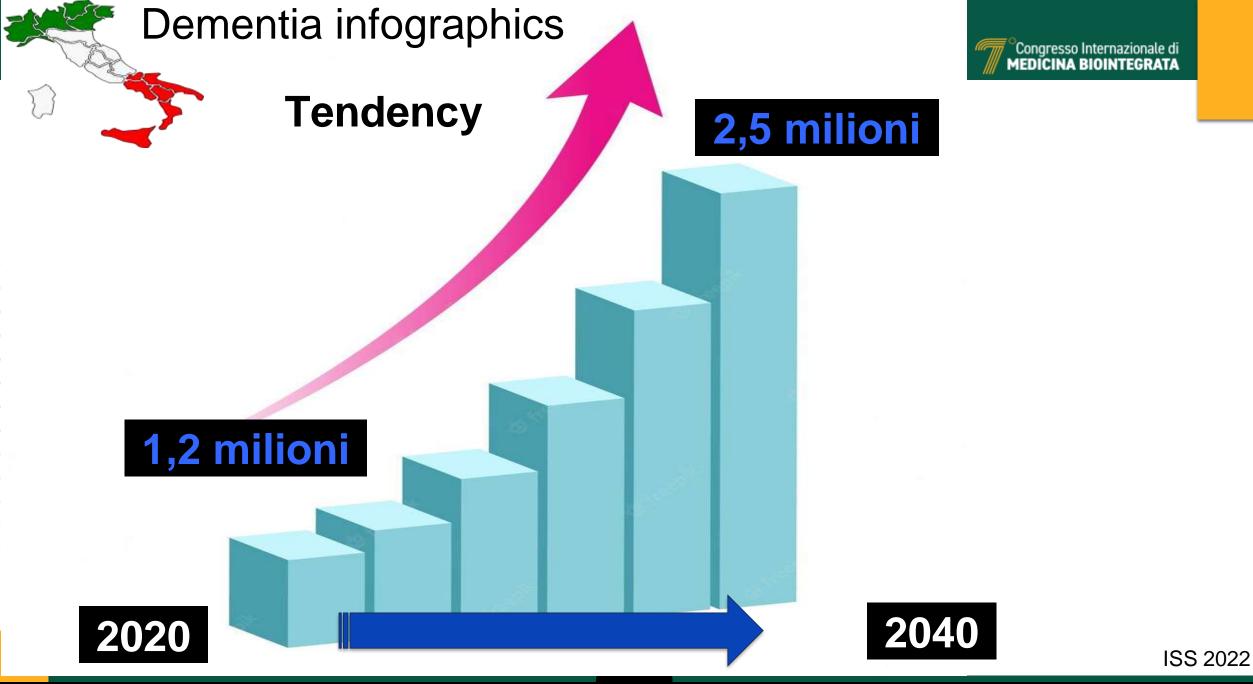
Dr. Massimo Veneziano



TROUBLE FOLLOWING CONVERSATION

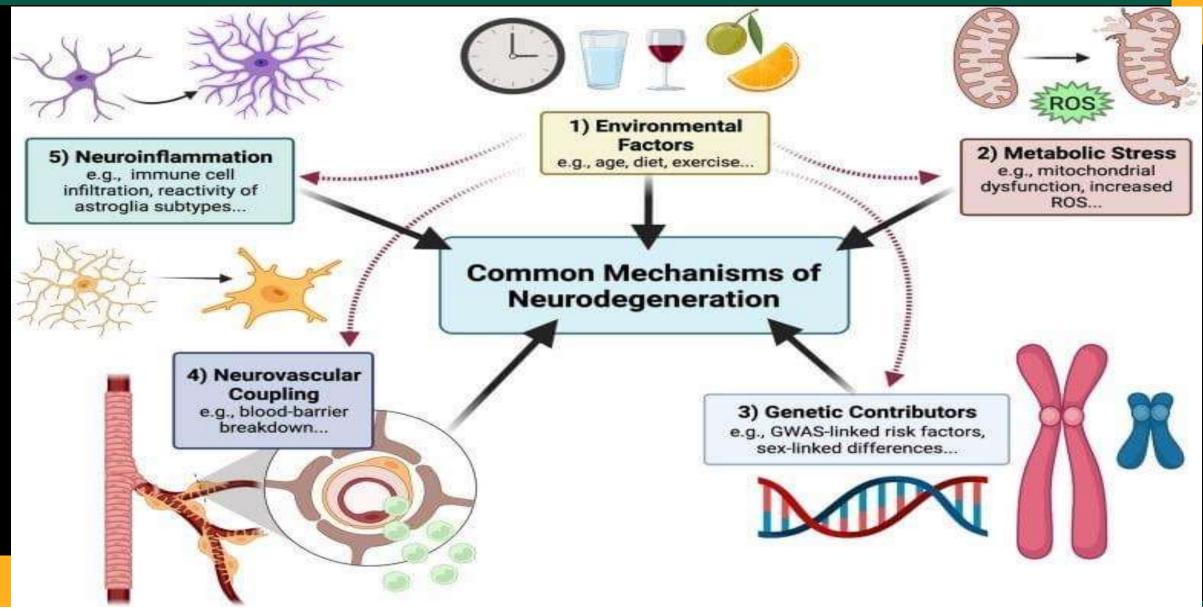








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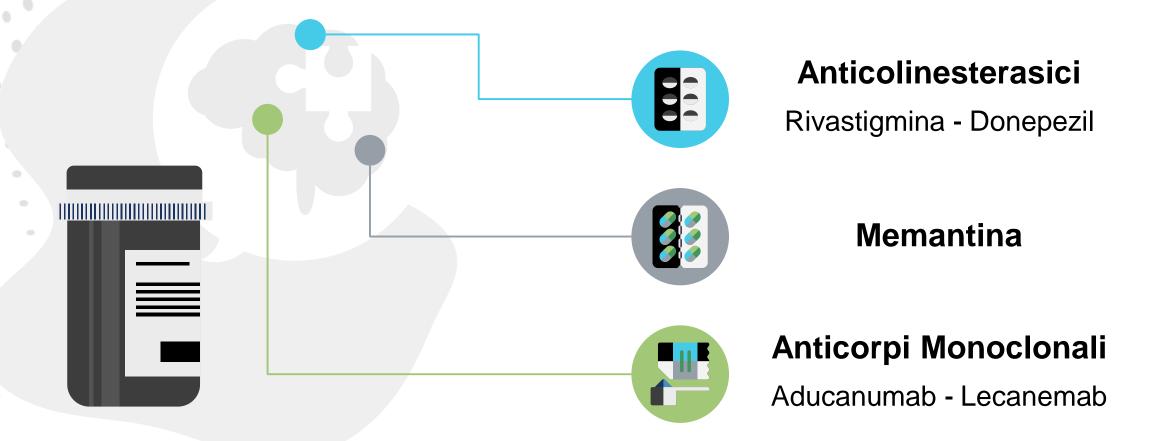


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Drugs that help dementia







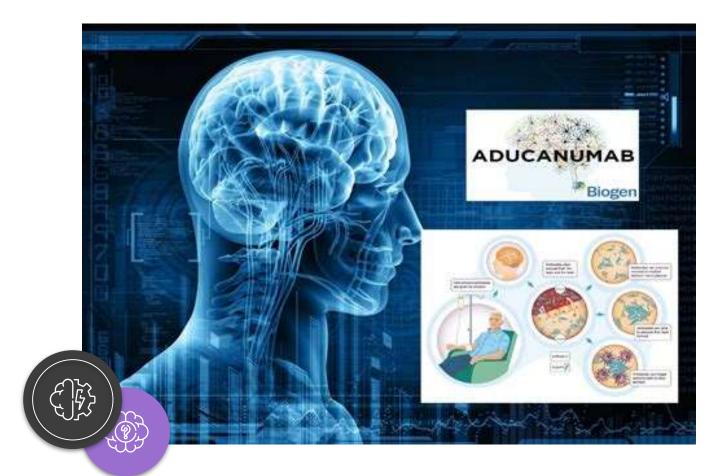
Dementia Anticorpi monoclonali



Aducanumab

Lecanemab

Una questione controversa



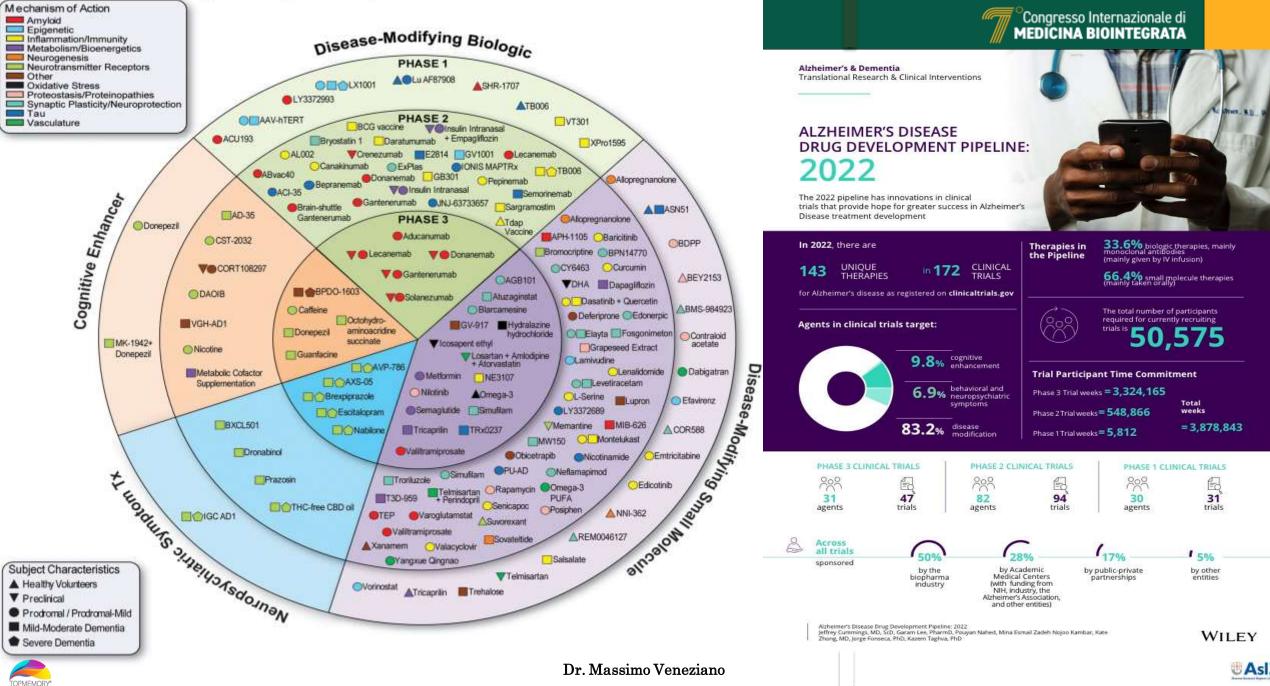
Aducanumab: Appropriate Use Recommendations. Cummings et al., 2021



Dr. Massimo Veneziano



2022 Azheimer's Drug Development Pipeline



CAsl3



The Lancet Commissions

Dementia prevention, intervention, and care: 2020 report of \mathcal{O} is the *Lancet* Commission

Gill Livingston, Jonathan Huntley, Andrew Sommerlad, David Ames, Clive Ballard, Sube Banerjee, Carol Brayne, Alistair Burns, Jiska Cohen-Mansfield, Claudia Cooper, Sergi G Costafreda, Amit Dias, Nick Fox, Laura N Gitlin, Robert Howard, Helen C Kales, Mika Kivimäki, Eric B Larson, Adesola Ogunniyi, Vasiliki Orgeta, Karen Ritchie, Kenneth Rockwood, Elizabeth L Sampson, Quincy Samus, Lon S Schneider, Geir Selbæk. Linda Teri, Naaheed Mukadam

Executive summary

The number of older people, including those living with dementia, is rising, as younger age mortality declines. However, the age-specific incidence of dementia has fallen in many countries, probably because of improvements in education, nutrition, health care, and lifestyle changes. Overall, a growing body of evidence supports the nine potentially modifiable risk factors for dementia modelled by the 2017 Lancet Commission on dementia prevention, intervention, and care: less education, hypertension, hearing impairment, smoking, obesity, depression, physical inactivity, diabetes, and low social contact. We now add three more risk factors for dementia with newer, convincing evidence. These factors are excessive alcohol consumption, traumatic brain injury (TBI), and air pollution. We have completed new reviews and meta-analyses and incorporated these into an updated 12 risk factor life-course model of dementia prevention. Together the 12 modifiable risk factors account for around 40% of worldwide dementias, which consequently could theoretically be prevented or delayed. The potential for prevention is high and might be higher in low-income and middle-income countries (LMIC) where more dementias occur.

Our new life-course model and evidence synthesis has paramount worldwide policy implications. It is never too early and never too late in the life course for dementia prevention. Early-life (younger than 45 years) risks, such as less education, affect cognitive reserve; midlife (45–65 years), and later-life (older than 65 years) risk factors influence reserve and triggering of neuropathological developments. Culture, poverty, and inequality are key drivers of the need for change. Individuals who are most deprived need these changes the most and will derive the highest benefit.

Policy should prioritise childhood education for all. Public health initiatives minimising head injury and decreasing harmful alcohol drinking could potentially reduce young-onset and later-life dementia. Midlife systolic blood pressure control should aim for 130 mm Hg or lower to delay or prevent dementia. Stopping smoking, even in later life, ameliorates this risk. Passive smoking is a less considered modifiable risk factor for dementia. Many countries have restricted this exposure. Policy makers should expedite improvements in air quality, particularly in areas with high air pollution.

We recommend keeping cognitively, physically, and socially active in midlife and later life although little evidence exists for any single specific activity protecting

www.thelancet.com Vol 396 August 8, 2020

against dementia. Using hearing aids appears to reduce the excess risk from hearing loss. Sustained exercise in midlife, and possibly later life, protects from dementia, perhaps through decreasing obesity, diabetes, and cardiovascular risk. Depression might be a risk for dementia, but in later life dementia might cause depression. Although behaviour change is difficult and some associations might not be purely causal, individuals have a huge potential to reduce their dementia risk.

In LMIC, not everyone has access to secondary Prof. Prof. education; high rates of hypertension, obesity, and hearing loss exist, and the prevalence of diabetes and Rese smoking are growing, thus an even greater proportion of (Poep dementia is potentially preventable.

Amyloid- β and tau biomarkers indicate risk of progression to Alzheimer's dementia but most people with normal cognition with only these biomarkers never develop the disease. Although accurate diagnosis is important for patients who have impairments and functional concerns and their families, no evidence exists to support pre-symptomatic diagnosis in everyday practice.

Our understanding of dementia aetiology is shifting, with latest description of new pathological causes. In Mukadami; Barmad Haringey Men oldest adults (older than 90 years), in particular, mixed dementia is more common. Blood biomarkers might hold promise for future diagnostic approaches and are more scalable than CSF and brain imaging markers.

Wellbeing is the goal of much of dementia care. People with dementia have complex problems and symptoms in many domains. Interventions should be individualised and consider the person as a whole, as well as their family carers. Evidence is accumulating for the effectiveness, at least in the short term, of psychosocial interventions tailored to the patient's needs, to manage neuropsychiatric symptoms. Evidence-based interventions for carers can reduce depressive and anxiety symptoms over years and be cost-effective.

Keeping people with dementia physically healthy is of old A intervention of the interv

G. Livingston et al., Lancet 2020 ⁴¹³

July 30, 2020 https://doi.org/10.1016/ S0140-6736(20)30867-6 Division of Psychiatry (Prof G Livingston MD, J Huntley PhD, A Sommerlad PhD, Prof E LSamspon MD, Prof E LSamspon MD, N Mukadam PhD), Dementia Research Centre, UK Dementia (Prof N Fox MD), and Department of Epidemiology

and Public Health (Prof M Klvimäki FMedSci), University College London, London, UK; Camden and Islington NHS Foundation Trust, London, UK

 (Prof G Livingston, J Huntley, A Sommerlad, Prof C Cooper, S G Costafreda, Prof R Howard,
N Mukadam); Barnet, Enfield, and Haringey Mental Health

(Prof E L Sampson); National Ageing Research Institute and Academic Unit for Psychiatry o Old Age, University of Melbourne, Royal Melbo Hospital, Parkville, VIC. Australia (Prof D Ames MD); University of Exeter, Exeter, Uk (Prof C Ballard MD): Faculty of Health: Medicine, Dentistry and Juman Sciences, University of Plymouth, Plymouth, UK (Prof S Banerjee MD); Cambridge stitute of Public Health University of Cambridge Cambridge, UK rof C Brayne MD); Departmen

(Prof C Brayne MD); bepartment of Old Age PSN; bepartment of Old Age PSN; UK (Prof A Burns MD); Department of Health Promotion, School of Public Health, Sackler Faculty of Medicine (Prof J Cohen-Mansfield), and Minerva Center for Interdisciplinary Study of End of Life (Prof J Cohen-Mansfield),

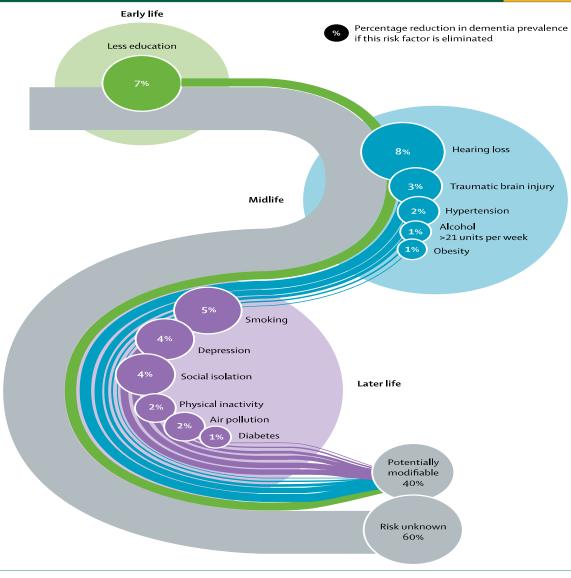


Figure 7: Population attributable fraction of potentially modifiable risk factors for dementia



Asl3



Multi-target therapies as an emerging strategy for **Alzheimer's** disease treatment

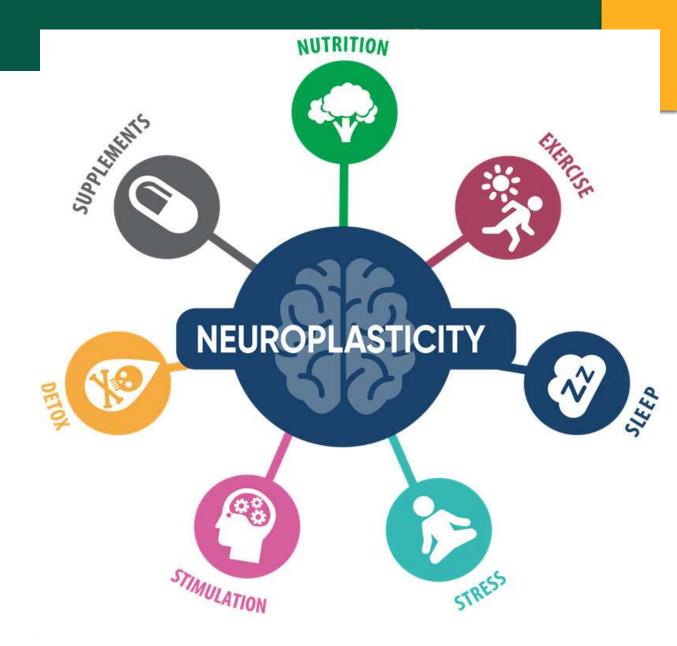
D. Elmaleh et al., 2019; J. Yaojun et al., 2022







"a multi-therapeutic program that simultaneously targets multiple factors underlying the AD network may be more effective than a monotherapeutico approch"



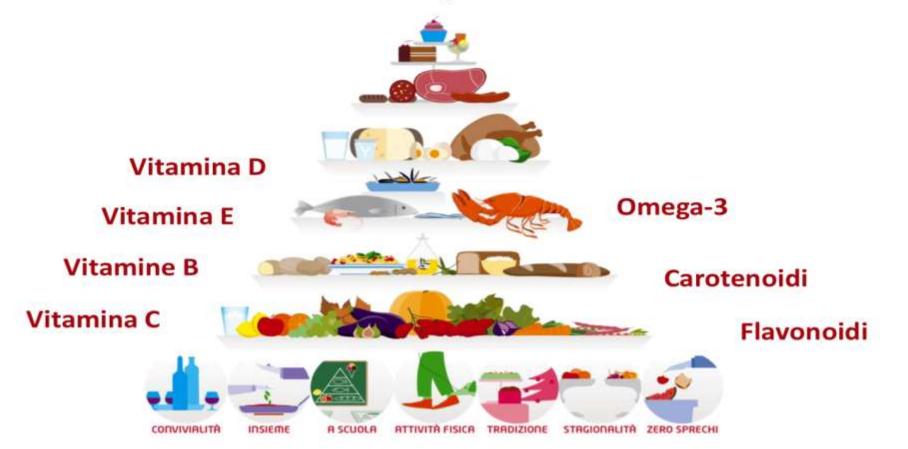






Numerosi studi negli ultimi anni si sono dedicati ad individuare nutrienti in grado di prevenire o rallentare il declino cognitivo.

Tra questi:









Nutrients and nutritional patterns in neurocognition and Alzheimer's disease risk

ficuloprotoctive roods.
Vegetables
Fruits
Whole grains
Soy beans
Nuts
Moderate fish intake
Reduced caloric intake or
caloric restriction mimetics
(e.g., resveratrol)
Extra virgin olive oil
Legumes
Berries
Dark green leafy vegetables
Probiotics

Neuroprotective foods:

Supplementation of neuroprotective nutrients: B vitamins n-3 PUFAs Vitamin E Vitamin D Curcumin/turmeric Sulforaphane Genistein Fortasyn Connect and other multi-component supplementations

Controversial evidence

Foods detrimental for neurocognition: Saturated or trans-unsaturated fats Red meat Poultry High-fat dairy products Processed foods Refined sugars (e.g., sweets, sugar-sweetened soft drinks) Pastries Fructose- and purine-rich foods

Other factors:

Impaired systemic availability of certain nutrients e.g., DHA, EPA, choline, B vitamins (e.g., B1, B12, folate), vitamin C, vitamin E, vitamin D, uridine, choline, minerals MetS-related risk factors (e.g., hyperhomocysteinemia, insulin resistance) Decrease of plasmatic phosphatidylcholine species Increase of plasmatic carbonyl proteins

Nutritional deficiencies in early life

High evidence

Neuroprotective

diets:

DASH

MIND

MeDi

High evidence

Beneficial effects on neurocognition

Detrimental effects on neurocognition





JAMA Neurology

Association of Antioxidant Supplement Use and Dementia in the Prevention of Alzheimer's Disease by Vitamin E and Selenium Trial (PREADVISE)

Richard J. Kryscio, Ph.D.^{1,2,3,4}, Erin L. Abner, Ph.D.^{1,2,3,5}, Allison Caban-Holt, Ph.D.^{1,2}, Mark Lovell, Ph.D.^{1,2,6}, Phyllis Goodman, M.S.7, Amy K. Darke, M.S.7, Monica Yee, B.A.⁸, John Crowley, Ph.D.⁹, and Frederick A. Schmitt, Ph.D.^{1,2,9}



Vitamin E for Alzheimer's dementia and mild cognitive airment (Review)

N, Llewellyn D, Isaac MGEKN, Tabet N



use of vitamin E and selenium did not forestall dementia and are not recommended as preventative agents

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R.J. Kryscio et al., 2017 Farina et al., 2018



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Dr. Massimo Veneziano



JAMA Neurology

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Neither

anti-oxidant

supplement

prevented

dementia

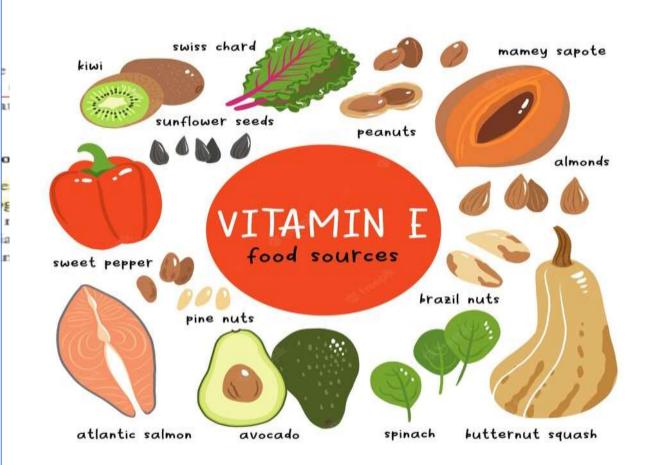
¹Sanders-Brown Center on Aging, University of Kentucky, Lexington, KY 40536, USA ²Alzheimer's Disease Center, University of Kentucky, Lexington, KY 40536, USA

Department of Biostatistics, University of Kentucky, Lexington, KY 40536, USA



Vitamin E for Alzheimer's dementia and mild cognitive impairment (Review)

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R.J. Kryscio et al., 2017 Farina et al., 2018



Dr. Massimo Veneziano





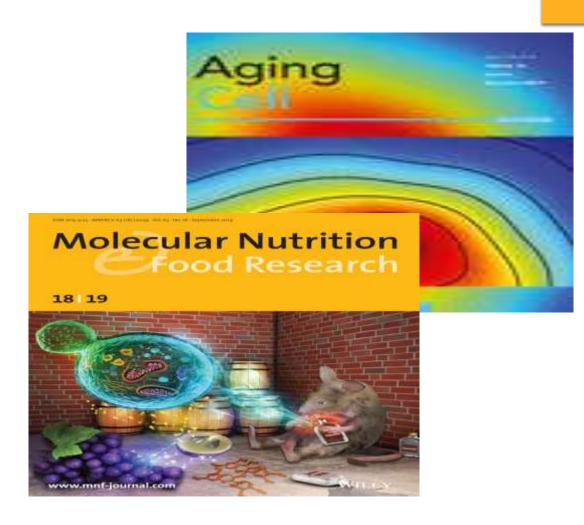
Nicotinammide adenina dinucleotide (NAD+) NAD+ supplementation reduces neuroinflammation and cell senescence in a transgenic mouse model of Alzheimer's disease

Y. Hou et al., 2021



Choline - Citicoline

Lifelong choline supplementation reduces Aß pathology in mice and produces profound benefits. **Suggest that simply** modifying diet throughout life may reduce AD pathology



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T.J. Mellot et al., 2017; Y. Wang et al., 2019; R. Velazquez et al., 2019; P. Jasielski et al., 2020





The current literature creates optimism that choline may be an avenue to ensure a graceful aging process without cognitive decline.

Lifelong Choline diet improves Alzheimer's symptoms Female mice bred to display Alzheimer's-like symptoms develop progressive cognitive decline. When mice received additional choline in their diet, they showed marked improvement in cognitive performance. Choline reduces the activation of microglia. **Overactivation of these** housekeeping cells in the brain is linked with neurodegeneration.







Bacoba Munnieri

^CCongresso Internazionale di MEDICINA BIOINTEGRATA

RESEARCH ARTICLE

Management of she will be

Anatomical markers and Phytochemical study of different plant parts of Bacopa monnieri (L.) Wettst.

Yor therey Asia *, Chandro Narrolt' and Patti Astanda'

Int. L of Life Sciences, 2017, Vol. 5 (3): 379-386

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Received BRAT 2017 dauge remnert (L) Waters (Scropfederiscov) conaccounted in Children "brahest", has been used in the traditional sectors of the Published in myord Receivers' on it increases mental startly and boats size also being used as ant-inflammatory, analysis; an anticoplant and at it concerning opent. The present study Br. Bretail Chiefes provide statuteista antisteast teachers for east, at with this mails preliminary photocharmost ansists war. the dot attely in Parabase Area, Diamb's Narmh and the presence of major considers antidolities which car Park Arreads (2017) Anatomical of hearthouty of the Afferson plant parts of Record mean select and Piptudeenal staty of chaitsgetiding horses for rost and stres are simple a different plant parts of Aurope measure (L.) Weiters, Aurora invest (torood with spirid theolerings, pitted trachelds and epidermiil kikar idultizet, zenille, neutizelleller intek 12/0 Streem 518: 575-896 colours scalate crystals. Pressure of fact, types of dom and discover in the same field of makes ander 453 marsh the nurface preparation as well as in the provise put estimated hall that is the mapse observation of the Departure in 2011 house bit. The chattenetiding furtures out by used as inclusioned at In all open protes attacks under the lates of the Crestin Germoni indeptioning of rest stem and leaf of the st phatechaestad analysis recealed the pressnes of a Intelligibles Reported in the Bertri Licence, which permits and Batomoids, turning, carboligidustry, proteins and and doublectors in any methods. different place parts of Recept sevenier while state president the original much it showed that alkedotik ting /a thy weight in rect, store a property stind the and in motto be 1.67 a 0.077, 47.00 a bill and 15.07 a 2.00 respect the second ball for sheathing on 79 my weight in rook, men and had seen 7.53 a 8.71 17.88 + 2.01 respectively and Revenuents (sog 7g day to

V. Anju et al., 2017

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Abstract

1855: 2120-7817[e5531: 2320-9645]

A.F. Cicero¹, M. Bove¹, A. Colletti¹, M. Rizzo², F. Fogacci¹, M. Giovannini¹, C. I Medical and Surgical Sciences Dept. Alma Mater Studiorum University of Bologna, Italy; 2. Biomedical Department University of Palermo. Italy

Corresponding Author: Arrigo F.G. Ckero, MD, PhD, Medical and Surgical Sciences Dept, Via Albertoni 15, 40138 Bologna, e-mail: arrigo.cicrotifumibo.it

Introduction Abstract BACKCROUND: The prevalence of senile dementia is increasing worldwide, especially in the developed countries. Nevertheless, drug therapy isn't often enough to treat this condition. Researchers are evaluating the possible impact of a preventive approach, based on an improvement of lifestyle and the intake of micronutrients. Moreover, there is an increasing interest for combined nutricenticals that an act is memory and the intake of micronutrients. Moreover, there is an increasing interest for combined nutraceuticals that can act as memory and learning enhancers, with a significant and beneficial potential on the cognitive disorders. on the cognitive disorders. OBJECTIVE: To evaluate the effects of a rational assemblage of nutraceuticals on cognitive functions in a sample of 30 elderly language. Many gen subjects. DESIGN: Double bind, cross-over designed trial versus placebo impairment in older a Stating: outpatient clinical practice. PARTICIPANTS: 30 elderly subjects with basal Mini-Mental State Examination score between 20 and 27 and self-perceived cognitive decline. State Examination score between 20 and 27 and self-perceived port State Stamination score between 20 and 27 and self-perceived port State Stamination (State State Sta (7). It is well known th Key words: Clinical trial, cognitive impairment, depression, dietary

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Received June 2, 2016 A control for multication June 30, 2016

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A. Cicero et al., 2018



Short-Term Impact of a Combined Nutraceutical on Cognitive Function, Perceived Stress and Depression in Young Elderly with Cognitive Impairment: A Pilot, Double-Blind, Randomized Clinical Trial

J Prov Alz Dis 2016 inpress Poslished online August 23, 2016, http://dx.doi.org/10.14280/jpad.2016.110

The evidence bas is expanding r

longer-lasting process attention across the ti Maybe its mechanism of of brain serotonin, do

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IOURNAL OF GERONTOLOGY AND AGING HEALTHCARE

Evaluation of the Long-Term Effectiveness of the Combined Nutraceutical Synaid® on a Large Cohort of Subjects with Different

Degree of Cognitive Impairment: Results from a 24-Month Prospective Clinical Trial Manufactory Venezitatio/+ and Rathery Scient?

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INTRODUCTION completes depline as something of a second backof regulate impairment and demonstraand of the The programs domag The programmer demographic aging of the ends population will deally the processing others provide the set to be the processing of the processing of the set of the processing of the set of the processing of the processing of the set of the processing of the processing of the processing of the set of the processing of the processing of the processing of the set of the processing of the processing of the processing of the set of the processing of the processing of the processing of the set of the processing of the processing of the processing of the set of the processing of the processing of the processing of the set of the processing of the processing of the processing of the set of the processing of the processing of the processing of the set of the processing of the processing of the processing of the set of the processing of the processing of the processing of the set of the processing of the processing of the processing of the set of the processing of the processing of the processing of the set of the processing of the processing of the processing of the set of the processing of the processing of the processing of the set of the processing of the set of the processing of the proc The bactering age in another of the second of the decision for the test of destands and all ones e become graph of the second second of the second of the second s Theoretical molecting the impact of any findly emity should reprove a goal in the light ignore demonster." which doubl puts and the completency of the agong related cares, maning the an called "longerity check". The longerity checks successed agong related reduccitizity regenters declars? a mounted frailer. Truity or addition for Among the operatural ideasa' digene using the risk of disability, mechanics, deterrors, deterring to fire over toth fire your relevant uncrussing torsid in terms of fire mendous and providence, dealthing in 4.00 would be takend to greater regulation valuesability." The lask between physical providence in the last 21 years 77 Convertinhading and requires thating wended assesses the base 110 and here of principle are allocated here 11th Olympic Tree comparisons," so much on that Advantage it does not from other linear a

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M. Veneziano et al., 2021

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Curcumin

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Curcumin, also known as diferuloyImethane, is a turmeric-derived polyphenol, with multiple applications in traditional medicine for more than 2000 years

H. Hatcher et al., 2008; T. Farooqui et al., 2019; B. Salehi et al., 2020





Traumatic Brain Injury

 Inhibits the expression of brain-derived neurotrophic factor (BDNF)

Multiple sclerosis

- Inhibits EAE, reduces the number of inflammatory cells
- Regulates CD4+ T helper cell response

Epilepsy

- Inhibits the mammalian target of the rapamycin (mTOR) pathway,
- Attenuates the expression of GFAP

Spinal Cord Injury

- Increases neurons survival
- Attenuates astrocytes reactivation
- Supresses the glial scar formation

Curcum

Inhibits MAO enzyme

Modulates the expression of

serotonin and dopamine

Stroke

- Inhibits iNOS expression
- Prevents peroxynitrite-mediated BBB alterations
- Prevents glial cells activation

Alzheimer disease

- Inhibits the accumulation of Aβ
- Inhibits Tau hyperphosphorylation
- Inhibits NF-κB
- Neuroprotective effects
- Antioxidant effects

Parkinson's disease

 Inhibits and reverse formation of α-synuclein aggregates

B. Salehi et al., 2020

CAsl3

Depression

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Curcumin

Dementia

The protective effects of **Curcumin toward** ameliorating the memory impairment and pathological deficits in AD mouse model. **Could be a potential food** supplement for long-term treatment of AD



H. Heng Tai et al., 2018





Curcumin



Curcumin has demonstrated beneficial effects on brain health through several mechanisms such as antioxidant, amyloid βbinding, anti-inflammatory, tau inhibition, metal chelation, neurogenesis activity, and synaptogenesis promotion.



B. Salehi et al., 2021







Curcumin

Dementia







E.K. Akkol et al., 2023



Curcumin



The therapeutic limitation of curcumin is its bioavailability, and to address this problem, new nanoformulations are being developed.



B. Salehi et al., 2020; 2021; E.K. Akkol et al., 2023



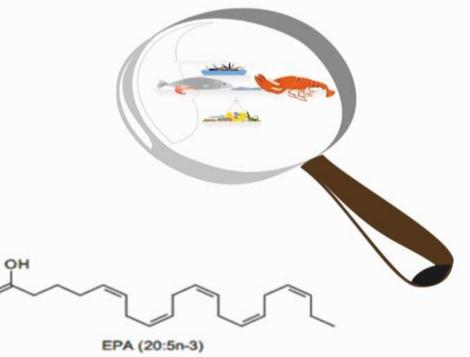




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- Azione diretta sull'integritá delle membrane neuronali
- Maggiormente studiati sono:
 - acido docosaesaenoico (DHA)
 - acido eicosapentaenoico (EPA)

DHA (22:6n-3)



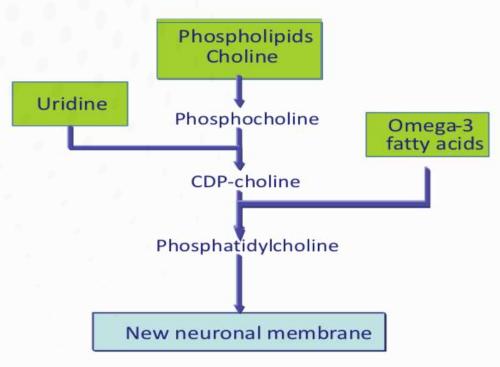




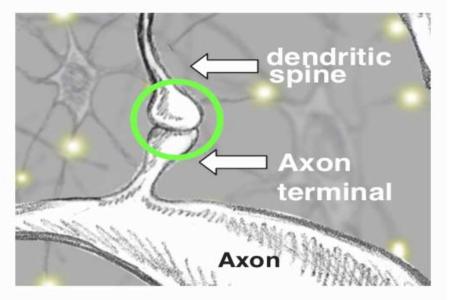




The Kennedy pathway for biosynthesis neuronal membrane







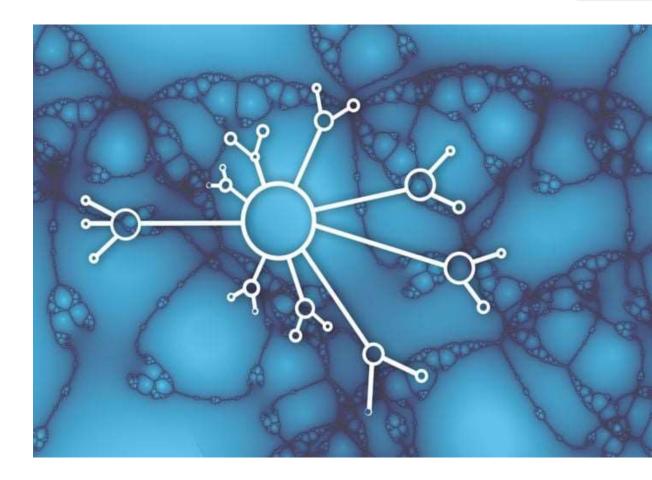








Lipoxidation derived protein damage also increases with age in a region specific manner



Horrocks et al., 1981; Soderberg et al., 1990; Svennerholm et al., 1991; Svennerholm et al., 1994; McNamara et al., 2008; Ledesma et al., 2012; Hancock et al., 2015, 2017; Norris et al., 2015; Dominguez et al., 2016; Cabre et al., 2017, 2018; Diaz et al., 2018; Dominguez-Gonzalez et al., 2018; Jove et al., 2019, 2021; Pamplona et al., 2019; Mota-Martorell et al., 2022

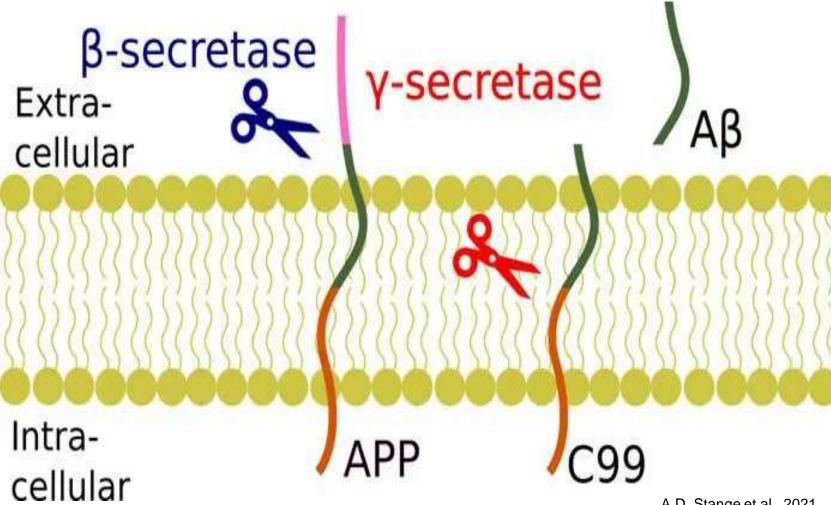




Omega 3

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Ruolo determinante dei lipidi nel funzionamento della C99, proteina generata dalla scissione dell'APP che porta alla formazione della β**Amiloide nell'AD**



A.D. Stange et al., 2021







Omega 3

Dementia

Brain lipidomic analyses in sAD have identified multiple diseasespecific lipid alterations and lipid derived molecular damage



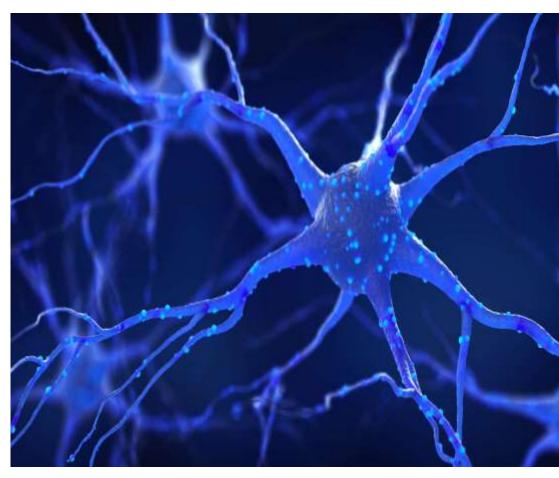
Farooqui et al., 1988; Pamplona et al., 2005; Han, 2010; Haughey et al., 2010; Martin et al., 2010; Terni et al., 2010; Frisardi et al., 2011; Wood et al., 2012; Zhu et al., 2012; Kosicek & Hecimovic, 2013; Sultana et al., 2013; Touboul & Gaudin, 2014; Naudi et al., 2015; Zabel et al., 2018; Jove et al., 2021





Omega 3

Non-targeted lipidomics analysis was conducted in post-mortem human frontal cortex area 8 and white matter of the frontal lobe centrum semi-ovale to identify lipidomes in middle-aged individuals with no neurofibrillary tangles and senile plaques, and cases at progressive stages of sporadic Alzheimer's disease.



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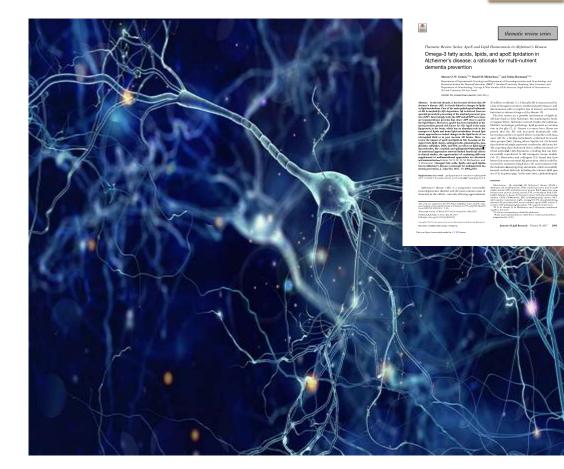


Omega 3

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AD is closely linked to changes in lipids or lipid metabolism

reduced brain atrophy and increased cognitive improvement of patients that had the highest bloodlevel of n3Fas, especially DHA



M. Grimm et al., 2018





Omega 3

Congresso Internazionale di MEDICINA BIOINTEGRATA

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¹⁰⁰⁰ A Namel Antichellammatary Role of Drange-I PUTAs in Prevention and Tradment of Athenna fermits and Vacular Cognitive Impairment and Demonta

Control Web, Hum, Yu-Wei, Yuanhao Yu, Hu Yu, Yu Yu, Hu Yu Yu, Hu Xu, Yu Xu,

This review describes the link between VCID (vascular cognitive impairment and dementia) and inflammation, as well as how omega-3 PUFA supplementation may be useful to prevent and treat inflammatory-related diseases.



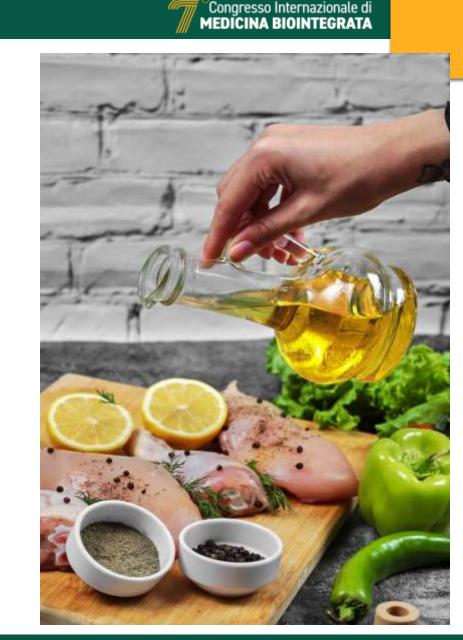
M. Simonetto et al., 2019





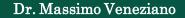
Mediterranean diet rich in antioxidants, fiber and omega-3 polyunsaturated fatty acids may have a protective effect on the neurodegenerative process.

G.C. Roman et al., 2019; S. Sliwinska et al., 2021; O. Stefaniak et al., 2022









Omega 3

Microbiota

Congresso Internazionale di **MEDICINA BIOINTEGRATA**

The Mediterranean diet (MeDi) may be neuroprotective by modulating gut microbiota.

MeDi was associated with a lower risk of AD.



intrai hornopaus



Review Article

Mediterranean diet adherence, gut microbiota, and Alzheimer's or Parkinson's disease risk: A systematic review

Rebecca J. Solch⁺, Julia O. Aigbogun⁺, Andrew G. Voyladjis⁺, Geant M. Talkington⁺, Revenda M. Darenskourg⁺, Samariha O'Connell⁺, Keith M. Pickett⁺, Sarah R. Perez⁺ Demetrius M. Maroganose^{+,+}

ABSTRACT

Inpariment of Neurology, Takine University School of Medicine, Anne Obiane, EA 199772, United States of America Office of Academic Affinite and Provent, Name University, How Obiani, LA 20112, Stimula of America Radiabil Massa University of the Head Resizure, School School, School 20112, Stimula School of America Namio School S

ARTICLEINFO

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1. Introduction

beneficial effects of adhering to the MeDi may be mediated by the gat microbial composition.

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Bitamining an enhance gat environment may be important for builty lovin aging, an dyrkolas, an imbalmon it the microkial environment, has been proposed as a mechanian for near-of-formating inding to A0 or 100 C). Got dyrkolas rung be unitgened by convening a dist tight in Effer and polyhomols, such as MoL, by increasing bending an bacterial to 122, MoL affective range process the A0 or D formula modulation of the gat microkios. This systematic review address incodesign pays the complexer informability between MoL, gat microlease the systematic review addresses.

The Witten that have in flowr, may be associated with AD or PD [2,4]. The Moditermenon dist [MeRich, high in numtion down foods, may be beneficial nor only for health overall, but not bo for handling brains angle, MeRi adherence is associated with a lower risk for dementio and, panality, PD [2,6]. MeRi is an aluminate source of fiber in contrast to the weeters det. A fiber is a num-energy solution to gat microbiolo, fiber

Aldrenizziow: AD, Alzheimer's Disease, PO, Parkiesser's Disease, MuDi, Wednerraman der

Corresponding autors, if-mail address: drassgammers(reduce.edu (0.00, Maragamore),

bing: video on (Ph.2014) (pp. 2002) 120306 Interview II Sentines U.B. Bentinet in restand form 1.4 Isomory 2022; Averagind 28 Assessy 2022 Available online 20 Assessy 2002 0023 51200 (d) 2022 The Analoss, Published by Elsevier B. This is an open access article and/or the CE BP-6C-90 House (http://orost/weistheat.org/foorsec/fr en el. 3.8.7).

biots, and AD or PD.

R. J. Solch et al., 2022





Microbiota

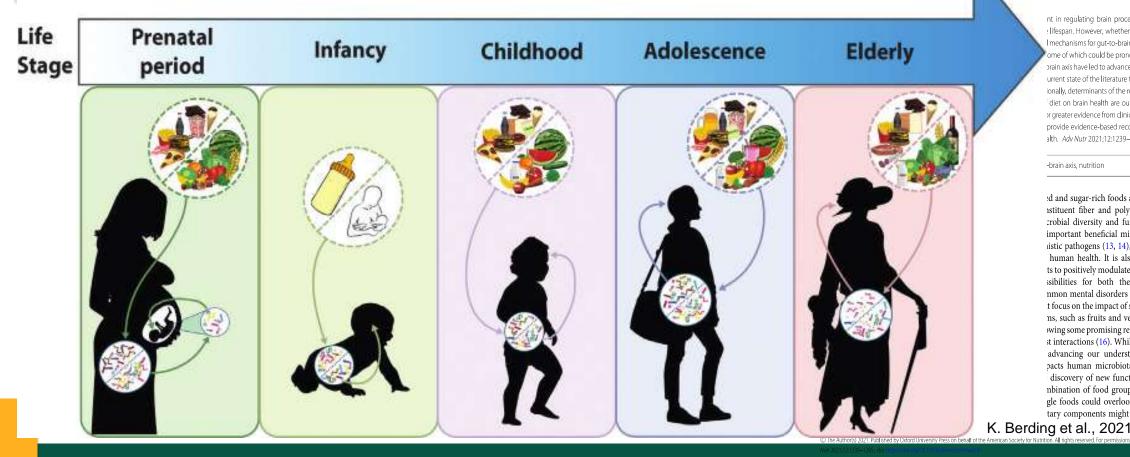
[©]Congresso Internazionale di MEDICINA BIOINTEGRATA

Diet and the Microbiota-Gut-Brain Axis: Sowing the Seeds of Good Mental Health

Kirsten Berding,¹ Klara Vlckova,¹ Wolfgang Marx,² Harriet Schellekens,^{1,3} Catherine Stanton,^{1,4} Gerard Clarke,^{1,5} Felice Jacka,^{2,6,7,8} Timothy G Dinan,^{1,5} and John F Cryan^{1,5}

¹APC Microbiome Ireland, Cork, Ireland; ²Deakin University, iMPACT – the Institute for Mental and Physical Health and Clinical Translation, Food & Mood Centre, School of Medicine, Barwon Health, Geelona, VIC, Australia; ³Department of Anatomy and Neuroscience, University Colleae Cork, Cork, Ireland; ⁴Teagasc Food Research Centre, Moorepark, Fermoy, Cork, Ireland; ⁵Department of Psychiatry and Neurobehavioural Sciences, University College Cork, Cork, Ireland: ⁶Centre for Adolescent Health. Murdoch Children's Research Institute. Parkville, VIC, Australia; ⁷Black Dog Institute, Randwick, NSW, Australia; and

ialas, OLD, Australia



Diet is one of the major factors involved

in shaping the gut microbiota

composition across the lifespan

nt in regulating brain processes and behavior. Diet is one of the : lifespan. However, whether and how diet can affect the brain via I mechanisms for gut-to-brain communication have been identified, ome of which could be prone to dietary modulation. Animal studies prain axis have led to advancements in our understanding of the role urrent state of the literature triangulating diet, microbiota, and host ionally, determinants of the responsiveness to a dietary intervention diet on brain health are outlined. In particular, we emphasize the or greater evidence from clinical populations. While promising results provide evidence-based recommendations for the development of alth. Adv Nutr 2021;12:1239-1285

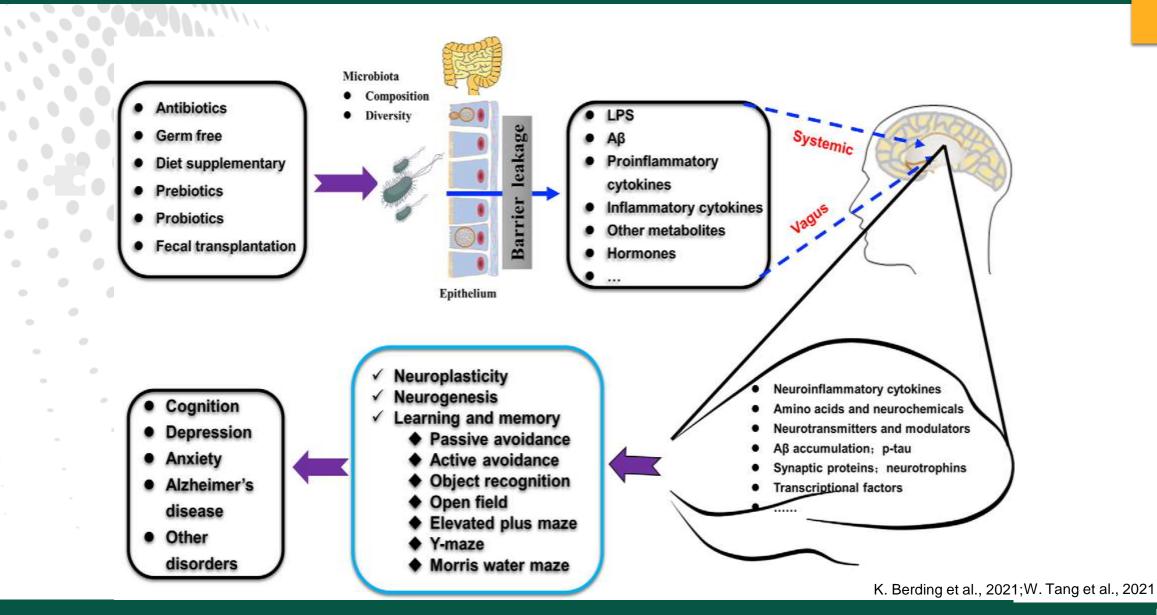
-brain axis nutrition

ed and sugar-rich foods and low in plant foods with their istituent fiber and polyphenols can lead to the loss of crobial diversity and function as well as the extinction important beneficial microbes and expansion of opporlistic pathogens (13, 14), with far-reaching consequences human health. It is also recognized that using healthy ts to positively modulate gut-brain communication holds ssibilities for both the prevention and treatment of nmon mental disorders (15). There are emerging studies t focus on the impact of supplementation with single food ns, such as fruits and vegetables high in prebiotic fibers, wing some promising results in modulating microbiomest interactions (16). While such approaches are important advancing our understanding of how a specific food pacts human microbiota and health and could lead to discovery of new functional foods, humans consume a nbination of food groups with every meal and studying gle foods could overlook the potential synergistic effect tary components might have, not just on overall health,

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Microbiota

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Role of gut dysbiosis in triggering inflammation in the brain and its contribution to Alzheimer's disease (AD) pathogenesis.

C. Chan et al., 2022



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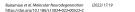


Microbiota

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There is strong increasing evidence supporting a role for the gut microbiome in the pathogenesis of Alzheimer's disease, including efects on synaptic dysfunction and neuroinfammation, which contribute to cognitive decline.

Putative early intervention strategies based on microbiota modulation appear therapeutically promising for Alzheimer's disease but still require further investigation.



Molecular Neurodegeneration

Microbiota in neuroinflammation and synaptic systematic dysfunction: a focus on Alzheimer's disease

Diane Bairamian^{1†}, Sha Sha^{1,2†}, Nathalie Rolhion^{3,4}, Harry Sokol^{3,4,5,6}, Guillaume Dorothée¹, Cynthia A. Lemere^{7†} and Slavica Krantic^{1+†}©

Abstract

Background: The implication of gut microbiots in the control of brain functions in health and disease is a novel, currently energing concept. Accumulating data suggest that the gut microbiots earth is action at sain i part by modulating neuroinflammation. Given the link between neuroinflammatory changes and neuronal activity. It is plausible that gut microbiot may affect neuronal functions indicated by impacting incrogla, a key player in neuroinflammation. Indeed, increasing evidence suggests that interplay between microgla and synaptic dysfunction may involve microbiota, among other factors. In addition to these indicet incroglad-seep player actions of microbiota on neuronal activity. It has been recently recognized that microbiota could also affect neuronal activity directly by stimulation of the vagus neve.

Main messages: The putative mechanisms of the indirect and direct impact of microbiota on neuronal activity are discussed by focusing on Alzheimer's disease, one of the most studied neurodegenerative disorders and the prime cause of dementia worldwide. More specifically, the mechanisms of microbiota-mediated microglal-alterations are discussed in the context of the perjetute and central inflammation corse-table. Next, we highlight the role of microbiota in the regulation of humonal mediators of peripheral immunity and their impact on vagus nerve stimulation. Finally, we address whether and how microbiota perturbations could affect synaptic neurotransmission and downteam cognitive dysfunction.

Conclusions: There is strong increasing evidence supporting a role for the gut microbiome in the pathogenesis of Alterner's disease, including effects to snapatic dyfurction and neuroinflammation, which combinate to cognitive decline. Plative early intervention strategies based on microbiota modulation appear therapeutically promising for Alterneris disease but sill require further investigation.

Keywords: Gut microbiota, Synaptic dysfunction, Alzheimer's disease, Peripheral immunomodulation, Neuroinflammation

ackground

hicakrantic@gmail.com

and Examinantia Carlo and Contract and Contr

Neurodegenerative diseases, such as Alzheimer's, Parkinon's and Huntington's diseases, are age-related neurodegenerative disorders, diagnosed chinically years after the pathogenesis has begun [1]. The development of a chronic inflammatory response in the brain, knowr as neuroinflammation, is a common exploring pathologica alleration in these disorders [2]. Remarkably, synaptic

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Dementia - Conclusioni - crisis -

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nutrients

The Role of Natural Antioxidants in the Prevention of Dementia—Where Do We Stand and Future Perspective

EINE-Charles Jonane Mannes Davids and State and State and State and State State State and State State and State State State and State S

Keywords: cognitive decline; Alcheimer's closure; midative strees; natural antioxidants; polyphor

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a (CC 10) house heye// memory/conserve/ fair", "opidemiology", and "cost" as keywords. Not, in order to gather relevant advances in research in the field of codative stress in Althemer's dense (AD) and the conditions Studi sull'uomo su grande scala

Miglioramento biodisponibilità di questi composti antiossidanti naturali

> Non sapremo mai il reale ruolo che svolgono nel curare o prevenire la demenza

Indicazioni su quando iniziare il trattamento e quali dosi utilizzare

A. Jurcau et al., 2022













Anxiety Disorders - Epidemiology



4% populazione monellale

WHO 2018



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Apprensione, agitazione, paura, senso di tensione interna.

DIAGNOSI

Presenza sintomi per almeno 6 mesi, per gran parte della giornata e in tutti gli ambiti di vita.

Sintomi non più controllabili e influiscono attività di vita quotidiana (sociale, professionale, famigliare).

Devono essere presenti almeno 3 dei seguenti sintomi: irrequietezza, disturbi del sonno, irritabilità, tachicardia, tensione muscolare, senso di soffocamento, astenia, facile affaticabilità, difficoltà cognitive.





DSM-5







The HUNT study

Bragantini, D., Sivertsen, B. et al., 2019



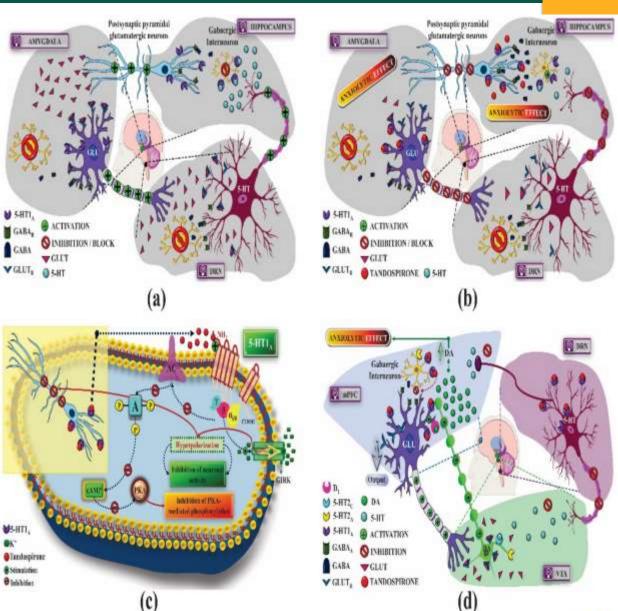


Biological factors have been implicated in the pathogenesis of anxiety. Neurochemical evidence suggests that the dysregulation of serotonin, norepinephrine, gamma-aminobutyric acid (GABA), glutamate, and peptides (corticotropin releasing factor, cholecystokinin, neuropeptide Y) transmission systems are strongly correlated with the pathophysiology of anxiety.

Pharmaceuticals **2021**, 14, 148



Asl

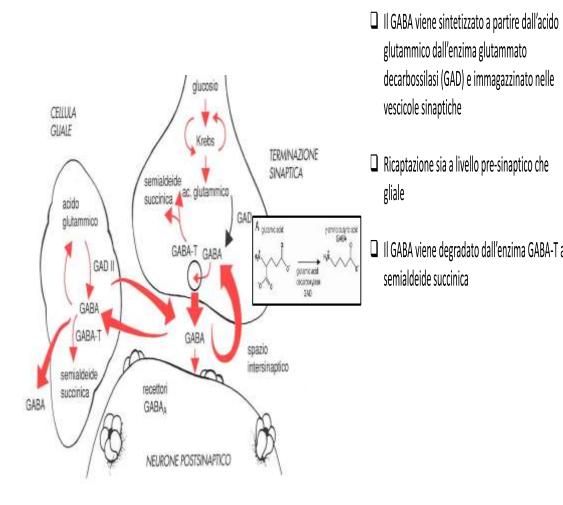




GABA attiva due principali tipi di recettori presenti a livello postsinaptico, presinaptico e/o siti extrasinaptici: il recettore GABA-A e il GABA-B

GABA-A canale ionico, media le azioni inibitorie del GABA aprendo II canale e prolungando l'afflusso di cloro per iperpolarizzare la membrana cellulare. I recettori GABA-A determinano il processo inibitorio dei circuiti cerebrali importanti nell'ansia;

GABA-B recettori metabotropici accoppiati alla proteinaG, prolungano l'inibizione influenzando i canali del potassio e del calcio.



L'acido gamma-amminobutirrico (GABA) è il neurotrasmettitore inibitorio più abbondante presente nel cervello dei

mammiferi (circa il 35-40% delle sinapsi sono GABAergiche)





Benzodiazepine

Farmaci più utilizzati nella maggior parte dei disturbi dello spettro ansioso (ridotti effetti sedativo-ipnotici ma diversi effetti collaterali)

Paura, preoccupazione, apprensione, irrequietezza,

Tachicardia, senso di soffocamento, sudorazione, bruciori di stomaco, etc.



Irritabilità, tensione muscolare, agitazione psicomotoria

Disturbi del sonno, difficoltà di attenzione, concentrazione e memoria





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ANSIOLITICI non benzodiazepinici



Betacarboline (Abecarnil)

Recettori Gaba A Azione sedativa associata

2

Barbiturici

Recettori Gaba A Azione sedativa associata

Agonisti del recettore 5HT1_A (Buspirone)

Attività sedativa assente. Latenza d'azione



Antidepressivi

Triciclici, inibitori – MAO, SSRI inibitori selettivi del reuptake di serotonina.





.....

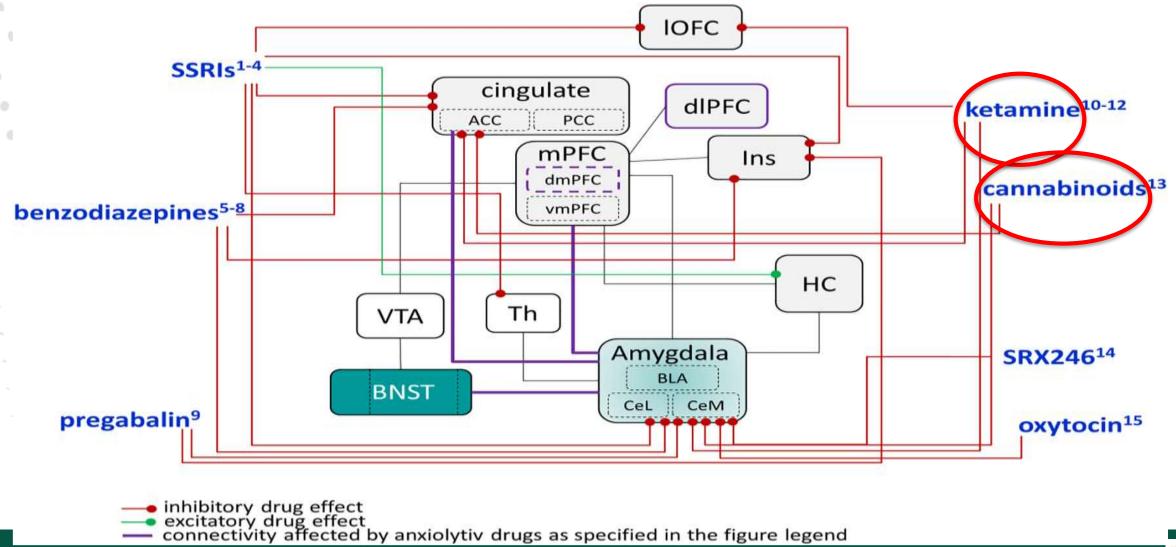
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S.B. Sartori, N. Singewald / Pharmacology & Therapeutics 204 (2019) 107402

APPROVED DRUGS

NOVEL DRUGS



Dr. Massimo Veneziano



- development of the second distribution of the

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Ketamine can be categorised as a dissociative anaesthetic, hallucinogenic and psychotomimetic drug with strong analgesic properties.

Il trattamento con ketamina è generalmente efficacia, sicuro e ben tollerato soprattutto per GAD refrattaria al trattamento e disturbo da stress post-traumatico in comorbilità con depressione trattamento-resistente.

Glue et al., 2018; Albott et al., 2018

L'**S-ketamina** (esketamina) è appena stata approvata per il trattamento delle forme d'ansia e di depressione resistenti al trattamento dalla FDA sotto forma di spray nasale.

FDA, 2019; The Scientist, 2019

Sicurezza è da valutare attentamente se somministrato a dosi più elevate su un periodo più lungo tempo in quanto suscita effetti euforici e dissociativi e può aumentare l'incidenza di effetti cardiovascolari, epatotossicità e cistite ulcerosa Cohen et al., 2018

Applicazione solo in ambiente clinico in cui può essere meglio controllata la somministrazione. S. Sartori et al., 2019 <text><section-header><section-header><section-header><section-header><section-header><image><section-header><section-header><section-header><section-header><section-header><section-header>







and vomiting, and in Wortern medicine it was commonly use

as an analgesic.⁴⁰ In the U8, physicians prescribed Ground-

sative for a multitude of illnesses until restrictions were put

in place in the 1930s and then finally stopped using it in 1970 when the fideral government listed marijuana as a Schedule l

substance, claiming it an illegal substance with no-medical value

California was the first state to go against the federal ban and

legalize medical marijaana in 1996.º As of June 2018, 9 state

and Washington, DC, have legalized recreational marijuana

and 30 states and Washington, DC, allow for use of medical maripaesa.⁷ The purpose of the present study is to describe the

effects of CHD on anxiety and sleep among patients in a clinic presenting with assisty or deep as a primary concern.

CIID has demonstrated preliminary efficient for a range of physical and montal health care problems. In the decade before

2012, there were only 9 published studies on the use of cannabinoide for medicinal treatment of pairs since then, 30 articles

have been published on this trooic, according to a PohMed sparch

Face 200102018-04

https://doi.org/10.7812/TVP/18-bit

^{Congresso Internazionale di MEDICINA BIOINTEGRATA}

ORIGINAL RESEARCH & CONTRIBUTIONS

ORIGINAL RESEARCH & CONTRIBUTIONS

Cannabidiol in Anxiety and Sleep: A Large Case Series

Sout Shannon, MO') Nixole Lewis, ND', Heather Lee, Ph-C', Shannon Hughes, PhD' E-out: 01/03/019

ARCTRACT

Contract Considering (202) is one of many considerant conpounds Revent in cartestini. It men not appear to alter consciencenovor trigger a 'Fight' & second sceparit according publications for to determine protections devidence decompting salitation (RD) a some more reporting to be a sporter, the holding splinging store and unbiangemental Endergy painty, taskand a splitting offers for CREATE the control carves system between in CREATE and in any article and the second system of the of a words categor of effectively has constrained, not low chronical interfers. of CRI and in the shellow income Digitative To detaining scheduer CED/relys reconcerdings will

original de la calendaria a mesendadaria. Energy. It is provide particular and a population and others dread application of URD for presenty and sives some planets at all address to pound benchment. The reference that evices excluded root/Ods documentation of states and clean

Main Outsines Measures: New and a sinty purer with sends at boardier and after CBD bookneets. Reading The local complex concerned of 74 which a presenting with printery concerns of printers in - 411 or poor steep in - 311. manually scores decreased writer the fast scored to 57 percents 29 2% and leman-advances of during the marky darphon. Shop coses; improved within the first market in 44 potents; 365 Paultan manage cost forms to the other newson. (Bill you wait transited to all that I parameters Construction Constitution may have been to be an any sended

INTRODUCTION

e Grunalis plant has been cultivated and used for its medictual and industrial brearfits during back to ancient times. antidepressive, and analogic benefits, r imnable savina and Cannable indica are the 2 main species.1 The General's plant contains more than \$8 different chemicals. CHD was shown to be helpful for de own as cannobinoids. The most abundant cannobinoid, ter- a simulated public speaking test at d ralephocannahinal (THC), is well known for its psychoactive in single-dose studies.¹²⁴⁰ Other str. properties, whereas cannabidial (CBD) is the second-most 10 mg/lig having a more anxiolytic bundant and is nonpercheactive. Different strains of the 100 mg/kg in sate 7 A conserver last are grove containing varying amounts of THC and aitsurpun found that high-dose CBD. Hence plants are grown for their fibers and high levels - the duration of deep.14 Acether rl CHD that can be entracted to make oil, but marijuana plan grown for recruitional use have higher concentrations of THC pated with CBD.¹ Industrial hemp must contain less that

4.76 THC to be considered level, and it is from this plant that CBD oil is entracted.¹ Many different cultures have used the Growal-Opiant to treat plethors of ailments. Practitioners in ancient China targeted malaria, memetrual symptoms, gour, and constipation. During ordieval times, cantabis was used for pain, epilepsy, nausea,

operation of Representing Medicine, Million Island of Issue Web. Colorado State Denset Institution, 80 (waited Experients controls consultation DBC down

Shannon et al., 2019

"Appartment of Parchistry, Indensity of Laborat

eminente Journal- Mps. (balang/11.7810/7997/18-0

Data Analysis

Cannabidiol in Anxiety and Seep: A Large Case Series

Deidentif ed patient data were evaluated using descriptive statistics and plotted graphically for visual analysis and interpretation of trends.

RESULTS

The average age for patients with anxiety was 34 years (range = 18-70 years) and age 36.5 years for patients with sleep disorders (range = 18-72 years). Most patients with an anxiety diagnosis were men (59.6%, 28/47), whereas more sleep-disordered patients were women (64.0%, 16/25). All 72 patients completed m and anxiety assessments at the onset of CBD treatment and st monthly follow-up. By the second monthly follow-up, 56.9%) remained on CBD treatment and completed 7 patients (37.5%) remained on CBD treatment hlv assessment.

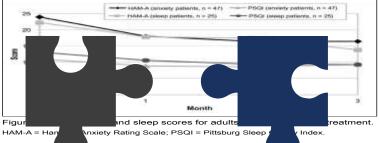
means and standard deviations for sleep and Nine and during the follow-up period for gure 1 graphically displays the trend in er the study period. On average, anxiety pst patients, and these improvements t the first monthly assessment after 79.2% (57/72) and 66.7% (48/72) mprovemen: in anxiety and sleep, nd 25.0% (18/72) experienced v and sleep, respectively. Two reatment, 78.1% (32/41) and improvement in anxiety and ne prior monthly visit; again, ectively, reported worsening month.

sustained response to anxirecords displayed a larger o scores. T e sleep scores anxiety scores decreased hed decreased during the

	y and sleep scores ent					
<u> </u>	SD)	PSQI, mean (SD)				
87)		10.98 (3.43)				
(7.56)		8.88 (3.68)				
(8.80) د		8.59 (2.91)				
. o.36 (9.80)		9.25 (2.46)				
22.18 (7.55)		13.08 (3.03)				
17.00 (0.70)		10.01 (0.00)				

	•	. ,	. ,	
3-month follow-up		13.78 (7.86)	9.33 (4.63)	
	2-month follow-up	17.36 (10.91)	9.39 (3.81)	
	onth follow-up	17.82 (9.72)	10.64 (3.89)	
	eline	22.18 (7.55)	13.08 (3.03)	

HAM-A = Hamilton Anxiety Rating Scale; PSQI = Pittsburg Sleep Quality Index; SD = standard deviation



CBD ell tolerated, with few patients rting side effects. Two ents discontinued treatment wi the frstweek because of fatigue. T reepatients noted mild sedation initially that appeared to abate in the first few weeks. One patient with a developmental disorder (aged 21 years) had to be taken of the CBD regimen because of increased sexually inappropriate behavior. TeCBD washeld, and the behavior disappeared. Te behavior reappeared on redosing 2 weeks later, and the CBD regimen was formally discontinued. Tetreating psychiatrist thought this was related to disinhibition because the patient's an xiety responded One patient noted dry eyes Reasons for patients dramatica not foll

patlaterassessment points	aly unknown
because of standard att	atienced in
tice. Tere was no evi	patients
because of tolerabi	trition
in nature and size	tinely
thisclinic.	
with CBD was in gen	pted, as

our patients

treatment because of religious or ethical condeclined he relation to cannabis. Nearly all patients easily cerns abo provided informed consent once the nature of the treatment was explained. Most patients appreciated the opportunity to try something natural and avoid further or initial psychiatric medication use.

inicians' and patients' resp.

DISCUSSION

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In an outpatient psychiatric population, sleep scores displayed ng sustained improvements during the 3-month study. Anxiety sheet every set of the rapidly, and this there was sustained of the rapidly set of the results are results are provided to the existing precision and clinical data of the there was well accepted and well tolerated in our patients. Side clicks were minimal (mainly fatigue) and may be related to dosing.

rule of the study (25 mg/d to 175 mg/d) were rule of the study (25 mg/d to 175 mg/d) were (so mg/d to 50 mg/d)^{12-14,17} for 2 reasons. T et rst is that in our experience lower doses appear to elicit an adequate clinical

fairly rapidity

improvements

The Permanente Journal • https://doi.org/10.7812/TPP/18-041

p alsoi ...

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conducted in December 2017. Most cotable was a study conducted at the University of California, San Disao's Center 9: Medicinal Canashis Research that showed cannabis cigarreduced pain by 34% to 40% compared with plaotho (20% decrease in pain).º In particular, CBD appear benefits for a wide range of neurologic disorder decreasing major sciences. A recent large, well-erof pediatric epilepsy documented a beneficial e educing seizure frequency by more than 509 endorphin release, the "ranner's high" experas been shown to be indoord in part by ar CBI receptors, eliciting anniolytic effects tivity of CBD at 5-HT., morphon may dr

Assesses. Compating chical analise are resoluti. of action by which CBD decreases

Author Millations





Low doses of THC are anxiolytic and high doses of THC are arousing and anxiogenic. **CBD** is able to block the anxiogenic effects of THC

B. Kamal et al., 2019







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"phytomedicines" may provide novel treatment options, to act as an adjunctive or alternative to existing anxiolytic medications.

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.

January 2018 Volume 32 Maun 1 (ESN 0861-418X

Phytotherapy Research

An international Journal devoted to clinical and pharmacological evaluation of herbal medicines, nutraceuticals and natural product derivatives

View this journal online at wileyonlinelibrary.com/journal/ptr





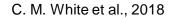
KAVA

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The pharmacology, pharmacokinetics, efficacy, and adverse events associated with Kava

 Gli studi clinici (almeno durata 4 sett.) hanno riscontrato buoni effetti ansiolitici (non immediati), ma una bassa tollerabilità e sicurezza (possono verificarsi effetti avversi di tipo dermatologico, epatologico e cognitivo).

 Necessario determinare la dose ottimale e lo schema posologico. The Journal of Clinical Pharmacology Official Publication of the American College of Clinical Pharmacology







Melissa

Congresso Internazionale di MEDICINA BIOINTEGRATA

Anti-anxiety properties of selected medicinal

plants

A. Khan et al., 2022

Current Pharmaceutical Biotechnology





Medicinal plants are being used as a potential source of novel drug for anxiety disorders.





Melissa

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"...Melissa officinalis leaf extract treatment has been demonstrated to *improve mild-to*moderate anxiety disorders and

insomnia..."

Mediterr J Nutr Metab (2011) 4:211–218 DOI 10.1007/s12349-010-0045-4

Julien Cases · Alvin Ibarra · Nicolas Feuillère

ORIGINAL ARTICLE

Marc Roller · Samir G. Sukkar

Pilot trial of *Melissa officinalis* L. leaf extract in the treatment of volunteers suffering from mild-to-moderate anxiety disorders and sleep disturbances

over 2010/Accepted: 2 December 2010/Public 2010. This article is published with open access

Kustratel Botanicals are an alternative option to prescription drugs for the alleviation of symptoms during matery disorders and insomnia. Molecular methods in the been shown as an anti-stress for any optimal access of methods by reported modernation of methods in the method by recording a standard or the constraint of the state of the state of the state of the state state of the state inhibit gamma-immutistic rest with the method by as a prospective, open-label of the state of the state inhibit gamma-immutistic rest with the state of anxiety manifestations by 18% (p < 0.01), as much as 90 to observe the state of the state of the state of the state of anxiety associated symptoms by 15% (p < 0.01), increased insomnia by 42% (p < 0.01). As much as 90 to observe the state of the state of the state of the state of anxiety and 70% (14/20) for both. Our study dem menutes, the the first time that chronic administration o the state of the

J. Cases - N. Feuillère - M. Roller Naturex SA, BP 1218, 84911 Avignon, France

A. Barra (63) Natures Inc., 375 Huyler Street, South Backers NU 07006, USA e-mail: a.iburra@natures.as S. G. Sukkar Disettics and Clinical Nutritication, Large Rosaria, San Martino University Hospital, Large Rosaria, termines of the similar america we and physiological event inclusion power in the sequence rainty, and is the number of the sequence of the sequence of the the event of the sequence of the s

into a stressor [4]. Insomnia is chronic and severe, it develops into a stressor [4]. Insomnia is a heterogeneous disorder that entails difficulties with sleep onset, maintenance and early

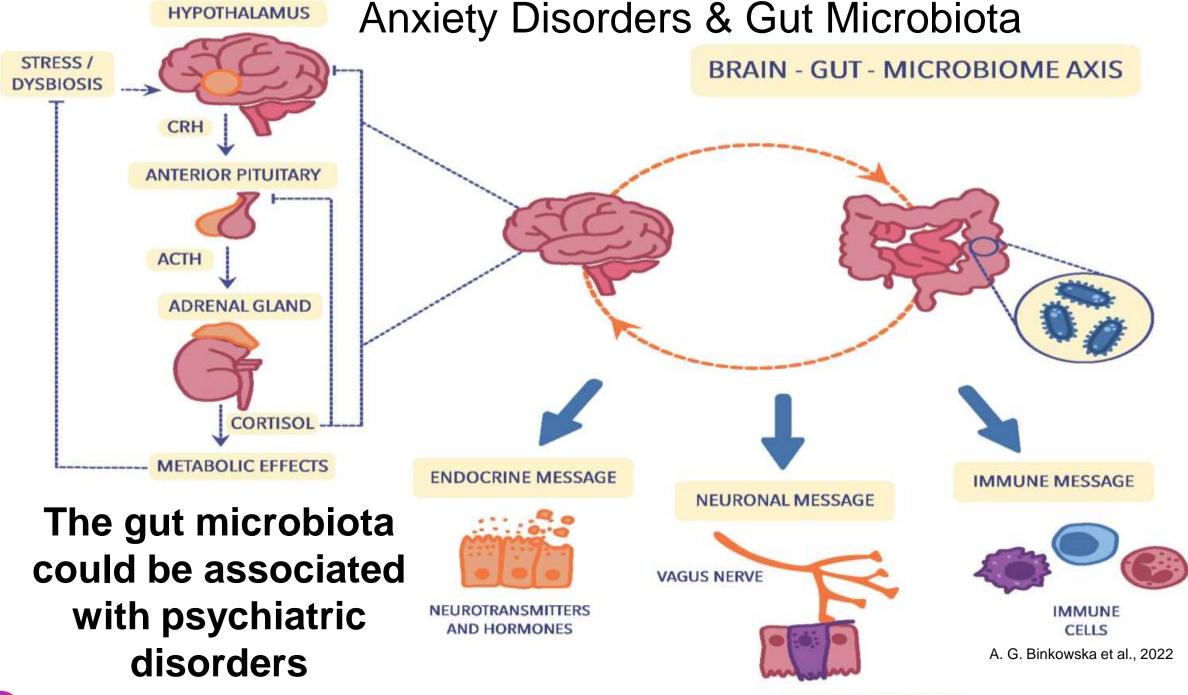
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Dr. Massimo Veneziano

J. Cases et al., 2019





TOPMEMORY*

Dr. Massimo Veneziano

ENTEROENDOCRINE CELL

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Identified different gut-microbial compositions in subjects with MDD, subjects with GAD. Identified a correlation between the

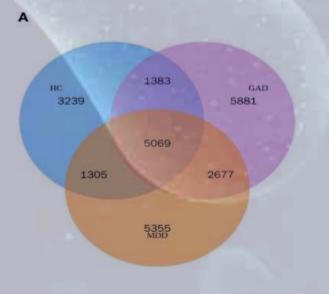
bacteria and clinical symptoms.

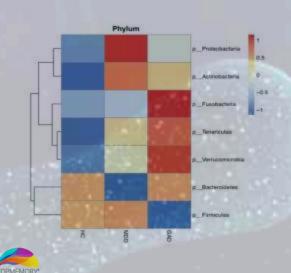
Z. Dong et al., 2022



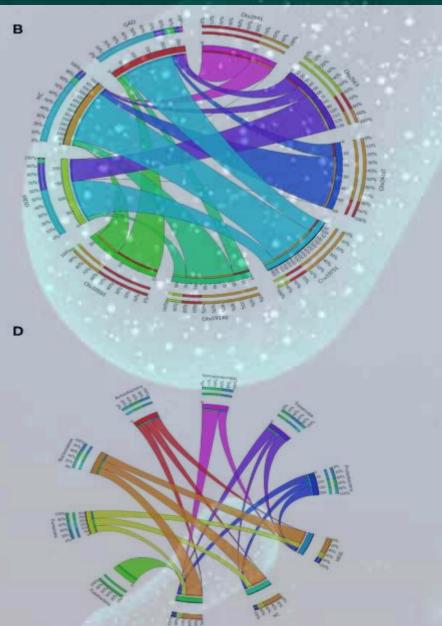








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Gut Microbiome: A Potential Indicator for Differential Diagnosis of **Major Depressive Disorder and General Anxiety Disorder**

Zaiguan Dong, Xiaoling Shen, Yanni Hao, Jin Li, Haoran Li, Haizheng Xu, Li Yin and Weihong Kuang*

Mental Health Center of West China Hospital, Sichuan University, Chenodu, China

Background: Major depressive disorder (MDD) and general anxiety disorder (GAD) share OPEN ACCESS many common features, leading to numerous challenges in their differential diagnosis. Given the importance of the microbiota-gut-brain axis, we investigated the differences in out microbiota between representative cases of these two diseases and sought to develop a microbiome-based approach for their differential diagnosis.

Methods: We enrolled 23 patients with MDD, 21 with GAD, and 10 healthy subjects Reviewed by Kiran Veer Sandhu. (healthy crowd, HC) in the present study. We used 16S rRNA gene-sequencing analysis University College Cork, Ireland to determine the microbial compositions of the out microbiome based on Illumina Miseo Danilo Amone. and according to the standard protocol. United Arab Emirates University, United Arab Emirate

Results: GAD showed a significant difference in microbiota richness and diversity as compared with HC. Additionally, Otu24167, Otu19140, and Otu19751 were significantly Weihong Kuang decreased in MDD relative to HC, and Otu2581 and Otu10585 were significantly kwhhli@163.com increased in GAD relative to MDD. At the genus level, the abundances of Sutterella and Fusicatenibacter were significantly lower in MDD relative to HC, and the abundances This article was submitted to of Fusicatenibacter and Christensenellaceae_R7_group were significantly lower in GAD than in HC. The abundance of Sutterella was significantly higher whereas that of Faecalibacterium was significantly lower in GAD relative to MDD. Moreover, we observed that Christensenellaceae_R7_group negatively correlated with the factor score (Limited Accepted: 19 August 2021 to Hopelessness) and total score of HAMD-24 (p < 0.05), whereas Fusicatenibacter negatively correlated with FT4 (p < 0.05). Furthermore, the GAD group showed significant differences at the genus level for Faecalibacterium, which negatively correlated with PTC Xu H, Yin L and Kuang W (2021) Gut Microbiome: A Potential Indicator for (p < 0.05).

Conclusions: This study elucidated a unique gut-microbiome signature associated with Depressive Disorder and General MDD and GAD that could facilitate differential diagnosis and targeted therapy.

doi: 10.3389/fpsyt.2021.651536 aut microbiome, anxiety, depression, 16S ribosomal RNA, differential diagnosis

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Differential Diagnosis of Major

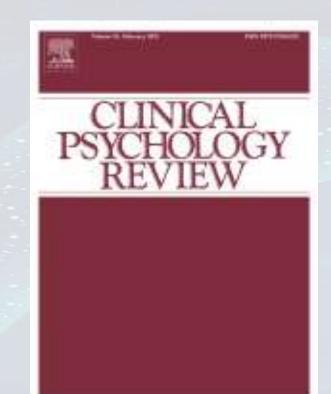
Front, Psychiatry 12:651536.

Anxiety Disorder.

September 2021 | Volume 12 | Article 651536

CAsl3

I soggetti affetti da disturbi d'ansia sembrerebbero avere una taxa batterica differente caratterizzata da una maggiore abbondanza di specie proinfiammatorie (ad es. Enterobacteriaceae e Desulfovibrio) e da una minore quantità di batteri produttori di acidi grassi a catena corta (ad es. Faecalibacterium).



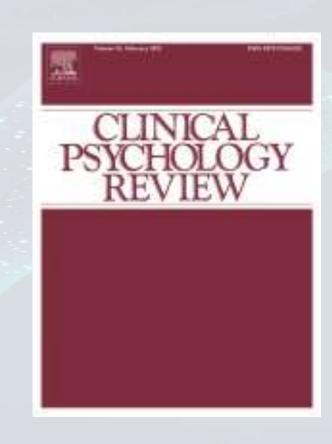
A. Carra et al., 2021

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Il microbiota intestinale obiettivo promettente per la ricerca. Studiare i fattori interferenti, in particolare la dieta e i farmaci psicotropi per migliorare gli interventi terapeutici e di prevenzione.



A. Carra et al., 2021

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Anxiety Disorders - Conclusioni

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Pharmaceuticals 2021, 14, 148

Problematiche e indirizzi per la futura ricerca

Le prove che supportano l'effetto dei medicamenti a base di erbe sui disturbi d'ansia sono aumentate negli ultimi anni, ma molte di queste derivano da studi su modelli animali e alcuni metodologicamente approssimativi (a breve termine e/o su piccoli campioni) Necessario condurre studi:

1. sugli esseri umani che siano più robusti e con un campione più ampio 2. verificare gli effetti dell'associazione tra alcune erbe e i farmaci

Table 2. Plant extracts that produce antidepressant-like and/or anxiolytic-like effects in animal	model
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Plant/Extract	Model/Test Used	Animal Species	Administration	Major Findings	Mechanisms of Action
<i>Achyranthes</i> <i>aspera</i> /methanolic extract	Hole cross, OF, forced swimming, tail suspension, elevated plus maze, and light/dark	Mice	Oral administration (50, 100, and 200 mg/kg) 30 min before tests	Anxiolytic and antidepressant effectiveness	Not assayed
Aloysia triphylla/methanolic, dicloromethane and hexanic extracts	Elevated plus maze test	Male ICR mice	Oral administration (125, 250, 500, and 750 mg/kg) 30 min before test	Anxiolytic effectiveness	Interaction with serotonergic transmission
Annona vepretorum/essential oil	Elevated plus-maze, hole-board, open-field, rota-rod, and tail suspension tests	Male albino Swiss mice	Intraperitoneal administration (25, 50, and 100 mg/kg)	Anxiolytic and antidepressant effectiveness	Not assayed
Camellia euphlebia / aqueous extract	Light/dark box, elevated plus maze, forced swimming, tail suspension, and open-field tests	Male Kunming mice	Intragrastrical administration (100, 200, or 400 mg/kg) 1 h before tests for 7 days	Anxiolytic and antidepressant effectiveness	Not assayed
<i>Camellia sinensis</i> /aqueous and ethanolic extracts	Elevated plus maze and OF tests	Male C57BL/6J mice	Oral administration (50 and 100 mg/kg) 1 hour before test	Anxiolytic effectiveness	Activation of serotonin 5-HT _{1A} receptors
<i>Cananga odorata</i> /essential oil	Open field, elevated plus maze, and light/dark box tests	ICR mice	10 mL inhalation 10 min before tests	Anxiolytic effectiveness	Increased 5-HT concentration in the hippocampus of male mice
Capparis thonningii/methanolic extract	Forced swimming, tail suspension, hole-board, light/dark, and elevated plus maze tests	Swiss albino mice	Oral administration (500–4000 mg/kg) 1 h before tests	Anxiolytic and antidepressant effectiveness	5-HT ₂ receptor inhibition
<i>Carthamus</i> <i>tinctorius</i> /ethanolic extract	Elevated plus maze and forced swim tests	White albino rats	Oral administration (100 and 200 mg/kg) 1 h before tests	Anxiolytic and antidepressant effectiveness	Not assayed
Cocos nucifera/hydroalcoholic extract	Elevated plus maze, hole-board, forced swimming, tail suspension, and open-field tests	Swiss mice	Oral administration (50, 100, or 200 mg/kg) 1 h before tests	Anxiolytic and antidepressant effectiveness	Inhibition of the 5-HT system



Take Home Message

La ricerca e la pratica clinica dovrebbero liberarsi dai condizionamenti di natura economica e politica per impegnarsi maggiormente a considerare anche altre forme di rattamento per i disturbi cognitivi e psicologici oltre ai farmaci..



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Grazie per la cortese attenzione



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