Neurological Disorders

DR. DEBBY HAMILTON, MD, MPH
Mechanisms of Disease

- Neuroplasticity
- Neuroinflammation
- Oxidative Stress
- Glutathione Depletion
- Mitochondrial dysfunction
- Nutritional Deficiency
- Infections
- Toxicity
Neurological Disorders

- Neurodegenerative Diseases: Alzheimer’s, Parkinson's disease, ALS
- Autism
- ADHD
- Mood disorders: depression, anxiety, bipolar disease, schizophrenia
- Traumatic Brain Injury
- Neurologic Lyme and tic borne infections
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*
Synaptogenesis

Hippocampus maturation

Pruning

Synaptogenesis

Myelination

Childhood

Adolescence

Adulthood

Dendritic spine number

Age
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
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

- Impact telomerase activity:
  - Stop breaking down telomeres so anti-aging
BDNF Functions

- 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
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<th>Sample</th>
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<td>13 young, healthy men</td>
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<td>62 healthy, sedentary males</td>
<td>Moderate-intensity aerobic PA for 2 wks</td>
<td>↑ serum BDNF following PA and ↑ memory on face name matching</td>
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<td>[247]</td>
<td>104 persons with partial response to antidepressants</td>
<td>Add-on high (16 kcal/kg/week) or low (4 KKW) PA for 12 wks to standard depression care</td>
<td>Persons entering with ↑ BDNF levels exhibited ↑ rate of response to antidepressants</td>
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<td>[248]</td>
<td>15 severely depressed adults</td>
<td>Add-on aerobic PA 16 kcal/kg/week for 3 d/wk for 3 wks to standard care for depression or medication-only group</td>
<td>Similar ↑ in BDNF in aerobic PA and medication-only group, but ↓ in oxidative stress markers seen only in PA group</td>
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Disease States Associated with Low BDNF

- Depression and mood disorders
- Traumatic brain injury
- ADHD
- Autism Spectrum Disorders?
- Degenerative Disease
- Aging
Bipolar Disorder and Low BDNF
Genetic SNP’s in BDNF
Val66 Met polymorphism
20 to 30% of Caucasians
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)
Mechanisms of Disease in ADHD

- Poor Neuroplasticity: low BDNF
- Neuroinflammation
- Mitochondrial dysfunction
- Oxidative stress
- Low glutathione
- Nutritional deficiency
- Toxicity
Prevalence of ASD

- 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
Microglia: Functions

- Phagocytosis
- Synaptic Pruning
- Development of CNS
- Maintenance of CNS cells
- Instigate inflammation
- Repair and regeneration in CNS inflammation
Activated Microglia: Cycle of inflammation and repair

1. Rapid proliferation of microglial cells
2. Migrate to site of insult or infection
3. M1 activated microglia: neurotoxic with release of pro-inflammatory cytokines including TNF-alpha, IL-1B, IL-6, COX, Reactive oxygen species (ROS), Nitric oxide
4. Engulf dying cells, infectious agents, toxic proteins, and cell debris
5. M2 activated microglia: secrete anti-inflammatory cytokines for repair including: IL-10, TGF-B, enzymes to inhibit ROS production (arginase), proteins to maintain extra-cellular matrix
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).

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

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2 Biomedical Network Research Centre on Mental Health (CIBERSAM), Barcelona, Catalonia, Spain
3 Department of Psychiatry and Legal Medicine, Universitat Autònoma de Barcelona, Cantabria, Spain
4 Psychiatry Genetics Unit, Vall d’Hebron Research Institute (VHIR), Barcelona, Catalonia, Spain

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 51 Caucasian ADHD adults, including the predominantly inattentive and combined types (aged 33.43 ± 8.99 yr) and 59 Caucasian 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 Scales. 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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First published online 3 January 2013

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).

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 (Galéa et al., 2011; Sagué et al., 2012). From a neurobiological point of view, different lines of evidence suggest the involvement of the dopaminergic and serotonergic systems (Solanto, 2002; Ribases et al., 2009; Landas et al., 2010; Nijmeijer et al., 2010) in the pathogenesis of ADHD. Experimental studies have shown a strong relationship between these monoaminergic systems and a member of the neurotrophin family, brain-derived neurotrophic factor (BDNF; Küppers and Beyer, 2001; Dlužen 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

ORIGINAL ARTICLE

Brain-Derived Neurotrophic Factor as a Biomarker in Children with Attention Deficit-Hyperactivity Disorder

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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

Meta-Analysis of BDNF Levels in Autism

Raluca Armeanu1 · Mikael Mokkonen1,2 · Bernard Crespi1

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 bias. 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

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; Oreifce 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 (Femandes 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; Halsepoto 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

- The found that 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.
Neurodegenerative diseases

- 5 million Americans suffer from Alzheimer's disease
- 1 million from Parkinson's
- 400,000 from multiple sclerosis (MS)
- 30,000 from amyotrophic lateral sclerosis (ALS or Lou Gehrig's disease)
- 30,000 from Huntington's

If left unchecked 30 years from now, more than 12 million Americans will suffer from neurodegenerative diseases.

http://neurodiscovery.harvard.edu/challenge
Alzheimer’s Neuroinflammation

- Accumulation of protein aggregates
  - Extracellular: B-amyloid plaques
  - Intracellular: Neurofibrillary tangles (NFT)
  - Cause loss of synaptic function leading to neuronal death
- Microglial activation
- Astrocyte activation
- Pro-inflammatory cytokines near B-amyloid protein deposits and NFT
Parkinson’s Neuroinflammation

- Loss of dopamine neurons in the substantia nigra
- Alpha-synuclein (Lewy body) protein inclusions in the nervous system
- Microglial activation
- Increase in pro-inflammatory cytokines

HIGHER BDNF
LESS DEMENTIA
Supplement Facts

Serving Size: 2 Capsules  Servings Per Container: 60

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<td>Choline (as Cytidine Diphosphate Choline Sodium Salt)**</td>
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<td>NeuroCyto Protect™ Blend</td>
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<td>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</td>
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<td>CDP Choline Sodium Salt, Sharp-PS® Phosphatidylserine</td>
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† 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.
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<td>Neurogenesis</td>
<td>stimulate brain regeneration</td>
<td>x</td>
<td>x</td>
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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 capacities, 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.

Skullcap: American

Scutellaria Lateriflora
Skullcap 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)
- Decrease oxidative stress
- Anti-inflammatory
Skullcap (*Scutellaria lateriflora*) (also known as Virginia Skullcap)

- **Scutellarin:**
  - Shown protective effect for cerebral injury via regulating expression of NOS isoforms & angiogenic molecules (Hu XM et al)
  - Protection against ConA-induced immunological liver injury in mice; mechanism: effect on pro-inflammatory cytokines (inhibition NF-kappaB-TNF-alpha-iNOS transduction pathway) (Tan ZH et al)
  - Study showed neuroprotective effects on brain ischemic injury-inhibition of the apoptosis-inducing factor pathway in rats (Zhang HF et al)
  - Anti-inflammatory activity in microglial cell (Wang S et al)
Bilberry: Vaccinium myrtillus
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
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
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 β-amyloid protein (Alzheimer’s)
- Decrease synuclein protein (Parkinson’s)
- Decrease oxidative stress
- Anti-inflammatory
Citicoline: CDP-choline Metabolic Pathway

Figure 2: Citicoline’s metabolic pathways.

Abbreviation: CTP, cytidine triphosphate.
Citicoline Benefits

- Improved cell membranes*
- Increase acetylcholine*
- Increase learning, memory, cognitive function
- Improve attention
- Decrease b-amyloid
Citocline improves memory performance in elderly subjects.

Abstract

Citocline 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 citocline alone (C1000:1000 mg/day; C500:500 mg/day) or in combination with nimodipine (C +N:300 + 90 mg/day) during 4 weeks on memory performance in elderly subjects with memory deficits and without dementia (N = 24; age = 66.12 +/- 10.76 years; MNS score = 31.69 +/- 2.76). Results indicated that citocline 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. 3.96 +/- 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 (6.5 +/- 2.1 vs. 6.7 +/- 2.4 omissions; p < 0.005) was observed after citocline treatment. Similar results were found in the three subgroups of treatment (8 subjects per group), suggesting that citocline 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 citocline. These effects are consistent with the vaso regulatory and neuroimmune actions of citocline 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 citocline improves memory performance in elderly subjects, we concluded that this molecule is suitable for the treatment of memory deficits in old people.
<table>
<thead>
<tr>
<th>Ischemic cascade level</th>
<th>Citicoline putative mode of action</th>
<th>Main effects</th>
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<tr>
<td>Cell energy balance</td>
<td>Stimulation/restoration of Na+/K+ ATPase activity</td>
<td>Cell energy deficiency correction</td>
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<td>Restoration/prevention of loss of neuronal ATP levels</td>
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<td>Hurtado et al^{34}</td>
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<td>Delay/prevention in the reversal of neuronal glutamate transporters</td>
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<td>Increased glutamate uptake by astrocytes</td>
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<td>Attenuation/prevention of PARP cleavage and DNA damage</td>
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<td>Endothelial barrier</td>
<td>TJ protein regulation</td>
<td>Reduction of brain edema</td>
<td>Schabitz et al^{10}</td>
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<td>disruption</td>
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<td>Decrease in permeability of endothelial barrier and restoration of TJ proteins linear structure</td>
<td>Ma et al^{19}</td>
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</table>
Cell Membrane

phosphatidylcholine
sphingomyelin
cholesterol
glycolipid
phosphatidylerine
phosphatidylethanolamine
phosphatidylinositol

EXTRACELLULAR SPACE
CYTOSOL

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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


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References


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- Liu DY et al. the physiology of BDNF and its relationship with ADHD. Molecular Neurobiology. 2015. 52(3): 1467-1476.


Manchanda S, Kaur G. Withania somnifera leaf alleviates cognitive dysfunction by enhancing hippocampal plasticity in high fat diet induced obesity model. BMC Complementary and Alternative Medicine. 2017;17:136. doi:10.1186/s12906-017-1652-0. (“At the molecular level, ASH treatment was observed to restore the levels of BDNF and its receptor TRKB as well as the expression of other synaptic regulators, which are highly implicated in synaptic plasticity.”)


