Neuroplasticity: Maintaining and Building Brain Health

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Objectives

- Describe the concept of neuroplasticity and why this is so important for brain health
- Learn about positive and negative influences on BDNF
- Learn about different neurological diseases including degenerative diseases, ADHD, autism, traumatic brain injury, and depression and the role that BDNF plays
- Learn about natural supplements that increase BDNF in order to foster neuroplasticity and cognitive function

NEUROPLASTICITY

The Ability of the Brain to Reorganize Itself, Both in Structure and How It Functions

HOW THE BRAIN CHANGES

NEUROGENESIS

Continuous generation of new neurons in certain brain regions

NEW SYNAPSES

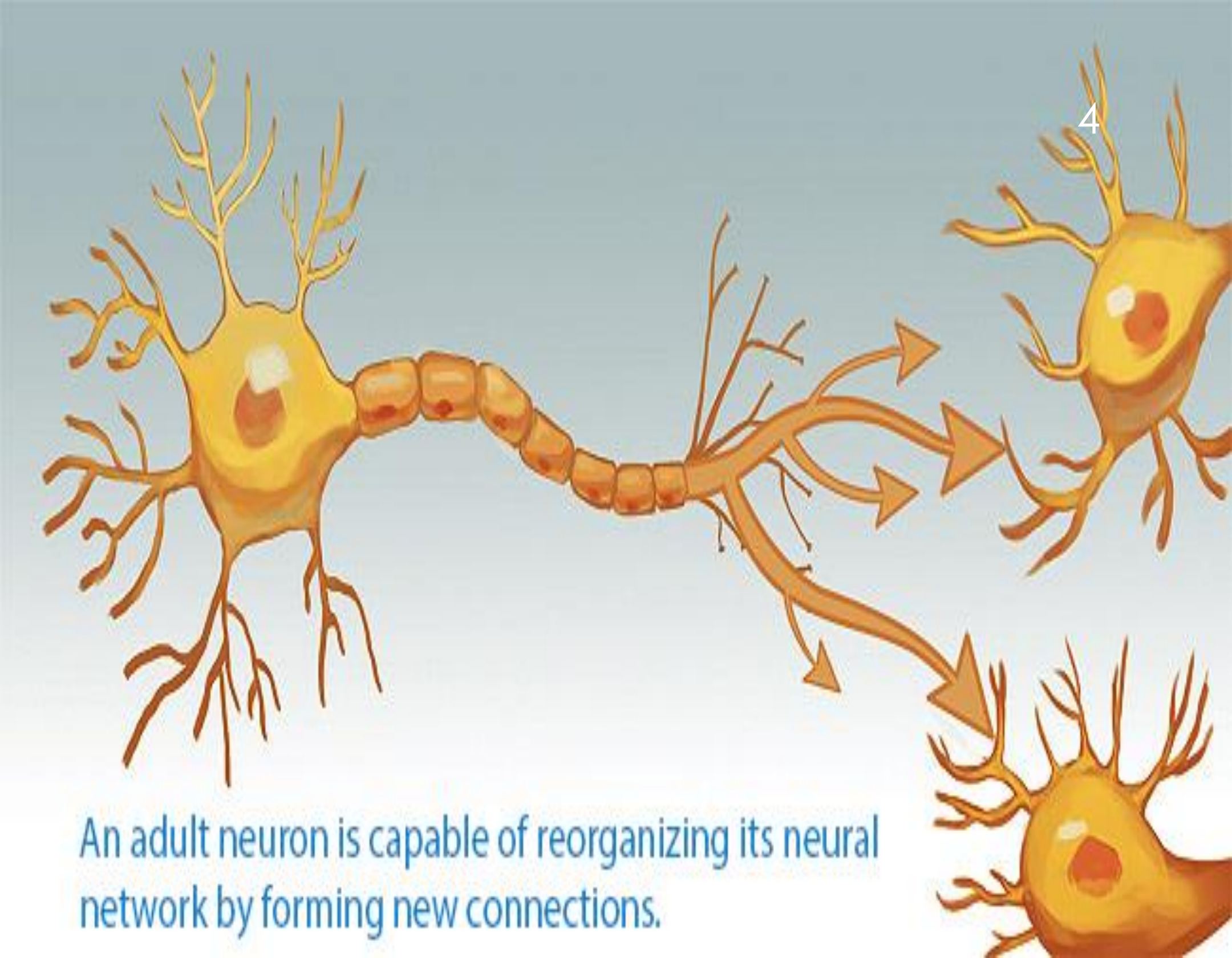
New skills and experiences create new neural connections

STRENGTHENED SYNAPSES

Repetition and practice strengthens neural connections

WEAKENED SYNAPSES

Connections in the brain that aren't used become weak



An adult neuron is capable of reorganizing its neural network by forming new connections.

Neurogenesis

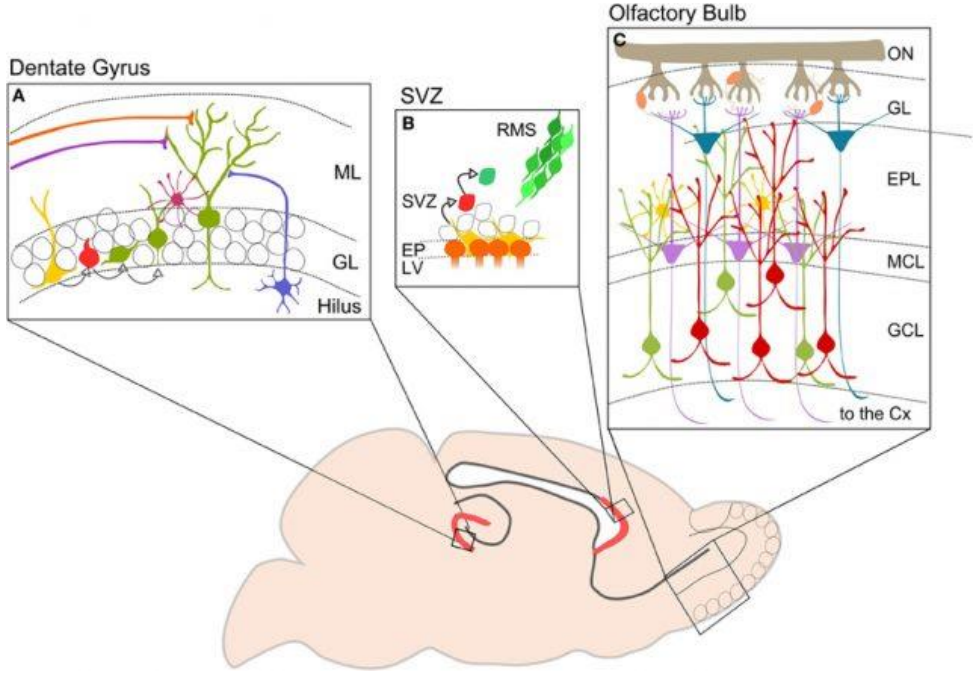
Only in 2 areas of the brain

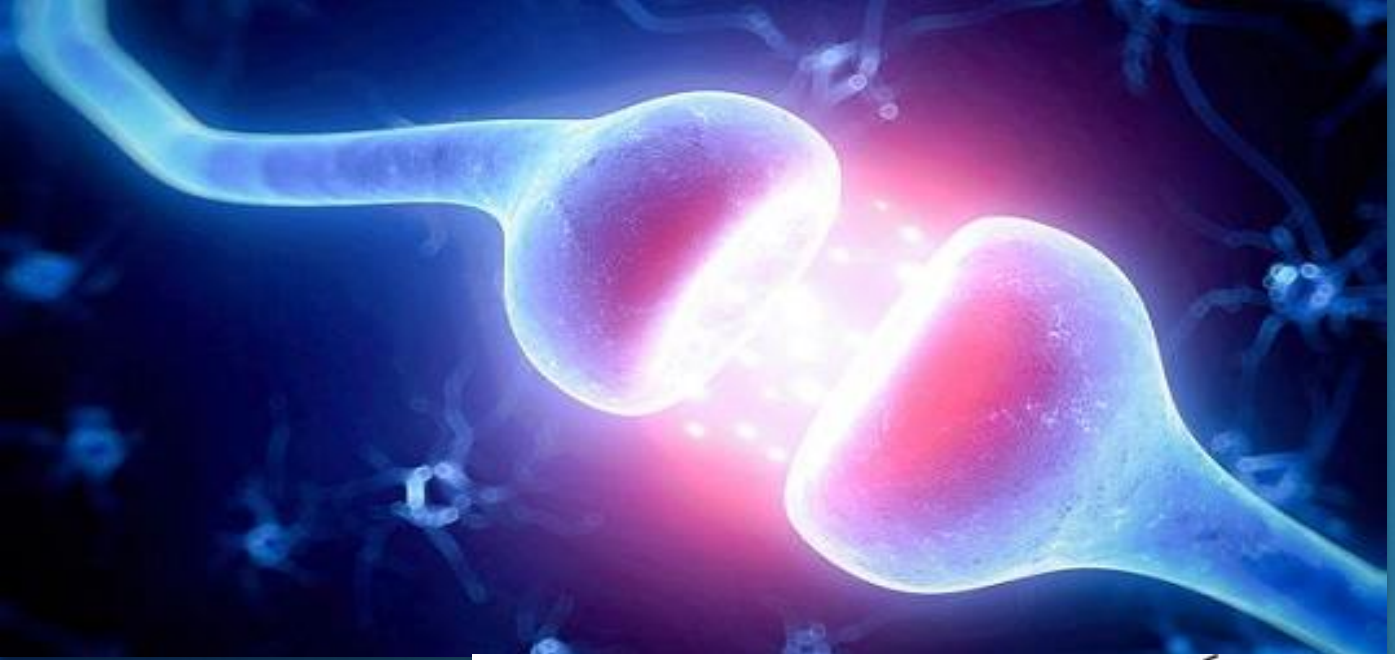
1. **Sub-ventricular zone(SVZ)**

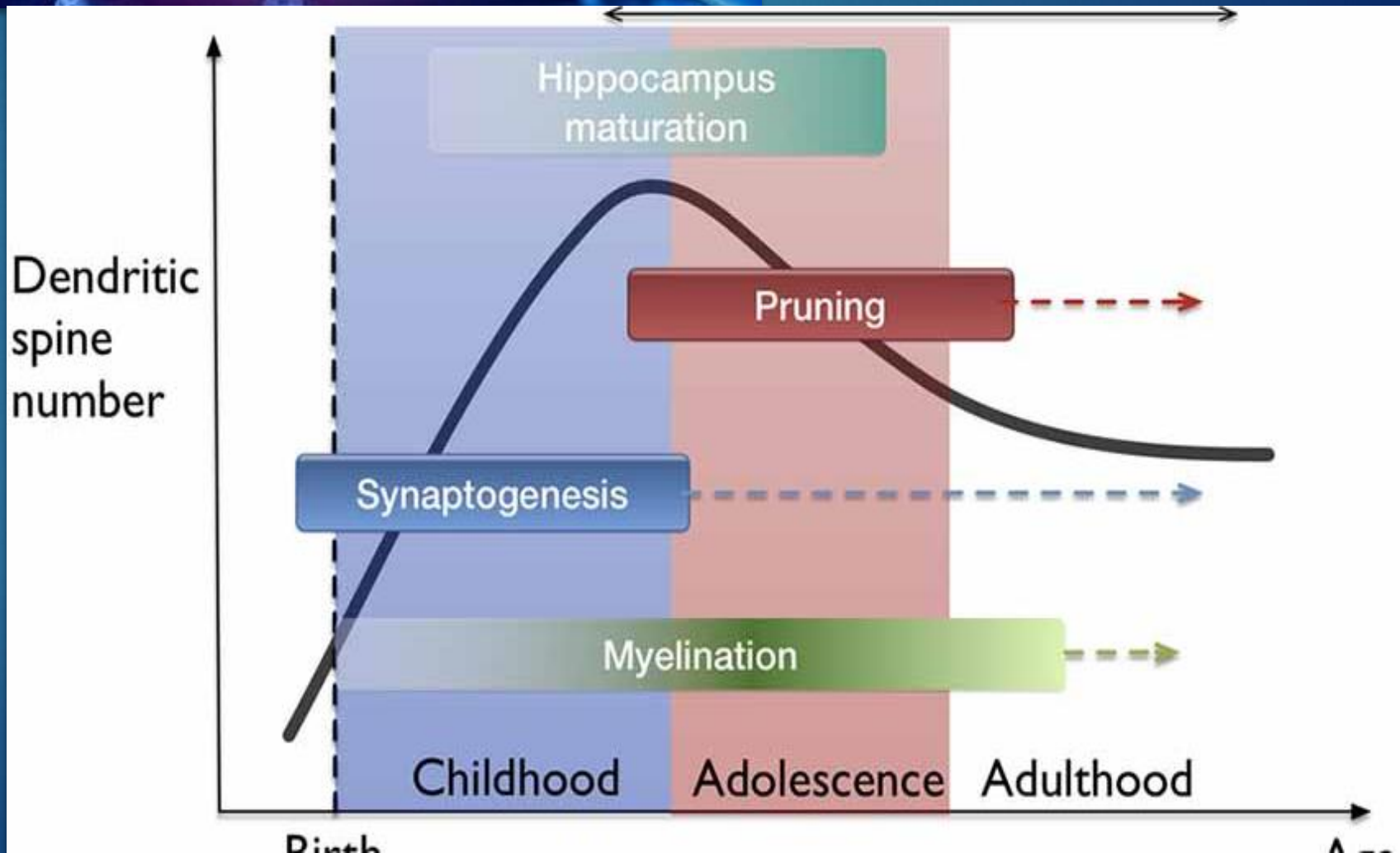
   Continuously generate neurons travel into olfactory bulb become interneurons

2. **Sub-granular zone(SGZ):** dendrate gyrus of the hippocampus

Stress has strong negative impact on hippocampal neurogenesis

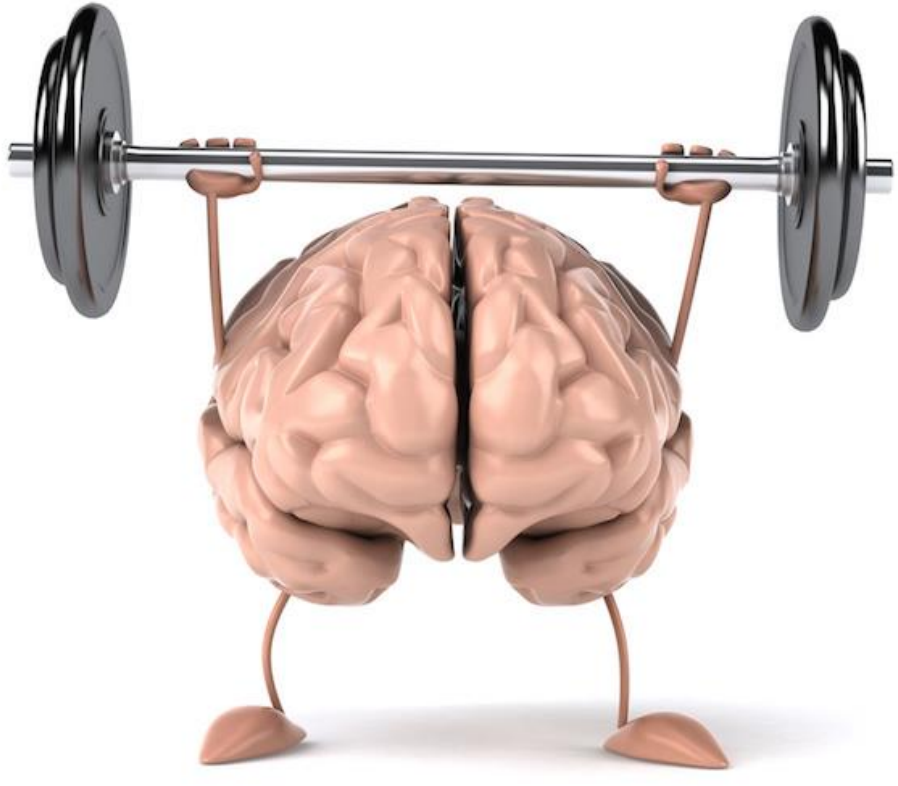





Hippocampus maturation
Pruning
Synaptogenesis
Myelination
Dendritic spine number
Childhood
Adolescence
Adulthood
Birth

Increase Neuroplasticity

- Physical Exercise
- Learning new skills
- Meditation
- Sleep
- Intermittent Fasting
- Increase BDNF(Brain Derived neurotrophic factor)
- Herbal supplements: (work by increasing BDNF, anti-oxidants, decreasing stress
- Good nutrition: omega three fatty acids

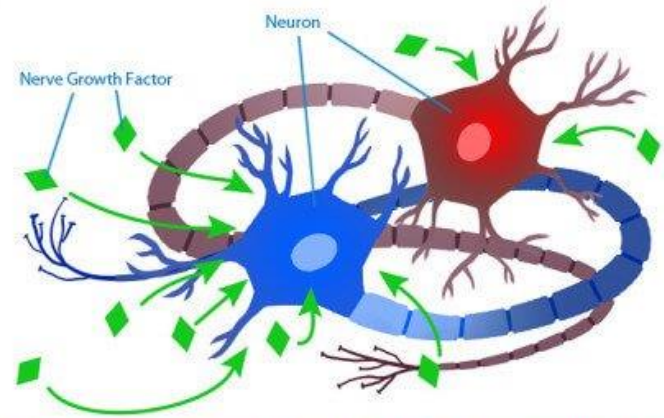


Decrease Neuroplasticity

- Stress: Increase cortisol, abnormal HPA axis
- Neurotoxins
- Physical and mental Inactivity
- Watching TV
- Poor nutrition
- Neuroinflammation from toxins, infections
- Traumatic brain injury
- Oxidative stress

Neurotrophic growth factors

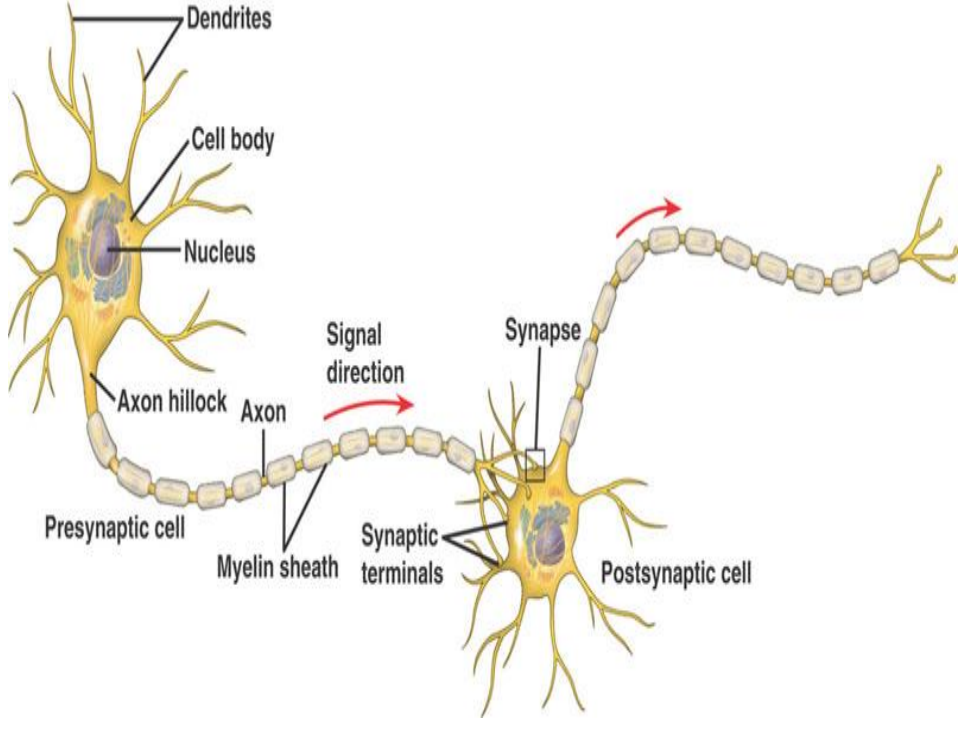
- Proteins that promote the survival, development, and function of neurons
  - Nerve Growth Factor (NGF): growth of sympathetic and sensory neurons
  - Brain Derived neurotrophic Factor (BDNF): primarily in the brain-central nervous system
  - NT-3, NT-4: peripheral and central nervous system



Nerve Growth Factors (shown in green) is required by neurons in order to survive. As they are a limited extracellular resource, some neurons (shown in blue) may uptake a disproportionate share of survival factors, leading to the eventual death of neighboring neurons (shown in red).

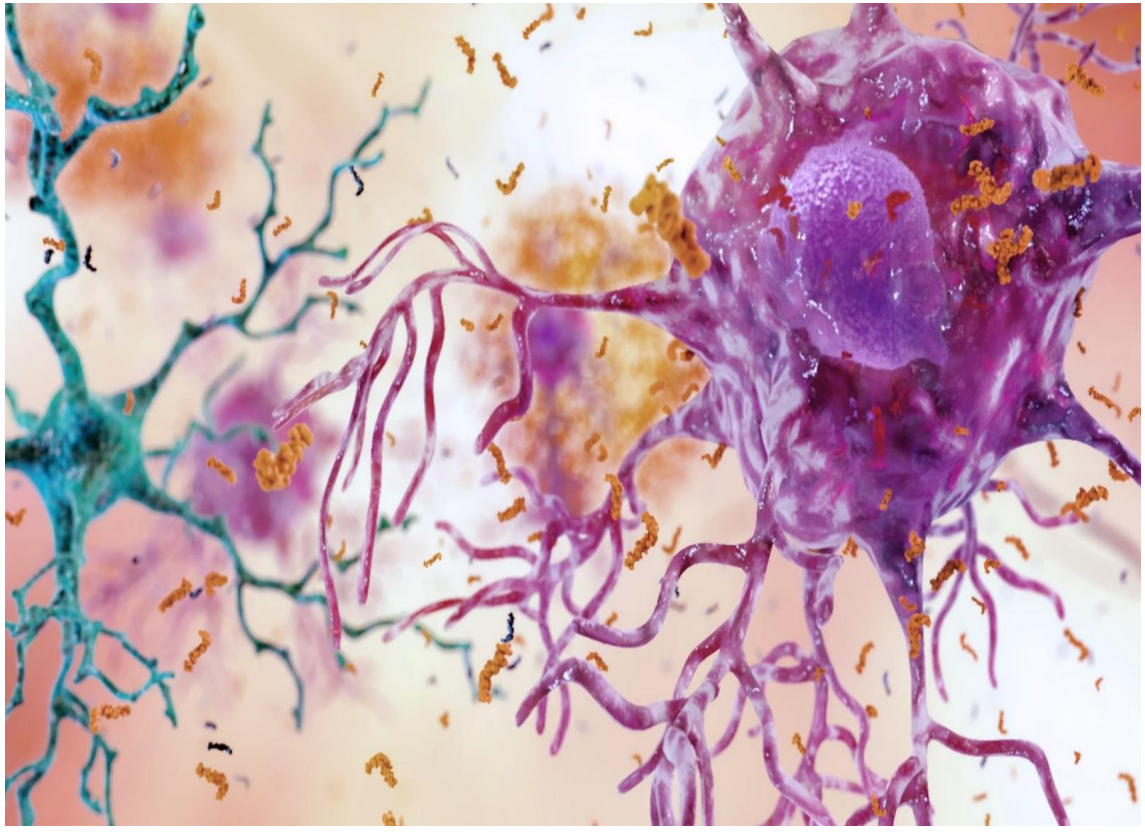
BDNF Functions

- Neuroplasticity:
  - Nervous system can change and adapt
- Neurogenesis:
  - New nerve cells
- Neuronal differentiation:
  - Nerve cells can change function
- Neuronal Repair
- Synaptogenesis:
  - Form new synapses
- Increase telomerase activity:
  - Stop breaking down telomeres so anti-aging



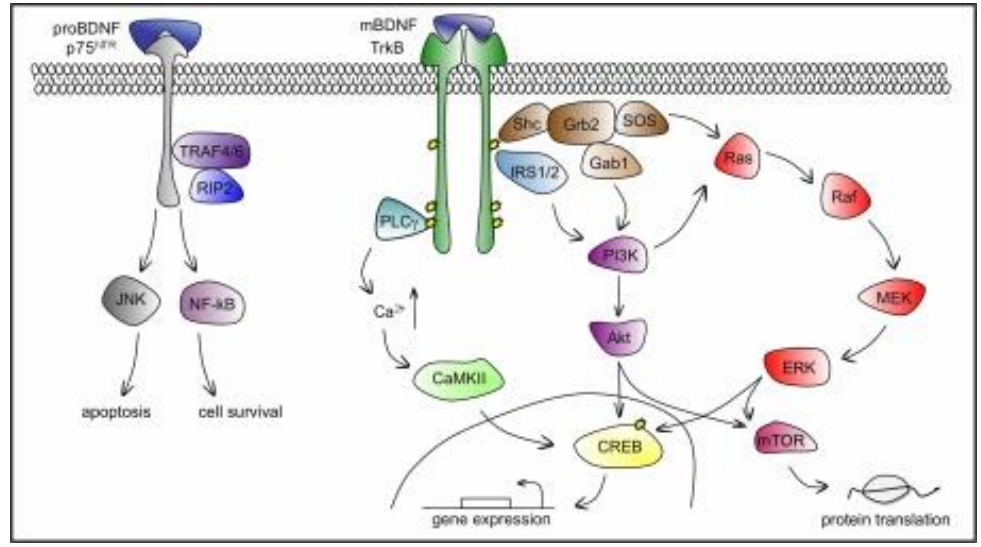
BDNF Functions: Clinical

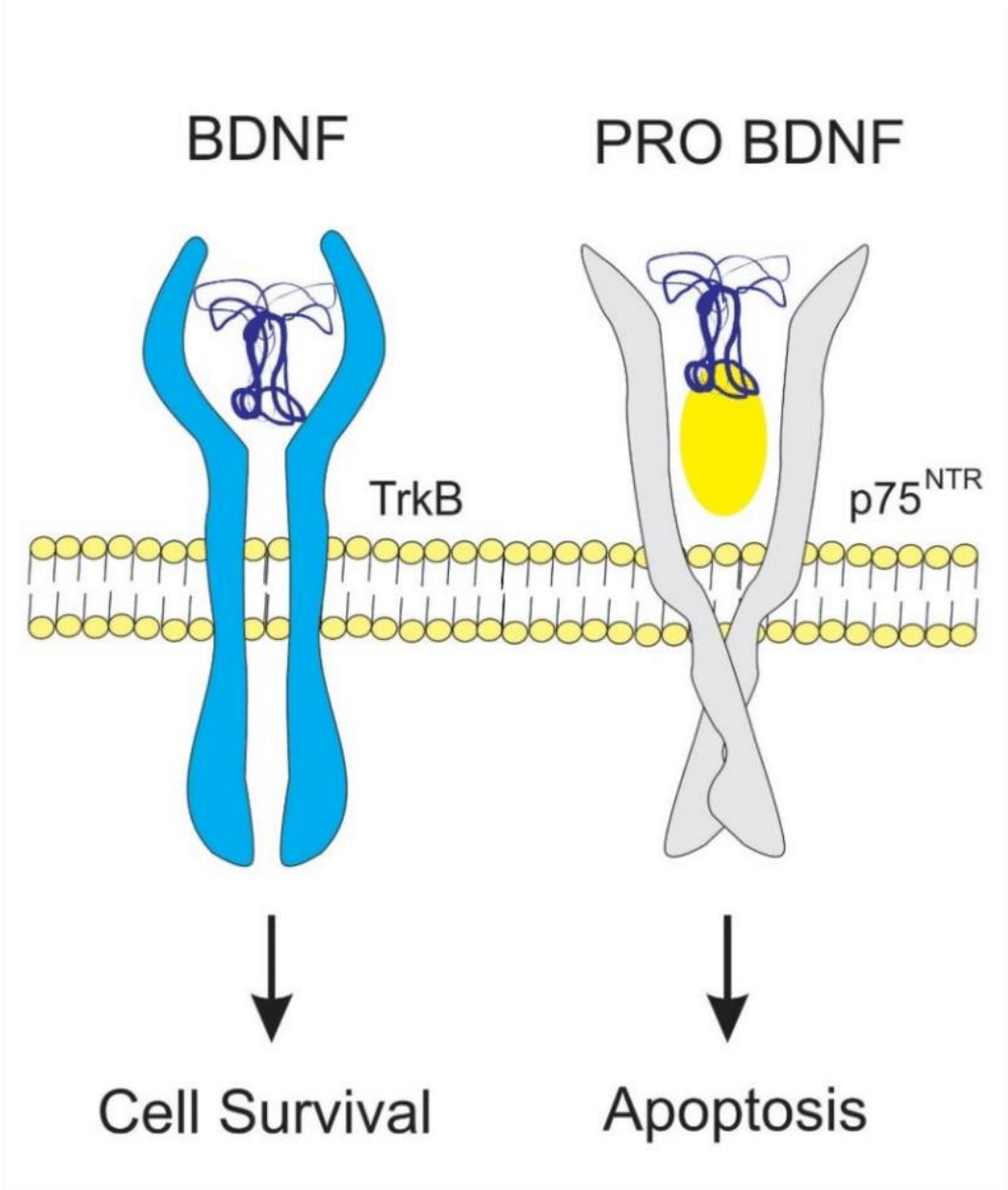
- Learning
- Memory
- Cognitive function
- Attention
- Resilience



BDNF Receptors

- Two receptors
  - TrkB: tropomyosin-related kinase
  - LNGFR: low affinity nerve growth factor receptor- also known as p75





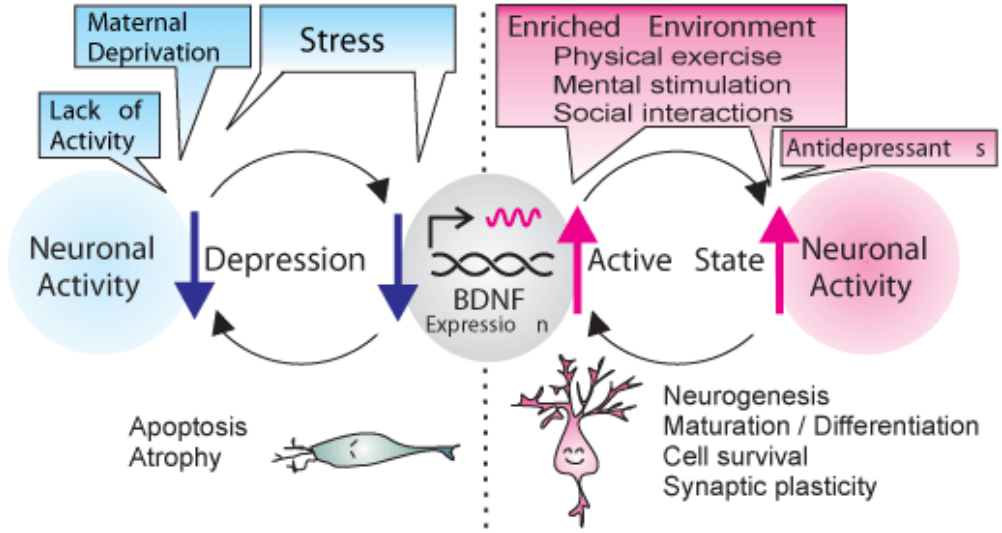
TrkB receptor:
BDNF

versus

p75 receptor:
Pro-BDNF

Brain Derived Neurotrophic Growth Factor

- Increased:
  - Exercise
  - Nutrition
  - Herbs
  - Learning
- Decreased
  - Stress
  - Poor diet
  - Depression
  - Low physical or mental activity



Neural Plasticity
Volume 2017, Article ID 7260130

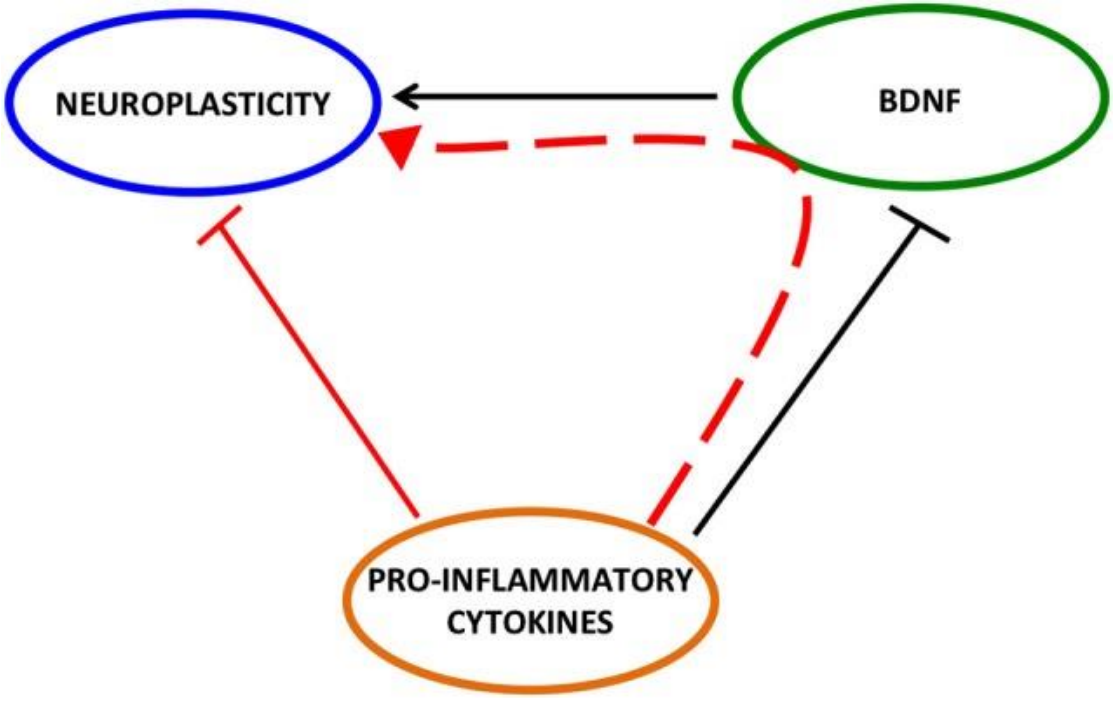
Review Article

Brain-Derived Neurotrophic Factor, Depression, and Physical Activity: Making the Neuroplastic Connection

Cristy Phillips

able 1: Effects of physical activity on brain-derived neurotrophic factor (BDNF).

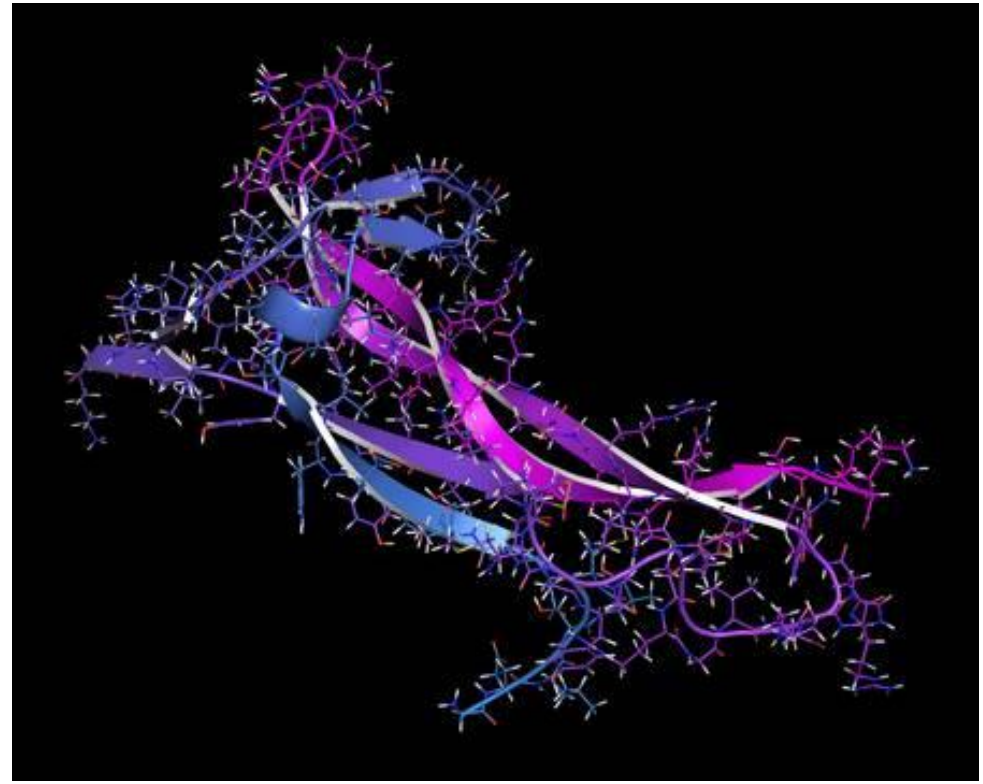
Reference	Sample	Treatment	Assessment outcome
[233]	13 young, healthy men	Moderate-intensity aerobic PA 4 d/wk for 5 wks	↑ plasma BDNF
[234]	7 healthy, sedentary males	Aerobic PA 7 d/wk for 12 wks	↑ plasma BDNF
[238]	60 older adults	Aerobic PA 3 d/wk for 60 wks	↑ BDNF and ↑ hippocampal volume
[236]	47 healthy, sedentary males	Aerobic PA 3 d/wk for 5 wks	↑ serum BDNF following PA and ↑ memory on face name matching
[235]	62 healthy, sedentary males	Moderate-intensity aerobic PA for 2 wks	↑ serum BDNF following PA and ↑ memory on face name matching
[247]	104 persons with partial response to antidepressants	Add-on high (16 kcal/kg/week) or low (4 KKW) PA for 12 wks to standard depression care	Persons entering with ↑ BDNF levels exhibited ↑ rate of response to antidepressants
[248]	15 severely depressed adults	Add-on aerobic PA 16 kcal/kg/week for 3 d/wk for 3 wks to standard care for depression or medication-only group	Similar ↑ in BDNF in aerobic PA and medication-only group, but ↓ in oxidative stress markers seen only in PA group

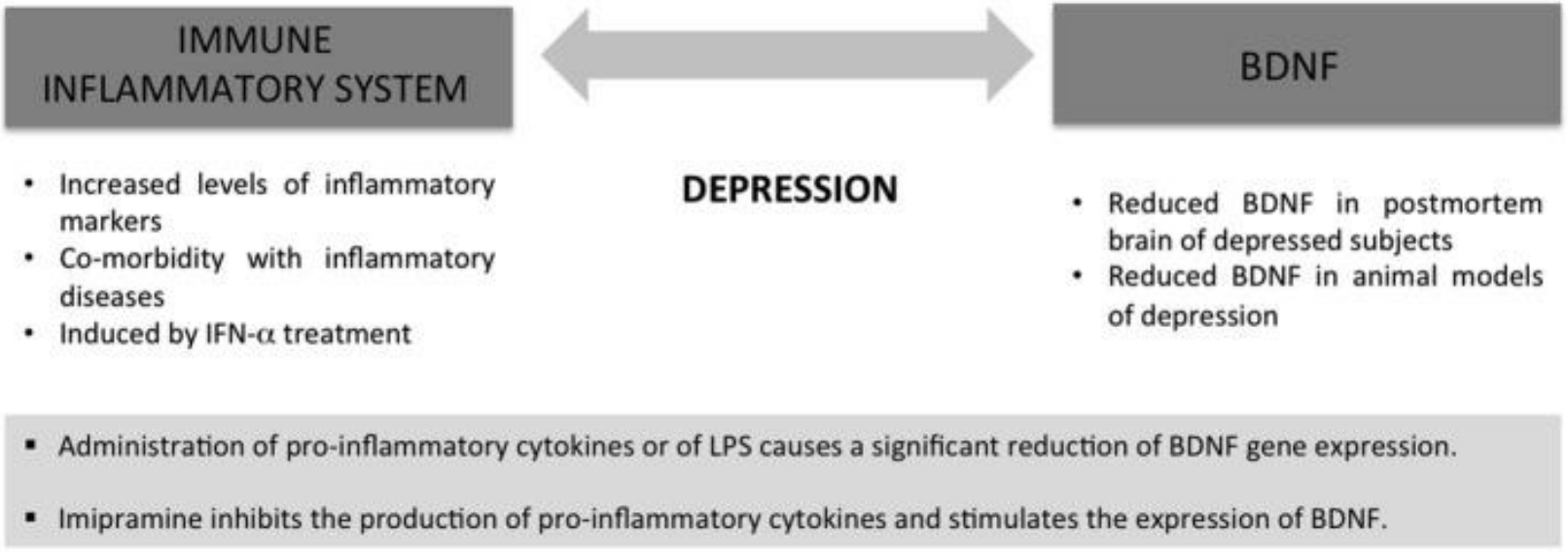


Calabrese F. et al. Brain-derived neurotrophic factor: a bridge between inflammation and neuroplasticity. Frontiers in Cellular Neuroscience. 2014;8:430.

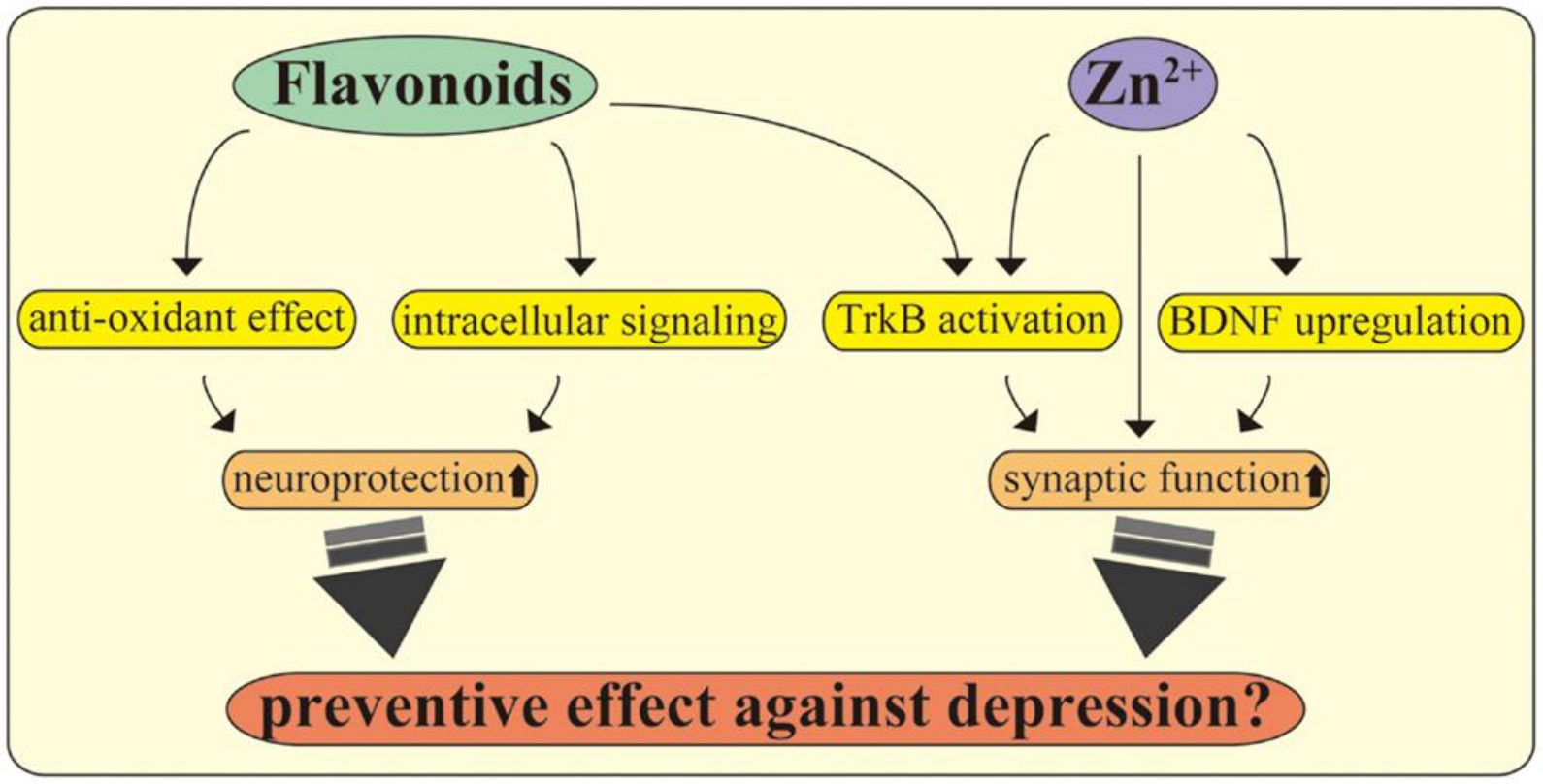
Disease States Associated with Low BDNF

- Depression and mood disorders
- ADHD
- Autism Spectrum Disorders?
- Traumatic brain injury
- Degenerative Disease





Calabrese F. et al. Brain-derived neurotrophic factor: a bridge between inflammation and neuroplasticity. Frontiers in Cellular Neuroscience. 2014;8:430.



The role of BDNF in comorbid depression: possible linkage with steroid hormones, cytokines and nutrition.
Numakawa T. et al. Frontiers in Psychiatry. 2014 Vol 5(136)

Genetic SNP's in BDNF

Val66 Met polymorphism

20 to 30% of Caucasians

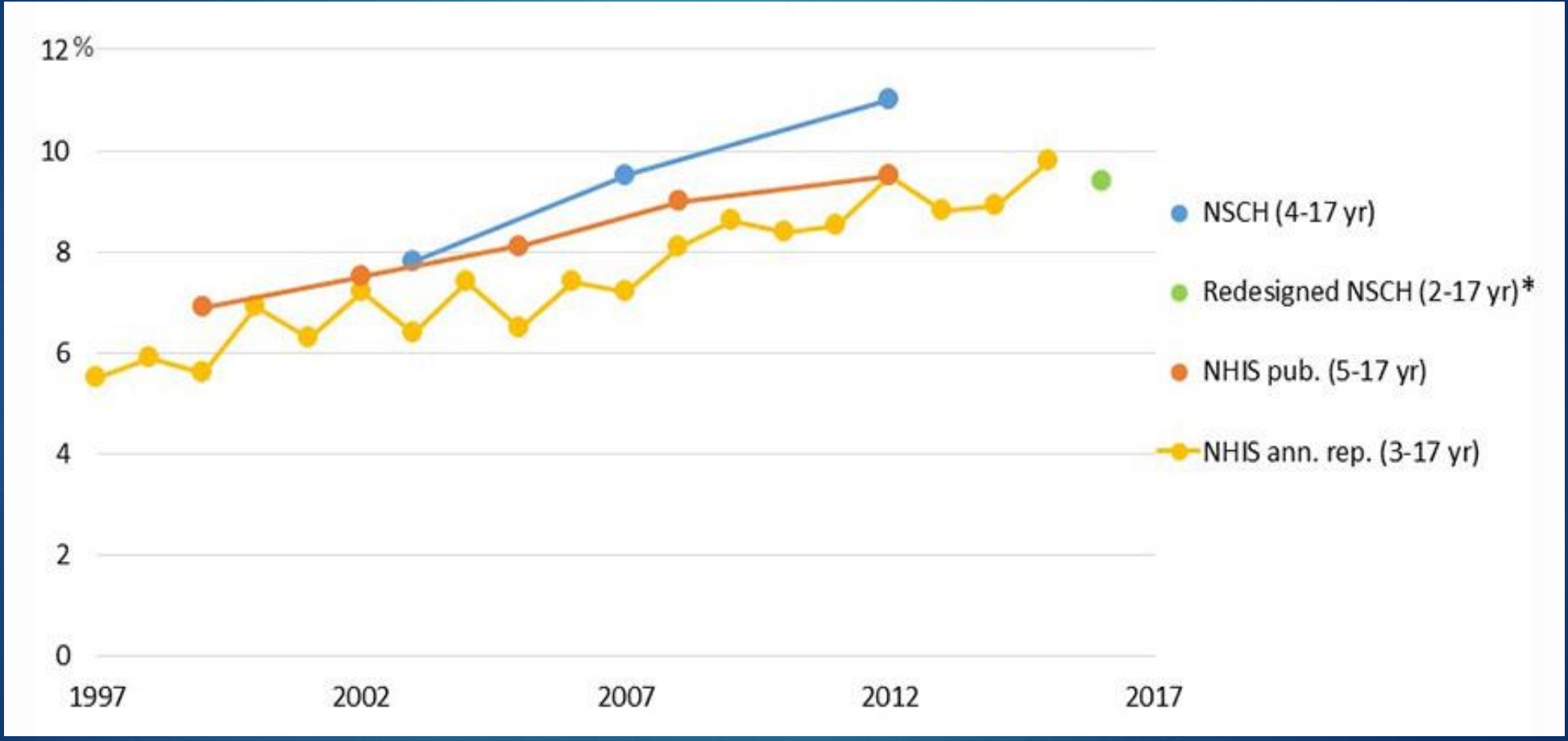
The association between *BDNF* Val66Met polymorphism and emotional symptoms after mild traumatic brain injury. *BMC Medical Genetics*. 2018. Wang Y-J, Chen K-Y, Kuo L-N, et al. ;19:13. doi:10.1186/s12881-017-0518-0.

- Patients with the BDNF Val66Met allele
  - Higher anxiety scores
  - Higher depression scores
  - Following traumatic brain injury

Prevalence of ADHD

https://www.cdc.gov/ncbddd/adhd/timeline.html

(Percent of children with a parent-reported ADHD diagnosis)



Inflammation in ADHD

METHODS: Sixty children were studied: 34 consecutive drug-naïve children with ADHD (30 males and 4 females; mean age of 10.10 years, sd=2.43 age) and 26 healthy control children (22 males and 4 females; mean age of 10.70 years, sd=1.81).

RESULTS: Data reveal higher IL-6 and IL-10 levels in ADHD patients than in the control group (p= .03).

- DonFrancesco. R. et al. Serum cytokines in paediatric neuropsychiatric syndromes: focus on Attention Deficit Hyperactivity Disorder. Minerva Pediatrica. 2016 Dec.

Prevalence of ASD

- About 1 in 59 children in 2016:CDC's Autism and Developmental Disabilities Monitoring (ADDM) Network. From 1 in 150 children in 2000
- ASD is about 4.5 times more common among boys (1 in 42) than among girls (1 in 189).
- Studies in Asia, Europe, and North America have identified individuals with ASD with an average prevalence of between 1% and 2%.
- About 1 in 6 children in the United States had a developmental disability in 2006-2008, ranging from mild disabilities such as speech and language impairments to serious developmental disabilities, such as intellectual disabilities, cerebral palsy, and autism.

- https://www.cdc.gov/ncbddd/autism/data.html

Summary of Neuroinflammation markers in ASD

- Microglial activation
- Astrocytic activation with elevated levels of GFAP(glial fibrillary acidic protein)
- Proinflammatory profile of cytokines in the brain, CSF and blood
- Nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB) activation

ADHD in adults and low BDNF

International Journal of Neuropsychopharmacology (2013), **16**, 1267–1275. © CINP 2013
doi:10.1017/S1461145712001629

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Decreased serum levels of brain-derived neurotrophic factor in adults with attention-deficit hyperactivity disorder

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Abstract

It has been hypothesized that brain-derived neurotrophic factor (BDNF) is involved in the pathogenesis of attention-deficit hyperactivity disorder (ADHD), although experimental data regarding the contribution of *BDNF* gene polymorphisms to this psychiatric disorder are controversial. Recently, changes in BDNF serum levels have been reported in children with ADHD, but there are no studies about the possible role of this neurotrophin in adults. A total of 54 Caucasoid ADHD adults, including the predominantly inattentive and combined types (aged 33.43 ± 8.99 yr) and 59 Caucasoid unrelated healthy controls (aged 35.52 ± 9.37 yr) were included in a study to evaluate BDNF levels in serum. Medical, neurological and psychiatric co-morbidities were excluded. Clinical data concerning ADHD diagnosis and blood samples for patients and controls were collected. BDNF serum levels were significantly lower in adults with ADHD compared to healthy controls ($p < 0.0001$). Although the combined type of ADHD subgroup displayed lower BDNF serum levels than the inattentive type, the differences did not reach statistical significance. No significant correlations were found between serum BDNF levels and scores on the Conners' Adult ADHD Rating Subscales. These results suggest a role for BDNF in ADHD, at least in those patients whose disorder persists throughout life. Low BDNF levels may contribute to the neurodevelopmental deficits of ADHD and to the persistence of the disorder into adulthood. BDNF differences between ADHD subtypes should be further studied.

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Key words: ADHD, BDNF, brain-derived neurotrophic factor, epigenetics, neurodevelopment.

Introduction

Attention-deficit hyperactivity disorder (ADHD) is a psychiatric condition that is defined by the core symptoms of inattention, hyperactivity and impulsivity and that begins in childhood, before the age of 7 yr, according to the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition Revised (DSM-IV-TR). Symptom intensity, especially hyperactivity, has been shown to decrease over time (Hart et al., 1995; Mick et al., 2004); however, for many patients the disorder persists into adulthood, although in some of them only some impairing symptoms remain (Rasmussen and Gillberg, 2000). The estimated prevalence of ADHD in adults ranges from 2.9% (Faraone and Biederman, 2005) to 4.4% (Kessler et al., 2006).

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Although the underlying pathogenesis of ADHD is still not well established, it is already accepted that it has a multi-factorial neurodevelopmental origin with a strong genetic component, with an estimated heritability of approximately 60% (Biederman and Faraone, 2005). Environmental risk factors also play a role in ADHD, especially if they are present in the pre- and early postnatal periods during the development of the brain (Galéra et al., 2011; Sagiv et al., 2012). From a neurobiological point of view, different lines of evidence suggest the involvement of the dopaminergic and serotoninergic systems (Solanto, 2002; Ribasés et al., 2009; Landaas et al., 2010; Nijmeijer et al., 2010) in the pathogenesis of ADHD. Experimental studies have shown a strong relationship between these monoamergic systems and a member of the neurotrophin family, brain-derived neurotrophic factor (BDNF; Küppers and Beyer, 2001; Dluzen et al., 2002; Goggi et al., 2003), which is widely expressed in the mammalian brain (Leibrock et al., 1989). BDNF has an important role in the development of the dopamine system (Yurek et al., 1996; Küppers and

ADHD in children and low BDNF

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ORIGINAL ARTICLE

Brain-Derived Neurotrophic Factor as a Biomarker in Children wi on Deficit-Hyperactivity Disorder

Farshid Saadat[1], Maryam Kosha[2], Ali Amiry[2], Gholamreza Torabi[2]*

[1]Department of Immunology, School of Medicine, Guilan University of Medical Sciences, Rasht-3477 Iran, [2]Department of Psychiatry, Shafa Hospital, Rasht, Iran

Abstract :

Background: Evidence suggests that Brain-Derived Neurotrophic Factor (BDNF) is involved in the pathogenesis of Attention-Deficit Hyperactivity Disorder (ADHD), although experimental data regarding the contribution of BDNF concentration to this psychiatric disorder are controversial. *Aim:* To evaluate the plasma levels of BDNF in patients with ADHD. *Material and Methods*: In this cross sectional study, ADHD and controls were recruited from the outpatient clinic of the Shafa Hospital, Rasht; between March 2012 and April 2013. Clinical data concerning ADHD diagnosis and blood samples for patients were collected before treatment. Medical, neurological and psychiatric co-morbidities were excluded. The mean of BDNF concentration measured and compared with healthy controls. BDNF assay was determined using ELISA kits according to manufacturer's instructions. Descriptive statistical analysis was used with analysis of variance to find the significance of data. *Results*: Statistical analyses showed that the mean BDNF levels were significantly lower in ADHD patients and its subgroups as compared with normal control subjects ($p<0.001$). *Conclusion*: This study showed a dramatically lower BDNF plasma levels in untreated patients with ADHD, which might be useful adjunct method for diagnosis of ADHD in society.

Keywords: Brain-Derived Neurotrophic Factor (BDNF), Attention-Deficit Hyperactivity Disorder (ADHD), BDNF Blood Level

Introduction:

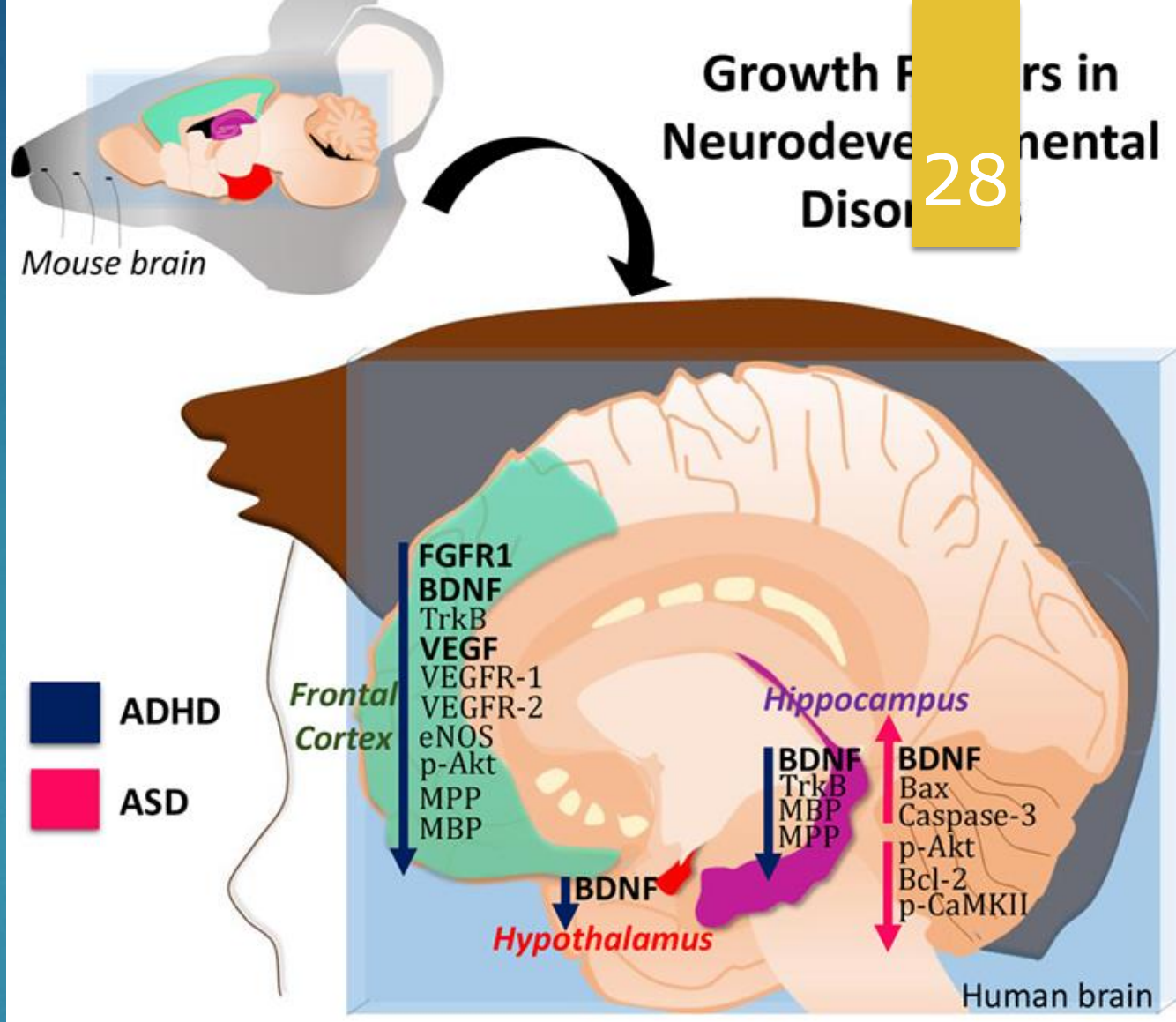
Attention deficit-hyperactivity disorder (ADHD) is a mental and neurobehavioral disorder characterized by inattention, impulsivity and hyperactivity. Diagnosing ADHD is based on its symptoms to inattention (ADHD-I), hyperactivity-impulsiveness (ADHD-H) or a combination of inattention and hyperactivity (ADHD-C) [1]. ADHD affects children globally and is diagnosed about twelve percent of Iranian kindergartens and school-aged children [2]. Moreover, its symptoms can be difficult to differentiate from other disorders, increasing the likelihood that the diagnosis of ADHD would be missed.

Although, the definite causes of ADHD are ambiguous, some factors such as genetics, dietary and the social environmental factors might be important to contributors in this disorder [3, 4]. Recently, there is evidence, which suggests that brain-derived neurotrophic factor, is involved in the pathogenesis of ADHD [5].

Brain-derived neurotrophic factor (BDNF) is a 25-kDa member of the neurotrophin family and highly expressed in cortical and hippocampal structures. It enhances the growth and maintenance of several neuronal systems as well

BDNF and other growth factors in Autism and ADHD

- Galvez-Contreras AY. Et al. Alterations of Growth Factors in autism and ADHD. Front Psychiatry.13 July 2017.



Expression levels of GF in blood

ADHD	ASD
↓ BDNF	BDNF ↑
↑ GDNF	TGF-β1 ↓
↑ NGF	EGF ↓
↑ NT3	NT4 ↓
↑ IGF2	HGF ↓

Autism and BDNF: mixed results

- Measurement of ProBDNF versus BDNF
- Different receptors with different actions

DOI 10.1007/s10571-016-0415-7

BRIEF COMMUNICATION

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Meta-Analysis of BDNF Levels in Autism

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Received: 18 May 2016 / Accepted: 3 August 2016

Abstract Brain-derived neurotrophic factor (BDNF) centrally mediates growth, differentiation and survival of neurons, and the synaptic plasticity that underlies learning and memory. Recent meta-analyses have reported significantly lower peripheral BDNF among individuals with schizophrenia, bipolar disorder, and depression, compared with controls. To evaluate the role of BDNF in autism, and to compare autism to psychotic-affective disorders with regard to BDNF, we conducted a meta-analysis of BDNF levels in autism. Inclusion criteria were met by 15 studies, which included 1242 participants. The meta-analysis estimated a significant summary effect size of 0.33 (95 % CI 0.21–0.45, $P < 0.001$), suggesting higher BDNF in autism than in controls. The studies showed notable heterogeneity, but no evidence of publication biases. Higher peripheral BDNF in autism is concordant with several neurological and psychological theories on the causes and symptoms of this condition, and it contrasts notably with the lower levels of BDNF found in schizophrenia, bipolar disorder, and depression.

Keywords Autism · BDNF · Meta-analysis · Schizophrenia · Bipolar disorder · Depression

Electronic supplementary material The online version of this article (doi:10.1007/s10571-016-0415-7) contains supplementary material, which is available to authorized users.

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Published online: 08 August 2016

Introduction

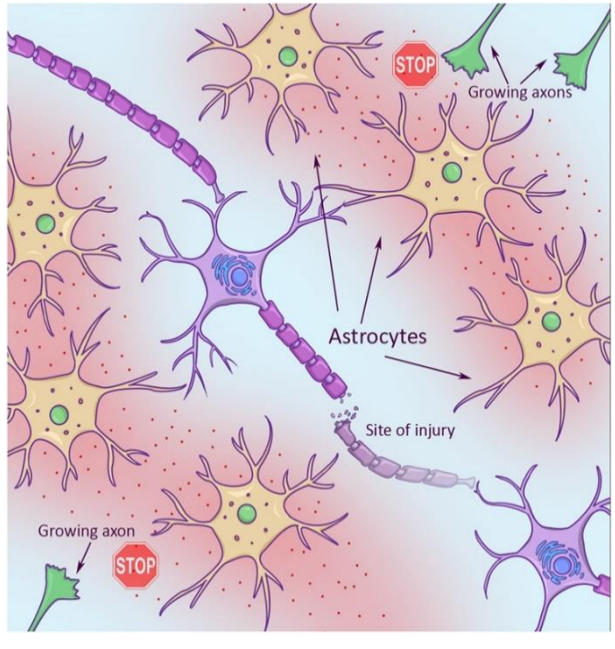
Brain-derived neurotrophic factor (BDNF) is a protein that belongs to the family of neurotrophins (Brigadski and Lessmann 2014). BDNF regulates dendritic spine maturation and pruning and plays important roles in promoting growth, differentiation, and survival of neurons (Binder and Scharfman 2004; Orefice et al. 2016). Expression of BDNF is regulated in part by neuronal activity induced by sensory stimulation (Woo and Lu 2009), and local protein synthesis at dendrites is mediated by BDNF, whereby it contributes to synaptic plasticity, learning, and memory (Lu et al. 2013; Bowling et al. 2016).

Given the considerable importance of BDNF, levels of this factor have been investigated among individuals with a range of psychiatric conditions. In particular, recent meta-analyses have demonstrated that BDNF levels in serum or plasma are significantly lower in subjects with schizophrenia (Ahmed et al. 2015), bipolar disorder (Fernandes et al. 2015), and depression (Molendijk et al. 2013) than in matched controls. The similar results across these three psychotic-affective disorders are not unexpected, given the strong overlap between them in their causes, phenotypic manifestations, and risk factors (e.g., Konstantareas and Hewitt 2001).

The pattern of association of BDNF levels with autism has been unclear (Tsai 2005; Halepoto et al. 2014). Serum or plasma BDNF is higher among individuals with autism compared with controls in some studies (e.g., Connolly et al. 2006; Ricci et al. 2013), but other studies have reported lower levels (e.g., Nelson et al. 2001; Hashimoto et al. 2007), or nonsignificant differences (e.g., Croen et al. 2008). The overall pattern of association between BDNF and autism has thus remained unresolved, and the causes of

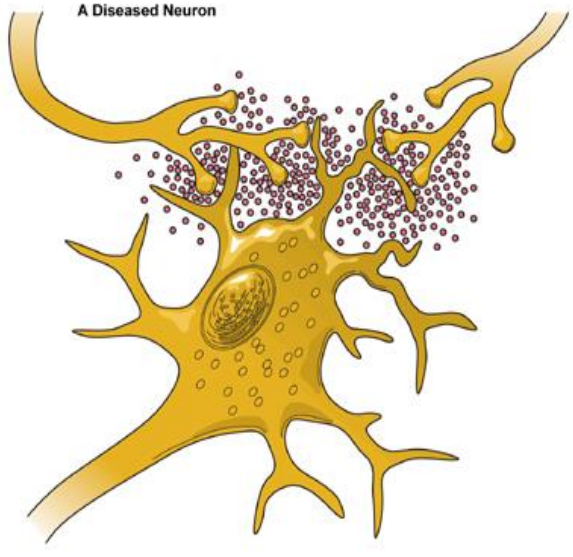
Circulating brain-derived neurotrophic factor has diagnostic and prognostic value in traumatic brain injury. *Journal of Neurotrauma*, Korley, F. et al. (2016). 33(2), 215-225. DOI: 10.1089/neu.2015.3949

- Levels of (BDNF), taken within 24 hours of someone's head injury, could predict the severity of a TBI and how a patient would fare.
  - Healthy BDNF: 60
  - Average head trauma: 20
  - Most severe head trauma: 4
- patients with high levels of BDNF had mostly recovered from their injuries 6 months later.
- patients with the lowest levels of BDNF, symptoms still lingered at follow-up 6 months later



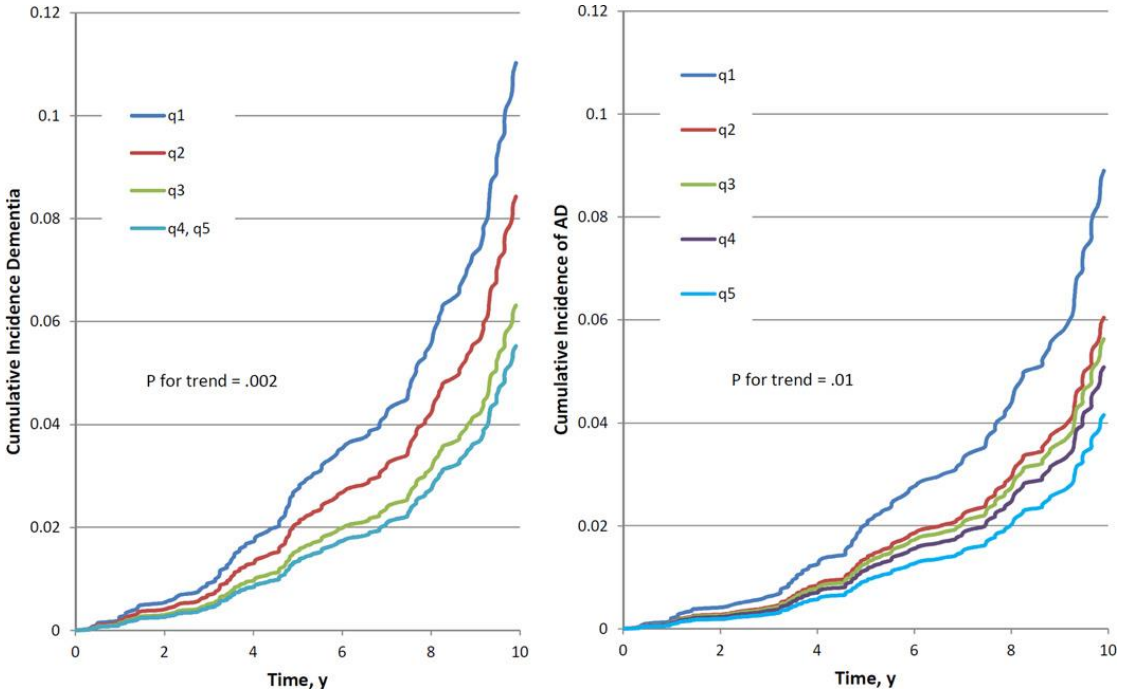
Preliminary associations between brain derived neurotrophic factor, memory impairment, functional cognition, and depressive symptoms following severe TBI Michelle D. Failla et al. Neurorehabil Neural Repair. 2016

- Abstract Background—Traumatic brain injury (TBI) often leads to mood and cognitive complications, impacting functional recovery. Brain derived neurotrophic factor (BDNF) is a likely target based on evidence of reduced BDNF signaling in experimental TBI
- Results:
  - Serum BDNF was reduced after TBI versus controls at all time-points.
  - At 12 months, chronic serum BDNF tended to be lower in participants with PTD

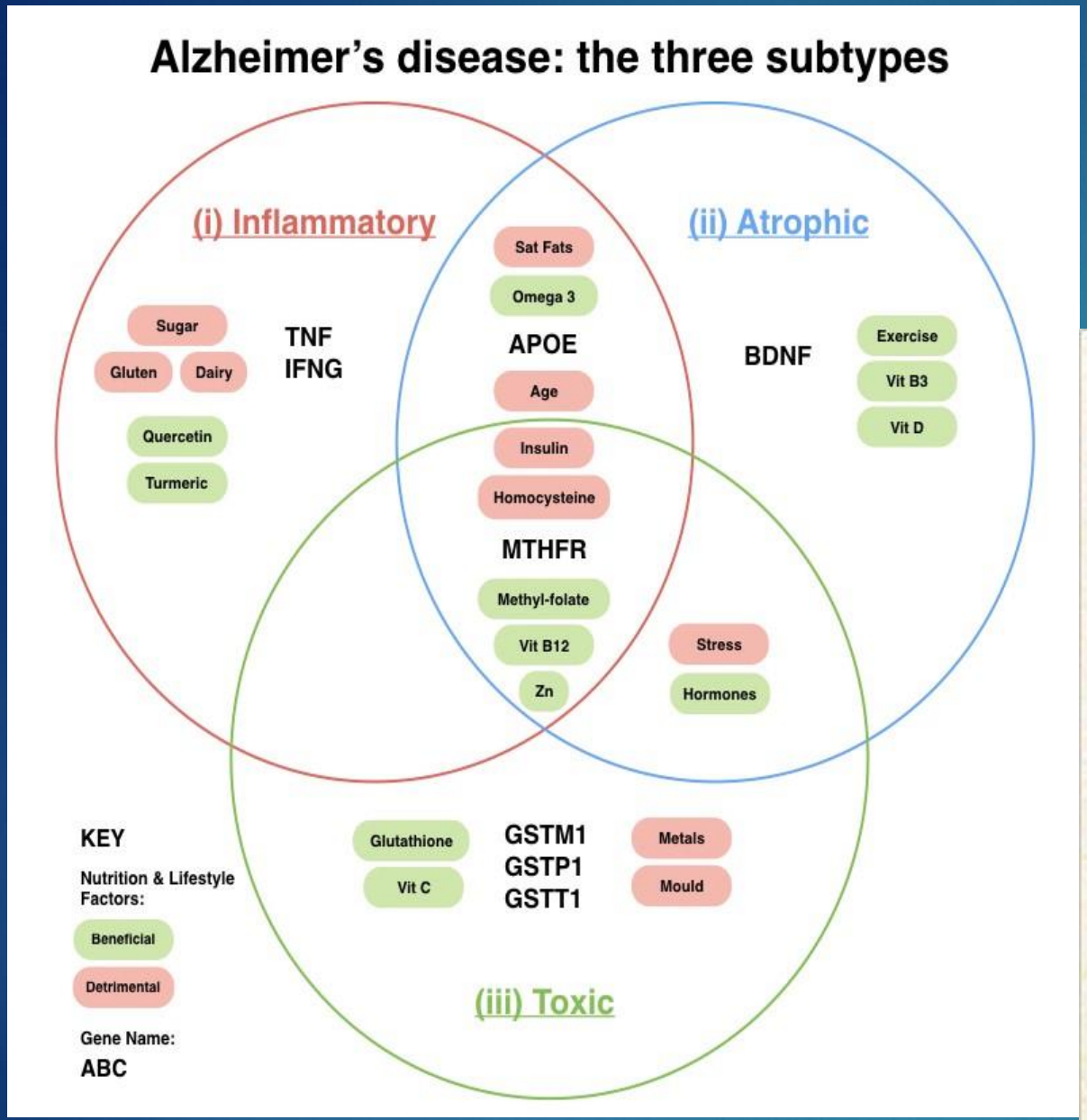


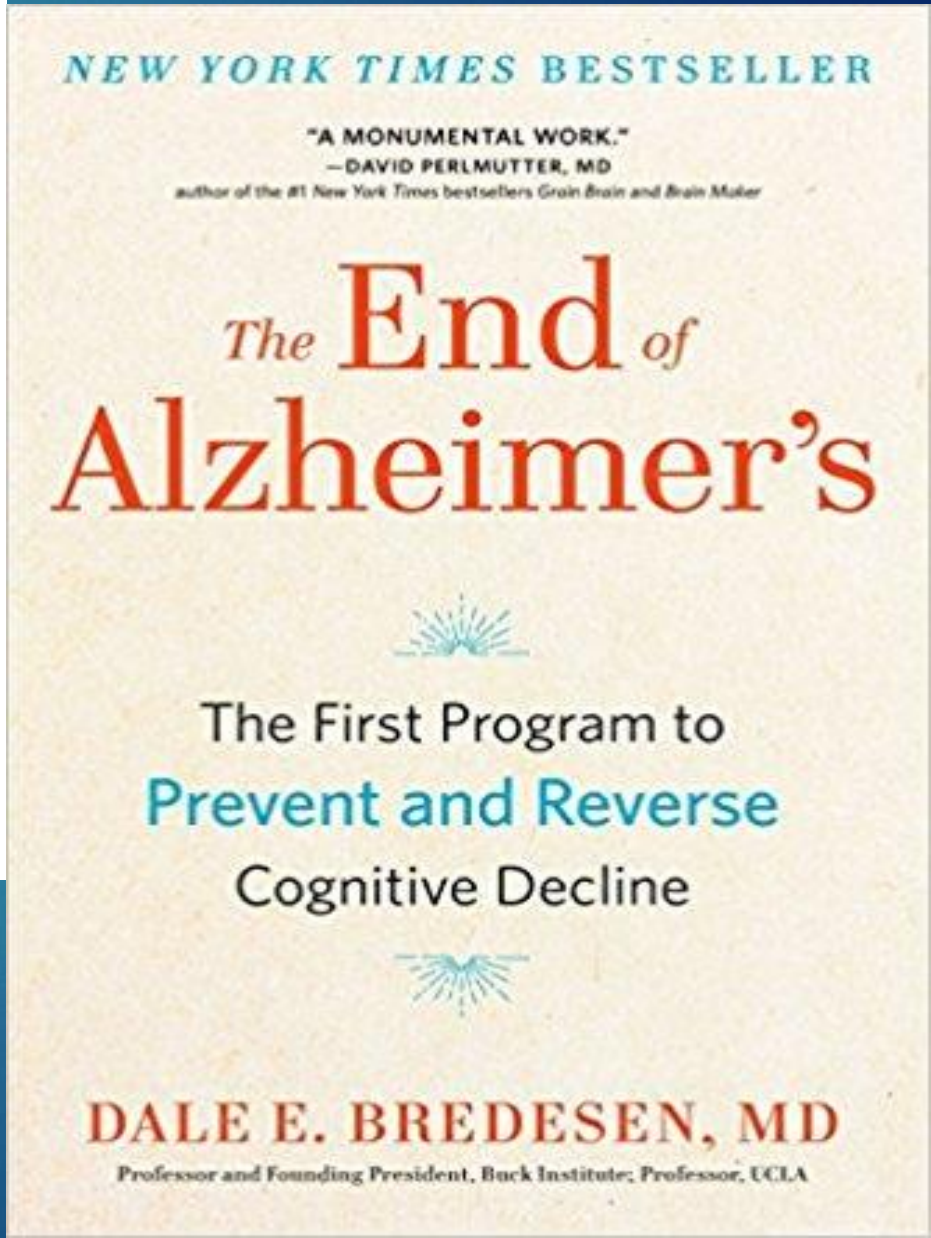
HIGHER BDNF

LESS DEMENTIA



Weinstein G, Beiser AS, Choi SH, et al. Serum brain-derived neurotrophic factor and the risk for dementia: the Framingham Heart Study. JAMA Neurol. 2014;71(1):55-61.


Alzheimer's disease: the three subtypes
(i) Inflammatory
(ii) Atrophic
(iii) Toxic
Sugar
Gluten
Dairy
Quercetin
Turmeric
TNF
IFNG
Sat Fats
Omega 3
APOE
Age
Insulin
Homocysteine
MTHFR
Methyl-folate
Vit B12
Zn
BDNF
Exercise
Vit B3
Vit D
Stress
Hormones
Glutathione
Vit C
GSTM1
GSTP1
GSTT1
Metals
Mould
KEY
Nutrition & Lifestyle Factors:
Beneficial
Detrimental
Gene Name:
ABC


NEW YORK TIMES BESTSELLER
"A MONUMENTAL WORK."
—DAVID PERLMUTTER, MD
author of the #1 New York Times bestsellers Grain Brain and Brain Maker
The End of Alzheimer's
The First Program to Prevent and Reverse Cognitive Decline
DALE E. BREDESEN, MD
Professor and Founding President, Buck Institute; Professor, UCLA

BDNF Essentials™

Supplement Facts

Serving Size: 2 Capsules Servings Per Container: 60

Amount Per Serving		%Daily Value
Choline (as Cytidine Diphosphate Choline Sodium Salt)**	25 mg	5%
Sodium (as Cytidine Diphosphate Choline Sodium Salt)**	5 mg	<1%
NeuroCyto Protect™ Blend Lions Mane Mushroom (*Hericium erinaceus*) mycelium Powder, Skullcap (*Scutellaria lateriflora*) Herb Powder, Bilberry (*Vaccinium myrtillus*) Fruit Extract, Bacopa (*Bacopa monnieri*) Herb Powder, Sensoril® Ashwagandha (*Withania somnifera*) Root and Leaf Extract	1175 mg	†
Cognition Blend CDP Choline Sodium Salt, Sharp-PS® Phosphatidylserine	175 mg	†

† Daily Value not established.

OTHER INGREDIENTS: Hypromellose (Capsule), Leucine.

**Choline and Sodium are from Cognition Blend
Sensoril® is a registered trademark of NutraGenesis, LLC.
Sharp-PS® is a registered trademark of Enzymotec USA, Inc.

Research area	Specifics	Skullcap	Lion's Mane	Bacopa	Ashwagandha	Blueberry	Citicoline	PS
Neuroplasticity	Increase BDNF	x	x	x	x	x		
	increase learning	x	x	x	x	x	x	x
	increase memory	x	x	x	x	x	x	x
	improve cognitive fxn	x	x	x	x	x	x	x
	increase executive fxn				x			
	improve psychomotor				x			
	improved acetylcholine						x	x
	improved attention			x	x		x	x
	improved processing speed			x	x		x	
	improved hippocampal fxn				x			
	improved telomerase activity				x			
Neurologic	Decrease glutamate		x					
	decrease seizures	x						
	improve mood	x			x			x
	decrease anxiety	x			x			x
	decrease depression					x		x
	decrease b-amyloid	x	x	x	x		x	
	improved optic fxn							
	improved sleep	x			x			x
	decrease synuclein protein	x	x					
Inflammation	Decrease oxidative stress	x	x	x		x	x	x
	decrease inflammation	x	x	x	x	x	x	x
	inhibit NF-KB				x			
	activate nrf2			x		x		
	increase antioxidants	x			x	x		
stress	decrease cortisol				x			x
	decrease stress symptoms				x			
	increased blood flow							
	formation of cell membranes						x	x
neurogenesis	stimulate brain regeneration	x	x					

Lion's Mane Mushroom (Hericium erinaceus)

- Increase BDNF*
- Increase neurogenesis*
- Decrease glutamate*
- Increase memory, learning, cognitive fxn
- Decrease b-amyloid protein(Alzheimer's)
- Decrease synuclein protein(Parkinson's)
- Decrease oxidative stress
- Anti-inflammatory

Lion's Mane (Hericium)

Lion's Mane Mushroom strongly stimulates the synthesis of nerve growth factor (NGF)

In this study, 6 months of taking Lion's Mane mushroom, 6 out of 7 dementia patients demonstrated improvements in their perceptual capacaties, and all 7 had improvements in their dressing, bathing and eating scores.

Scientists believe that Lion's Mane may be a powerful reducer of brain inflammation and a strong inducer of brain tissue regeneration.

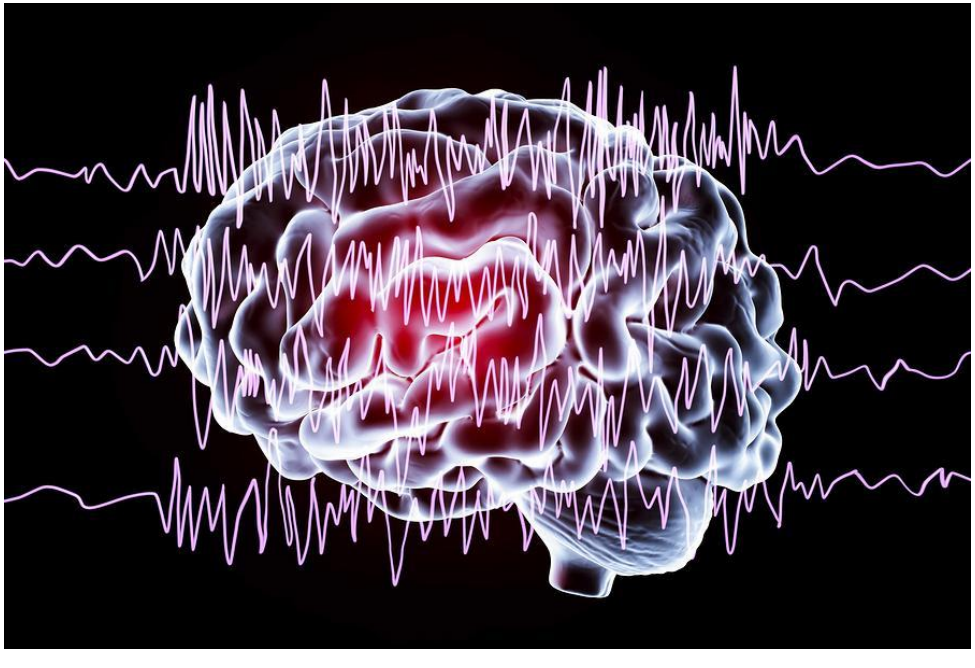
Alzheimers Issue. Phytotherapy Research. Volume 23, Issue 3, pages 367-372, March 2009

Skullcap: American

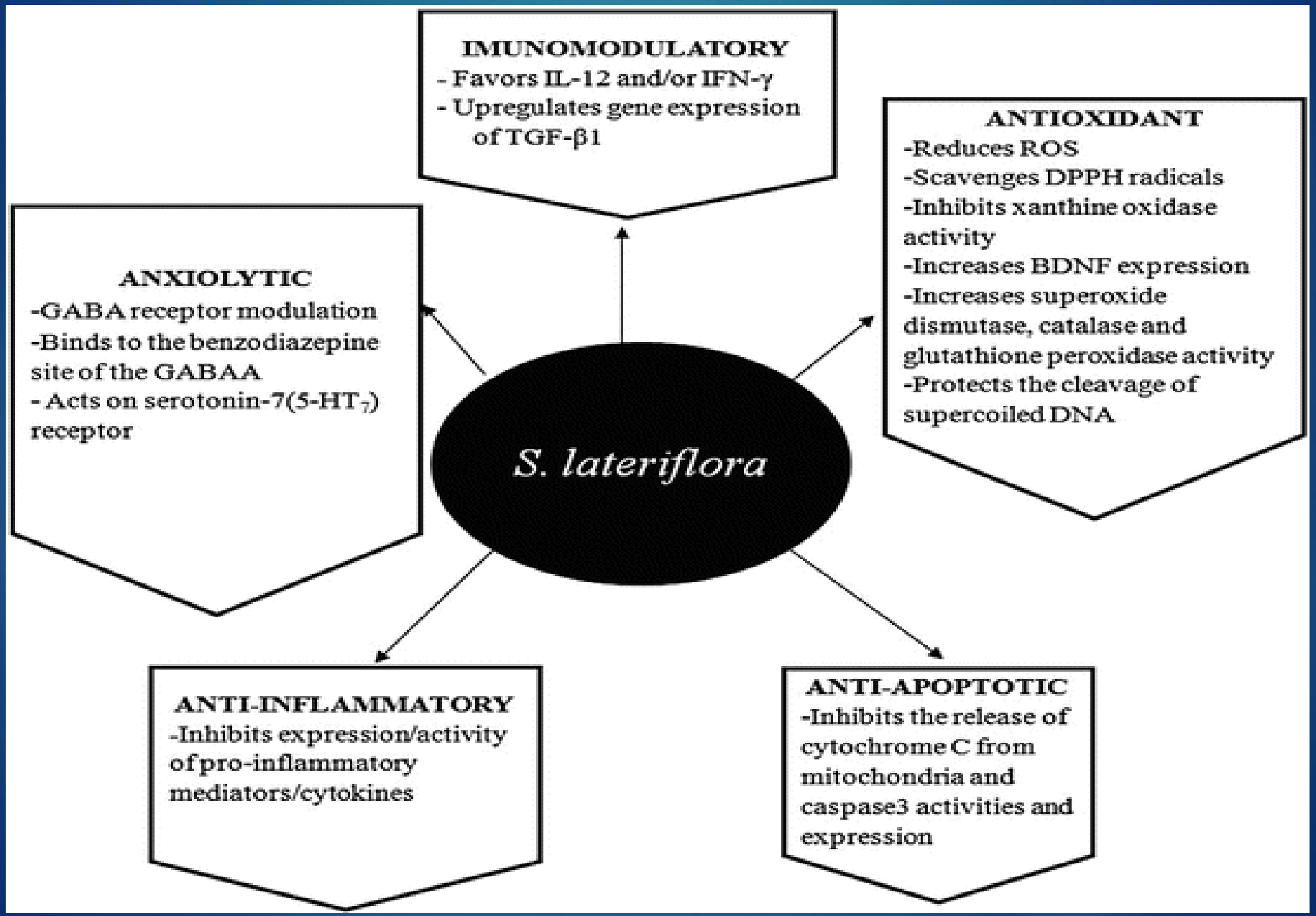
Scutellaria Lateriflora

Skullcap Neurologic Functions

- Increase BDNF*
- Increase neurogenesis*
- Decrease seizures*
- Increase memory, learning, cognitive fxn
- Improved sleep
- Decrease anxiety
- Decrease b-amyloid protein(Alzheimer's)
- Decrease synuclein protein(Parkinson's)



Skullcap Functions



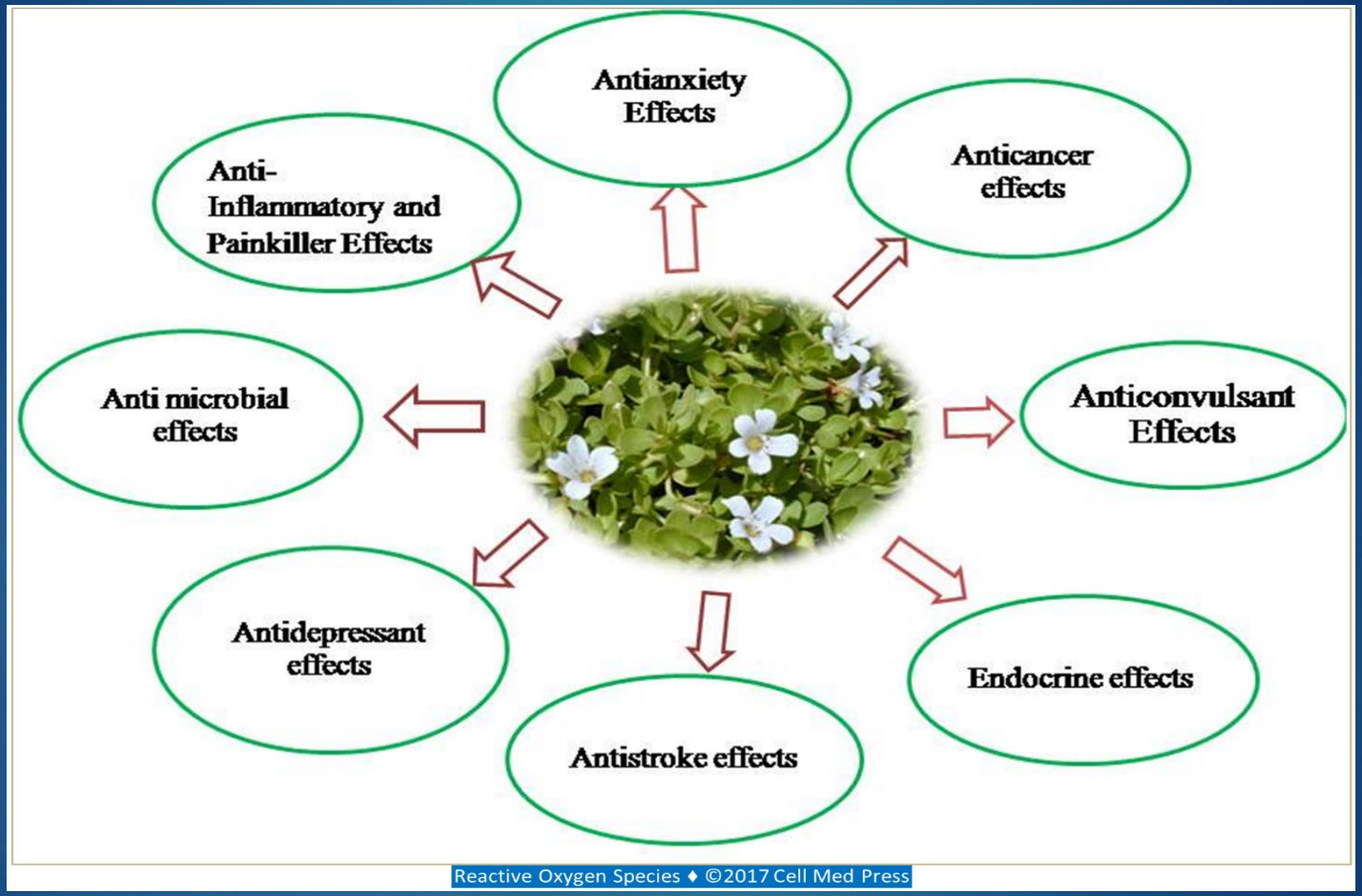
Blueberry/Bilberry

- Increase BDNF*
- Increase neurogenesis*
- Activate Nrf2*: Brain anti-oxidant*
- Increase attention
- Increase processing speed
- Increase memory, learning, cognitive function
- Improved sleep
- Decrease seizures
- Decrease depression
- Decrease oxidative stress
- Anti-inflammatory

Bacopa:

Bacopa Monnieri

Bacopa: Functions



Ashwagandha

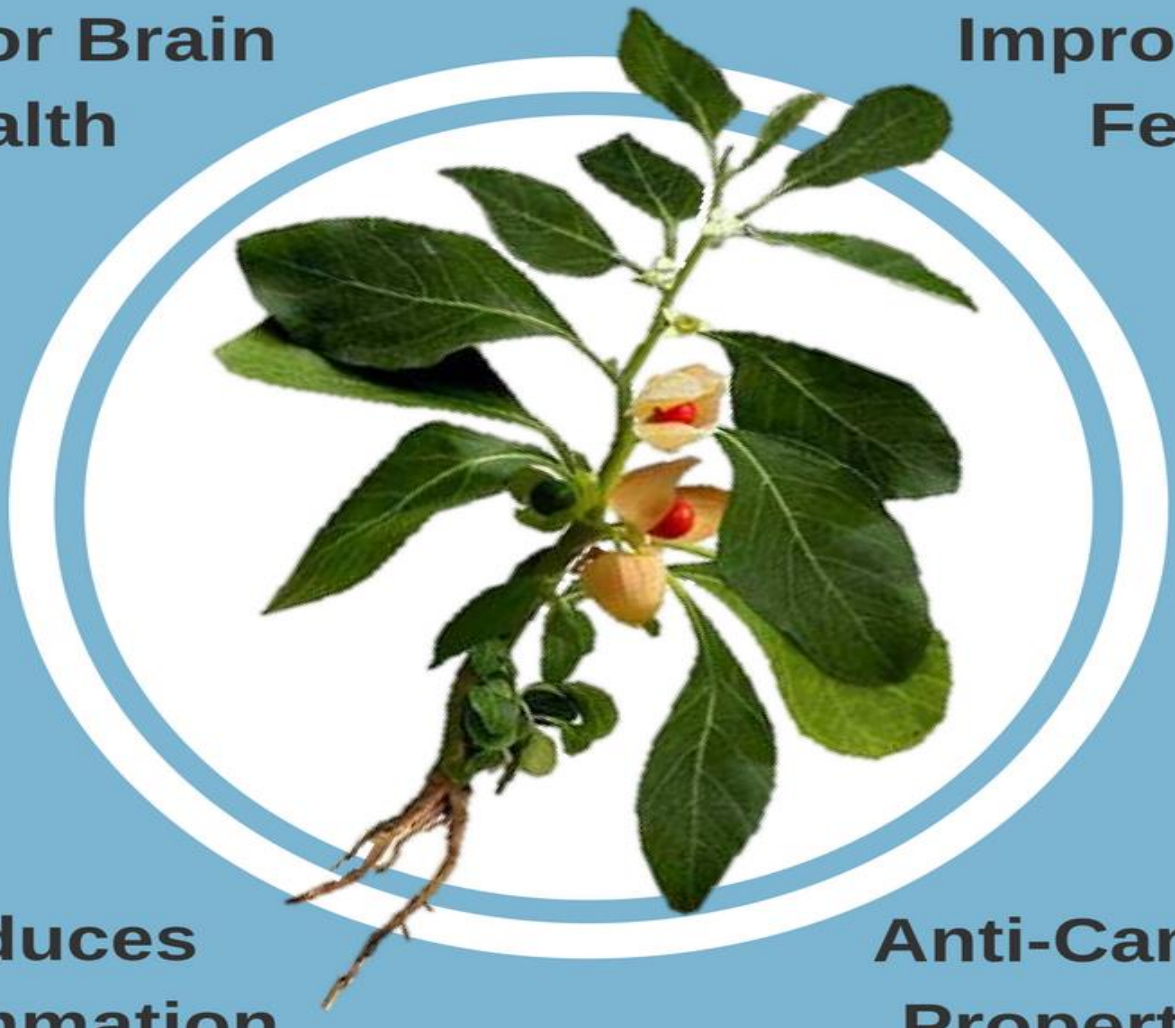
Withania Somnifera

Benefits of Ashwagandha

Great for Brain Health

Improves Male Fertility

Boosts Immune System



Increases Energy Naturally

Lowers Blood Sugar

Reduces Stress & Anxiety

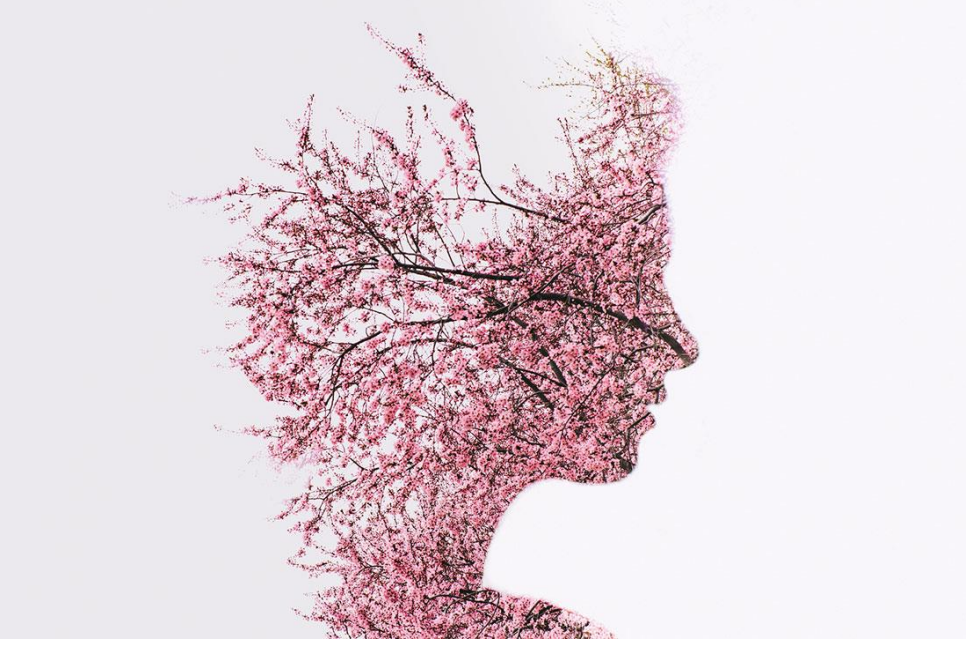
Reduces Inflammation

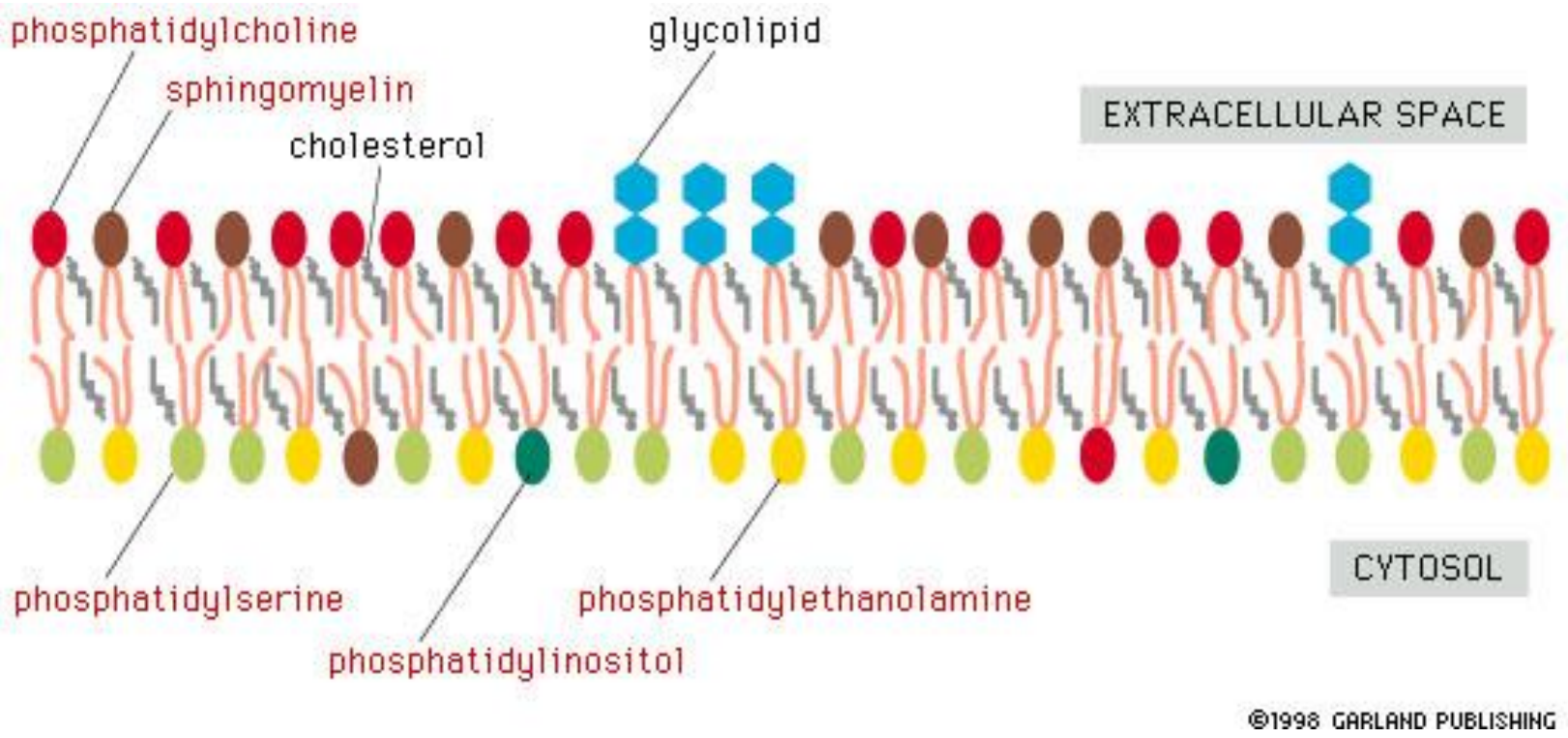
Anti-Cancer Properties

STRESSRX

Neurologic Benefits of Ashwagandha

- Increase BDNF*
- Increase neurogenesis*
- Decrease cortisol and stress*- adaptogen
- Increase memory, learning, cognition
- Improved sleep
- Increase telomerase activity
- Decrease anxiety, depression
- Improve mood
- Decrease b-amyloid protein(Alzheimer's)
- Decrease synuclein protein(Parkinson's)
- Decrease oxidative stress
- Anti-inflammatory

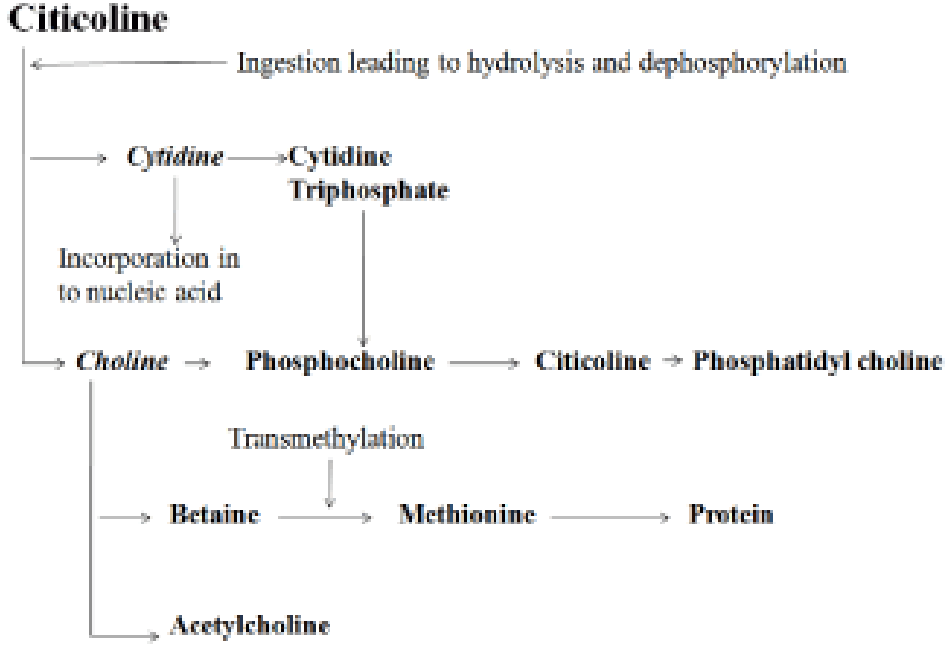




Cell Membrane

Citicoline Benefits

- Improved cell membranes*
- Increase acetylcholine*
- Increase learning, memory, cognitive function
- Improve attention
- Decrease b-amyloid
- Methyl donor



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Abstract

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Methods Find Exp Clin Pharmacol. 1997 Apr;19(3):201-10.

Citicoline improves memory performance in elderly subjects.

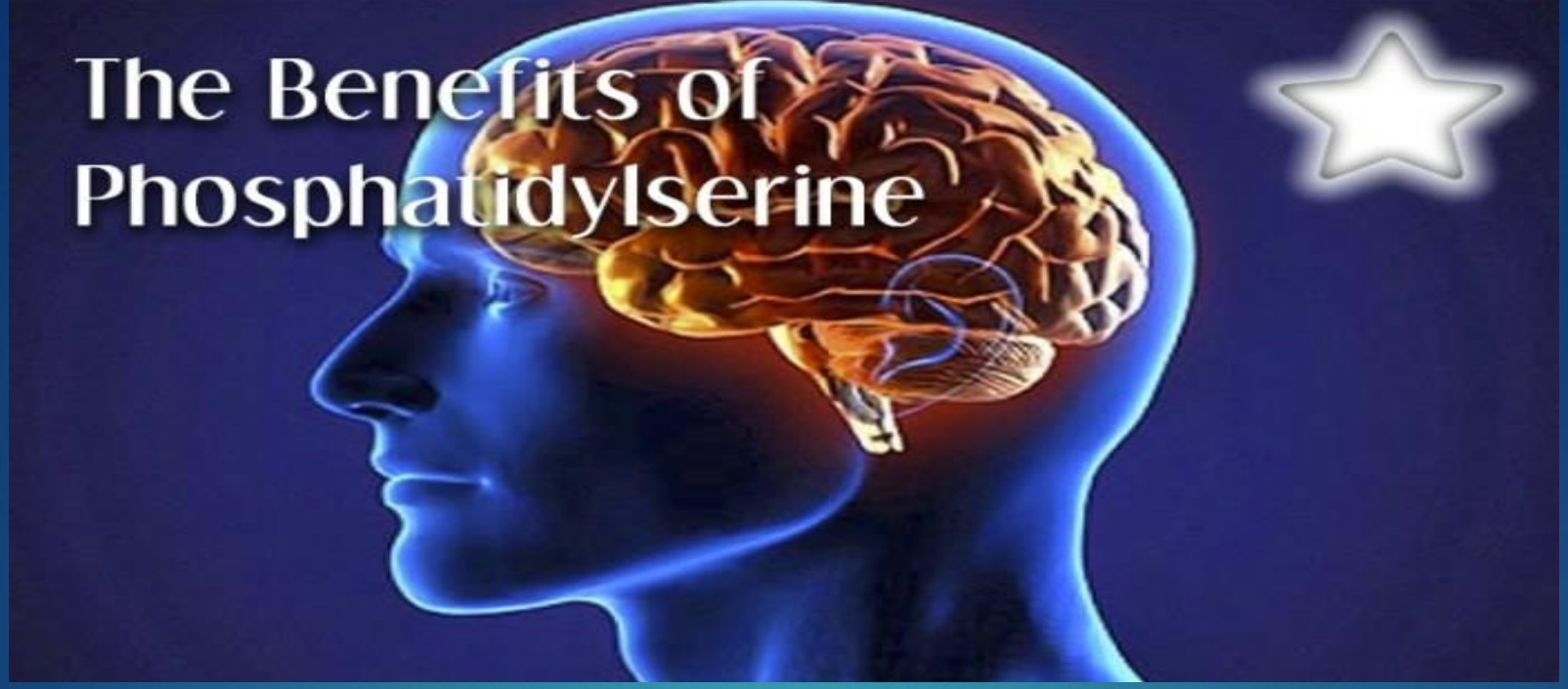
Alvarez XA[1], Laredo M, Corzo D, Fernández-Novoa L, Mouzo R, Perea JE, Daniele D, Cacabelos R.

Author information

[1]EuroEspes Biomedical Research Center, La Coruña, Spain.

Abstract

Citicoline is a choline donor involved in the biosynthesis of brain phospholipids and acetylcholine extensively used in the treatment of neurodegenerative diseases. In this study we investigated the effects of the oral administration of citicoline alone (C1000:1000 mg/day; C500:500 mg/day) or in combination with nimodipine (C +NI:300 + 90 mg/day) during 4 weeks on memory performance in elderly subjects with memory deficits and without dementia (N = 24; age = 66.12 +/- 10.78 years; MMS score = 31.69 +/- 2.76). Results indicated that citicoline in comparison with placebo improves memory in free recall tasks, but not in recognition tests. A significant improvement in word recall (5.17 +/- 1.1 vs. 3.95 +/- 1.2 omissions; $p < 0.005$), immediate object recall (6.5 +/- 1.6 vs. 5.5 +/- 1.2 omission; $p < 0.05$) and delayed object recall (8.5 +/- 2.1 vs. 6.7 +/- 2.4 omissions; $p < 0.005$) was observed after citicoline treatment. Similar results were found in the three subgroups of treatment (8 subjects per group), suggesting that citicoline possesses memory-enhancing activity at doses of 300-1000 mg/day. A decrease in systolic blood pressure and minor changes in lymphocyte cell counting were also observed in old subjects after receiving citicoline. These effects are consistent with the vasoregulatory and neuroimmune actions of citicoline and suggest that this compound may improve memory by acting on mechanisms of brain neurotropism and cerebrovascular regulation. According to the present results, showing that citicoline improves memory performance in elderly subjects, we concluded that this molecule is suitable for the treatment of memory deficits in old people.



- Improved cell membranes*
- Increase acetylcholine*
- Decrease cortisol and stress*
- Increase learning, memory, cognitive function
- Improved sleep
- Decrease anxiety, depression
- Improve attention
- Decrease b-amyloid

Key concepts
BDNF Essentials™

- Increases BDNF
- Increases Neuroplasticity
- Supports cognitive functioning: memory, attention, learning
- Decreases cortisol and stress: helps increase BDNF
- Anti-inflammatory and anti-oxidant
- **NOT** activating

Key concepts *Neuroplasticity*

- Exercise both body and brain
- Low glycemic diet with good fats
- Supportive herbs and nutrition
- Decrease stress so normalize HPA axis
- Decrease inflammation
- Decrease oxidative stress
- Minimize and remove neurotoxins

References

- Alvarez XA. Et al. Double-blind placebo-controlled study with citicoline in APOE genotyped Alzheimer's disease patients. Effects on cognitive performance, brain bioelectrical activity and cerebral perfusion. *Methods Find Exp Clin Pharmacol.* 1999 Nov;21(9):633-44.
- Auddy B. et al. A standardized *Withania somnifera* extract reduces stress related parameters in chronically stressed humans – a double-blind, randomized, placebo-controlled study. *JANA. 2008.* Vol. II, No. I, pp. 50-56.
- Baumeister et al. Influence of phosphatidylserine on cognitive performance and cortical activity after induced stress. Nutr Neuroscience. 2008 Jun;11(3):103-10.
- Bowtell JL. Et al. Enhanced task-related brain activation and resting perfusion in healthy older adults after chronic blueberry supplementation. *Applied Physiology, Nutrition, and Metabolism*, 2017, 42(7): 773-779.
- Cenacchi T, et al. Cognitive decline in the elderly: a double-blind, placebo-controlled multicenter study on efficacy of phosphatidylserine administration. *Aging* (Milano). 1993 Apr;5(2):123-33.
- Chandrasekhar K. et al. A prospective, randomized double-blind, placebo-controlled study of safety and efficacy of a high-concentration full-spectrum extract of *Ashwagandha* root in reducing stress and anxiety in adults. *Indian journal of psychological medicine*. 2012. 34(3), 255.
- Choudhary D. et al. Efficacy and Safety of Ashwagandha (Withania somnifera (L.) Dunal) Root Extract in Improving Memory and Cognitive Functions. *Journal of Dietary Supplements.* 2017. *1-14.*
- Dutta K. et al. *Withania somnifera* Reverses Transactive Response DNA Binding Protein 43 Proteinopathy in a Mouse Model of Amyotrophic Lateral Sclerosis/Frontotemporal Lobar Degeneration. *Neurotherapeutics*. 2017 Apr; 14(2): 447–46.

References

- EghbaliFeriz S. et al. Centeral nervous system diseases and Scutellaria: a review of current mechanism studies. Biomed Pharmacother. 2018. 2018 Mar 16;102:185-195.
- Glade MJ. Et al. Phosphatidylserine and the human brain. Nutrition. 2015 Jun;31(6):781-6.
- Hazra, S. et al. Reversion of BDNF, Akt and CREB in Hippocampus of Chronic Unpredictable Stress Induced Rats: Effects of Phytochemical, Bacopa Monnieri. *Psychiatry Investigation*. 2017. 14. 74. 10.4306/pi.2017.14.1.74.
- Jayaprakasam B. et al. Withanamides in Withania somnifera fruit protect PC-12 cells from beta-amyloid responsible for Alzheimer's disease. *Phytotherapy Research*. 2010, 24(6):859-63
- Kidd PM. A review of nutrients and botanicals in the integrative management of cognitive dysfunction. *Altern Med Rev*. 1999 Jun;4(3):144-61.
- Krikorian R. et al. Blueberry Supplementation Improves Memory in Older Adults. *Journal of agricultural and food chemistry*. 2010;58(7):3996-4000.
- Lai P. et al. Neurotrophic properties of the Lion's mane medicinal mushroom, Hericium erinaceus (Higher Basidiomycetes) from Malaysia. *Int J Med Mushrooms*. 2013;15(6):539-54.
- Lohani M. et al. Anti-oxidative and DNA protecting effects of flavonoids-rich Scutellaria lateriflora. *Nat Prod Commun*. 2013 Oct;8(10):1415-8.
- Manchanda S. et al. *Withania somnifera* leaf alleviates cognitive dysfunction by enhancing hippocampal plasticity in high fat diet induced obesity model. *BMC Complement Altern Med*. 2017; 17: 136.

References

- McGlade E. et al. The Effect of Citicoline supplementation on motor speed and attention in adolescent males. *J Atten dis*. 2015. July. 1087054715593633.
- Palmieri, G., et al., Double-blind controlled trial of phosphatidylserine in patients with senile mental deterioration. *Clin. Trials J.* 1987;24:73-83.
- Pase MP. et al. (2012) The cognitive-enhancing effects of Bacopa monnieri: a systematic review of randomized, controlled human clinical trials. *Journal of alternative and complementary medicine*. 2012.18, 647-652.
- Raghav S Et al. Randomized controlled trial of standardized *Bacopa monniera* extract in age-associated memory impairment. *Indian Journal of Psychiatry*. 2006;48(4):238-242.
- Raguraman, V. et al. Withania somnifera Root Extract Enhances Telomerase Activity in the Human HeLa Cell Line .*Advances in Bioscience and Biotechnology. 2016.* 7(04), 199.
- Stough C. Et al. The chronic effects of an extract of Bacopa monniera (Brahmi) on cognitive function in healthy human subjects *Psychopharmacology(Berl)*. 2001 Aug;156(4):481-4.
- Zhang Z. et al. Characterization of chemical ingredients and anticonvulsant activity of American skullcap (Scutellaria lateriflora). *Phytomedicine*. 2009 May;16(5):485-93.
- Zhu M. et al. The Flavonoid Baicalein Inhibits Fibrillation of a-Synuclein and Disaggregates Existing Fibrils. *Journal of Biological Chemistry*. 2004 279, 26846-26857.