Dr. Ryan Lazarus DC, MSc, CNS

Neuroplasticity
Part II

Presentation Objectives

- Review the Various Conditions Associated with Neuroplasticity
- Discuss BDNF Dynamics
- Discuss the lifestyle strategies for neuroplasticity enhancement
- Review the science linking nutrition to neuroplasticity

Neuroplasticity for Specific Conditions

- Alzheimer's
- Dementia
- Emotional Trauma
- Stroke
- Depression
- Anxiety
- Chronic Pain
- ADHD
- OCD
- ASD

Neuroplasticity Rehabilitation for Stroke Recovery

Neuroplasticity has been observed quite often in those recovering from strokes. Strokes often leave patients with brain damage, ranging from moderate (e.g., some facial muscular impairment) to severe (e.g., serious cognitive impairments, memory problems).

According to the experts at stroke-rehab.com, the best way to encourage neuroplasticity in stroke recovery is to use two key methods:

- Task repetition
- Task-specific practice

Neuroplasticity for Depression

- The bad news is that, when it comes to psychiatric disorders, there's a sort of negative neuroplasticity; depression can cause damage to the brain, encouraging unhealthy and maladaptive pathways and discouraging healthy and adaptive ones (Hellerstein, 2011).

- The good news is that some treatments for depression seem to be able to halt the damage and perhaps even reverse. The even better news is that research on neuroplasticity has shown us that "your day-to-day behaviors can have measurable effects on brain structure and function," which can offer healing and recovery from psychiatric disorders (Hellerstein, 2011).

- It may not be easy and it will likely take sustained effort, but we have the ability to "remodel" our brains at any age in ways that can help us to function more effectively.

Neuroplasticity for Anxiety

- The same principles apply to managing and treating anxiety disorders—our brains are also perfectly capable of rewiring and remodeling to improve our ability to manage anxiety.

- “Any brain changes are at the expense of other changes. The development of these parts of our brain that effortlessly trigger anxiety, it is at the detriment of the ones that aid calmness & confidence… it is not enough to just stop anxiety in any given moment which is often people’s focus. The anxiety wiring is still there and waiting to be triggered. We need to create competitive wiring. We need to create specific wiring of what we want to achieve which is ‘competitive wiring’ to the problem. Without this we loop endlessly in anxiety with no neural pathway to take us forward.”

- Basically, neuroplasticity can be applied to help you manage, treat, and perhaps even “cure” anxiety, but it takes some time and effort! These more permanent brain changes can be achieved through adapting and changing thought patterns, through recall and memory patterning, breathing exercises, eye patterning, modifying postural habits, increasing body awareness, and targeting sensory perception (Cleary, 2015).

Neuroplasticity for Chronic Pain

A recent study on the subject found that there are at least four methods that can help your brain adapt and manage chronic pain:

- Transcranial direct current stimulation (electrodes implanted in certain areas of the brain to stimulate certain responses)
- Transcranial magnetic stimulation (non-invasive magnetic stimulation of the brain via a “wand” to engage specific areas)
- Intermittent fasting (periods of fasting followed by periods of normal food intake)
- Glucose administration (taking glucose supplements to replace what we lose due to normal aging; (Sibille, Fartsch, Reddy, Fillingim, & Keil, 2016)

Five Main Factors that Stimulate Neuroplasticity

- Exercise
- Ketones
- Meditation
- Music
- DHA

Neuroplasticity Lifestyle

- Intermittent fasting
- Sleeping
- Traveling
- Mnemonic devices
- Learning a musical instrument
- Non-dominant hand exercises
- Reading fiction
- Creating artwork
- Dancing or Tai Chi

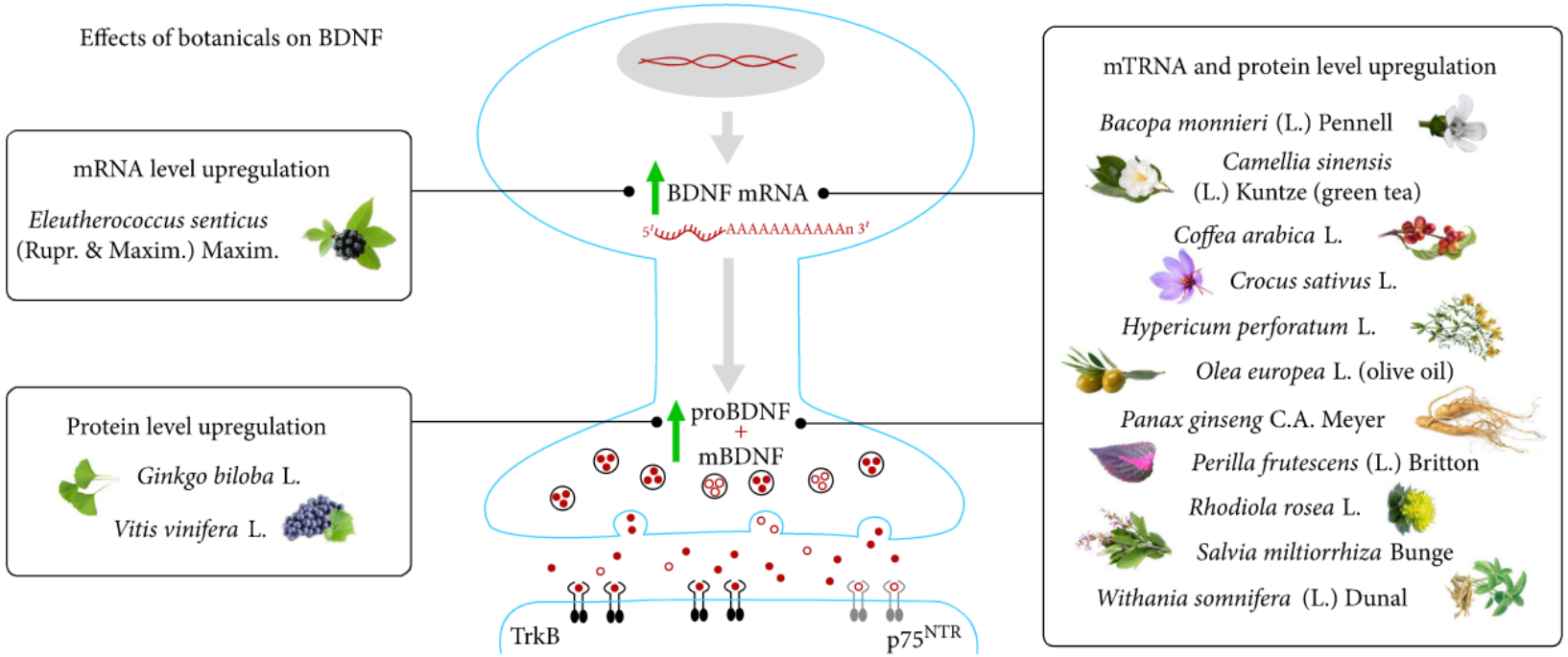

Figure 1: Effects of botanicals on BDNF mRNA and protein levels. The figure shows botanicals acting at transcriptional and translational levels.

Brain-Derived Neurotrophic Factor (BDNF)

Brain-derived neurotrophic factor (BDNF) is a nerve growth agent with a role to support, grow, and differentiate existing neurons of the central and peripheral nervous system.

Phytonutrients and Neuroplasticity

“Polyphenols can mitigate risk for neurodegenerative diseases, age-related cognitive decline, and oxidative stress via mechanisms involving the maintenance of metabolic homeostasis and the promotion of synaptic plasticity.

“Several dietary choices of polyphenols with putative neuroprotective, neuroplastic, neurogenic, and anti-inflammatory effects have been explored, with a particular emphasis on curcumin, catechins, resveratrol, and omega-3 fatty acids.”

. Murphy, G. P. Dias, and S. Thuret, “Effects of diet on brain plasticity in animal and human studies: mind the gap,” Neural Plasticity, vol. 2014, Article ID 563160, 32 pages, 2014.

Neurobiol Dis. 2017 Jul;103:89-100. doi: 10.1016/j.nbd.2017.04.001. Epub 2017 Apr 7.

B-vitamin and choline supplementation increases neuroplasticity and recovery after stroke.

Jadavji NM[1], Emmerson JT[2], MacFarlane AJ[3], Willmore WG[4], Smith PD[2].

⊕ Author information

Abstract

Folates are B-vitamins that play an important role in brain function. Dietary and genetic deficiencies in folate metabolism result in elevated levels of homocysteine which have been linked to increased risk of developing a stroke. Reducing levels of homocysteine before or after a stroke through B-vitamin supplementation has been a focus of many clinical studies, however, the results remain inconsistent. Animal model systems provide a powerful mechanism to study and understand functional impact and mechanisms through which supplementation affects stroke recovery. The aim of this study was to understand the role of B-vitamins in stroke pathology using in vivo and in vitro mouse models. The first objective assessed the impact of folate deficiency prior to ischemic damage followed by B-vitamins and choline supplementation. Ischemic damage targeted the sensorimotor cortex. C57Bl/6 wild-type mice were maintained on a folic acid deficient diet for 4weeks prior to ischemic damage to increased levels of plasma homocysteine, a risk factor for stroke. Post-operatively mice were placed on a B-vitamin and choline supplemented diet for a period of four weeks, after which motor function was assessed in mice using the rotarod, ladder beam and forepaw asymmetry tasks. The second objective was to determine how a genetic deficiency in methylenetetrahydrofolate reductase (MTHFR), an enzyme involved in folate metabolism, increases vulnerability to stroke. Primary cortical neurons were isolated from $Mthfr^{+/+}$, $Mthfr^{+/-}$ and $Mthfr^{-/-}$ embryos and were exposed to in vitro models of stroke which include hypoxia or oxygen glucose deprivation. Cell viability was measured 24-h after exposure stroke like conditions in vitro. In supplemented diet mice, we report improved motor function after ischemic damage compared to mice fed a control diet after ischemic damage. Within the perilesional cortex, we show enhanced proliferation, neuroplasticity and anti-oxidant activity in mice fed the supplemented diet. A genetic MTHFR deficiency resulted in neurodegeneration after exposure to in vitro models of stroke, by activating apoptosis promoting p53-dependent mechanisms. These results suggest that one-carbon metabolism plays a significant role in recovery after stroke and MTHFR deficiency contributes to poor recovery from stroke.

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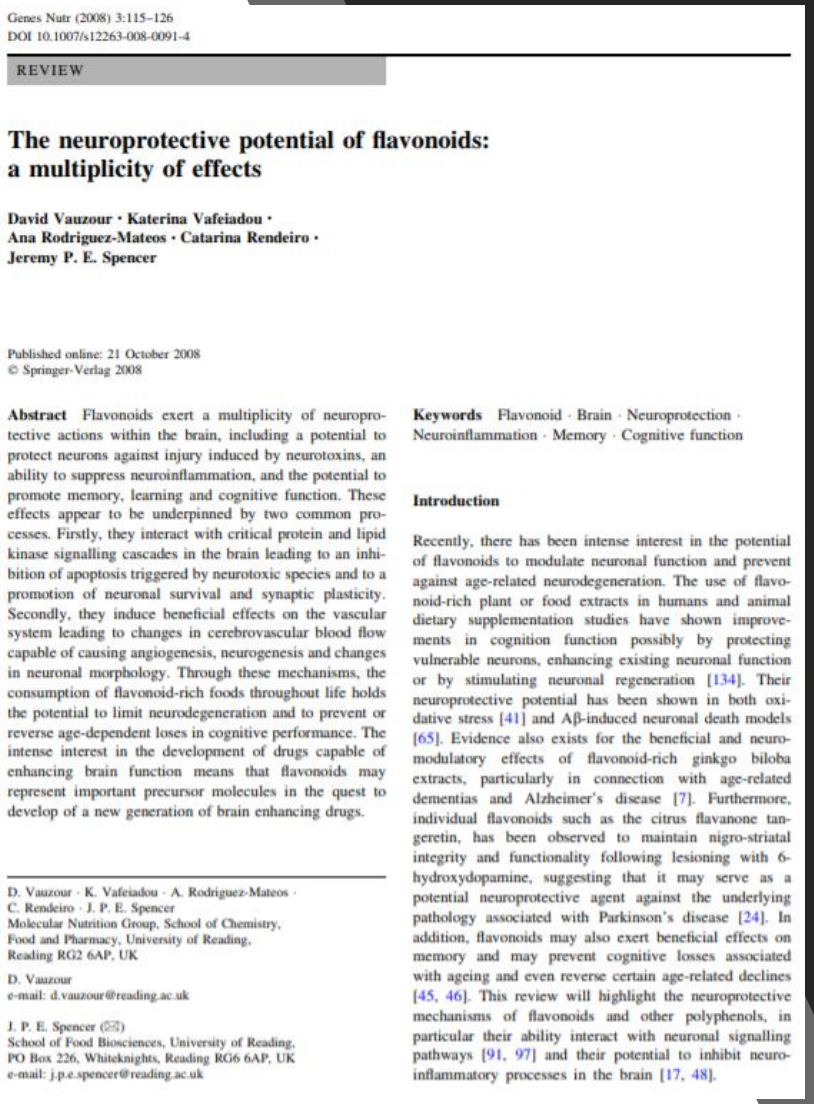
Choline & Neuroplasticity

"Effects of choline are correlated with modifications in histone and DNA methylation in brain, and with alterations in the expression of genes that encode proteins important for learning and memory processing, suggesting a possible epigenomic mechanism of action."

"Dietary choline intake in the adult may also influence cognitive function via an effect on PC containing EPA and DHA; polyunsaturated species of PC whose levels are reduced in brains from AD patients, and is associated with higher memory performance, and resistance to cognitive decline."

Neuroprotective Actions of Dietary Choline. Nutrients. 2017 Jul 28;9(8)



Genes Nutr (2008) 3:115–126
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REVIEW

The neuroprotective potential of flavonoids: a multiplicity of effects

David Vauzour · Katerina Vafeiadou · Ana Rodriguez-Mateos · Catarina Rendeiro · Jeremy P. E. Spencer

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Abstract Flavonoids exert a multiplicity of neuroprotective actions within the brain, including a potential to protect neurons against injury induced by neurotoxins, an ability to suppress neuroinflammation, and the potential to promote memory, learning and cognitive function. These effects appear to be underpinned by two common processes. Firstly, they interact with critical protein and lipid kinase signalling cascades in the brain leading to an inhibition of apoptosis triggered by neurotoxic species and to a promotion of neuronal survival and synaptic plasticity. Secondly, they induce beneficial effects on the vascular system leading to changes in cerebrovascular blood flow capable of causing angiogenesis, neurogenesis and changes in neuronal morphology. Through these mechanisms, the consumption of flavonoid-rich foods throughout life holds the potential to limit neurodegeneration and to prevent or reverse age-dependent loses in cognitive performance. The intense interest in the development of drugs capable of enhancing brain function means that flavonoids may represent important precursor molecules in the quest to develop of a new generation of brain enhancing drugs.

Keywords Flavonoid · Brain · Neuroprotection · Neuroinflammation · Memory · Cognitive function

Introduction

Recently, there has been intense interest in the potential of flavonoids to modulate neuronal function and prevent against age-related neurodegeneration. The use of flavonoid-rich plant or food extracts in humans and animal dietary supplementation studies have shown improvements in cognition function possibly by protecting vulnerable neurons, enhancing existing neuronal function or by stimulating neuronal regeneration [134]. Their neuroprotective potential has been shown in both oxidative stress [41] and Aβ-induced neuronal death models [65]. Evidence also exists for the beneficial and neuromodulatory effects of flavonoid-rich ginkgo biloba extracts, particularly in connection with age-related dementias and Alzheimer's disease [7]. Furthermore, individual flavonoids such as the citrus flavanone tangeretin, has been observed to maintain nigro-striatal integrity and functionality following lesioning with 6-hydroxydopamine, suggesting that it may serve as a potential neuroprotective agent against the underlying pathology associated with Parkinson's disease [24]. In addition, flavonoids may also exert beneficial effects on memory and may prevent cognitive losses associated with ageing and even reverse certain age-related declines [45, 46]. This review will highlight the neuroprotective mechanisms of flavonoids and other polyphenols, in particular their ability interact with neuronal signalling pathways [91, 97] and their potential to inhibit neuroinflammatory processes in the brain [17, 48].

D. Vauzour · K. Vafeiadou · A. Rodriguez-Mateos · C. Rendeiro · J. P. E. Spencer
Molecular Nutrition Group, School of Chemistry, Food and Pharmacy, University of Reading, Reading RG2 6AP, UK

D. Vauzour
e-mail: d.vauzour@reading.ac.uk

J. P. E. Spencer (✉)
School of Food Biosciences, University of Reading, PO Box 226, Whiteknights, Reading RG6 6AP, UK
e-mail: j.p.e.spencer@reading.ac.uk

Pine Bark

One study shows that flavonoids, which are antioxidant nootropics found in Pine Bark Extract, may be what initiates this BDNF production.

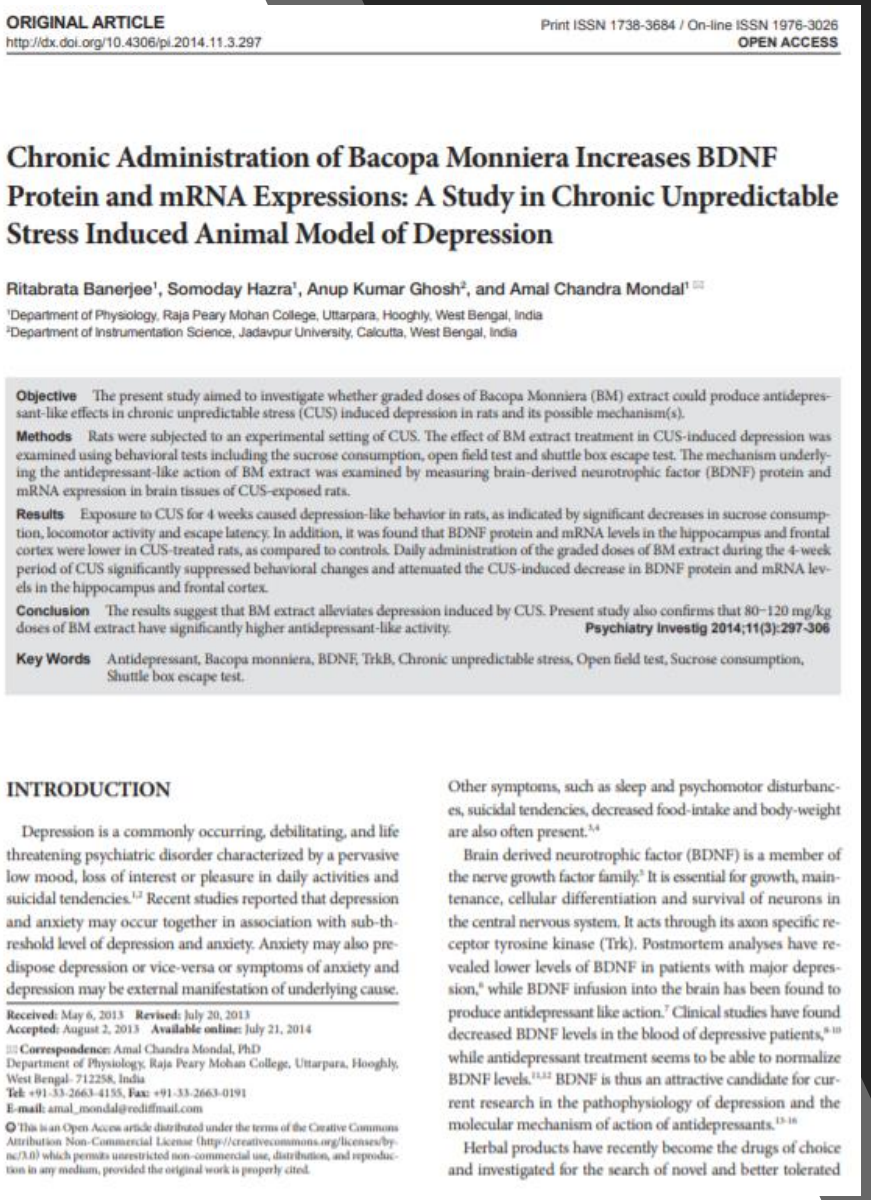
- "Pine Bark Extract may promote the production of BDNF in the hippocampus and prefrontal cortex."

- "Pine bark extract may increase support for neural synapses and plasticity in these brain regions, ultimately providing benefits to our ability to remember information, learn and maintain a balanced mood.

Resveratrol

- “Resveratrol attenuated stress-induced learning deficits, depressive symptoms, and hippocampal degeneration by mechanisms that involved the restoration of BDNF.
- Altogether, this preclinical data provides evidence that resveratrol treatment may be efficacious for improving mood and cognitive function.”

D. Liu, Q. Zhang, J. Gu et al., “Resveratrol prevents impaired cognition induced by chronic unpredictable mild stress in rats,” Progress in Neuro-Psychopharmacology & Biological Psychiatry, vol. 49, pp. 21–29, 2014



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Chronic Administration of Bacopa Monniera Increases BDNF Protein and mRNA Expressions: A Study in Chronic Unpredictable Stress Induced Animal Model of Depression

Ritabrata Banerjee[1], Somoday Hazra[1], Anup Kumar Ghosh[2], and Amal Chandra Mondal[1]

[1]Department of Physiology, Raja Peary Mohan College, Uttarpara, Hooghly, West Bengal, India
[2]Department of Instrumentation Science, Jadavpur University, Calcutta, West Bengal, India

Objective The present study aimed to investigate whether graded doses of Bacopa Monniera (BM) extract could produce antidepressant-like effects in chronic unpredictable stress (CUS) induced depression in rats and its possible mechanism(s).

Methods Rats were subjected to an experimental setting of CUS. The effect of BM extract treatment in CUS-induced depression was examined using behavioral tests including the sucrose consumption, open field test and shuttle box escape test. The mechanism underlying the antidepressant-like action of BM extract was examined by measuring brain-derived neurotrophic factor (BDNF) protein and mRNA expression in brain tissues of CUS-exposed rats.

Results Exposure to CUS for 4 weeks caused depression-like behavior in rats, as indicated by significant decreases in sucrose consumption, locomotor activity and escape latency. In addition, it was found that BDNF protein and mRNA levels in the hippocampus and frontal cortex were lower in CUS-treated rats, as compared to controls. Daily administration of the graded doses of BM extract during the 4-week period of CUS significantly suppressed behavioral changes and attenuated the CUS-induced decrease in BDNF protein and mRNA levels in the hippocampus and frontal cortex.

Conclusion The results suggest that BM extract alleviates depression induced by CUS. Present study also confirms that 80–120 mg/kg doses of BM extract have significantly higher antidepressant-like activity.

Psychiatry Investig 2014;11(3):297-306

Key Words Antidepressant, Bacopa monniera, BDNF, TrkB, Chronic unpredictable stress, Open field test, Sucrose consumption, Shuttle box escape test.

INTRODUCTION

Depression is a commonly occurring, debilitating, and life threatening psychiatric disorder characterized by a pervasive low mood, loss of interest or pleasure in daily activities and suicidal tendencies.[1,2] Recent studies reported that depression and anxiety may occur together in association with sub-threshold level of depression and anxiety. Anxiety may also predispose depression or vice-versa or symptoms of anxiety and depression may be external manifestation of underlying cause. Other symptoms, such as sleep and psychomotor disturbances, suicidal tendencies, decreased food-intake and body-weight are also often present.[3,4]

Brain derived neurotrophic factor (BDNF) is a member of the nerve growth factor family.[5] It is essential for growth, maintenance, cellular differentiation and survival of neurons in the central nervous system. It acts through its axon specific receptor tyrosine kinase (Trk). Postmortem analyses have revealed lower levels of BDNF in patients with major depression,[6] while BDNF infusion into the brain has been found to produce antidepressant like action.[7] Clinical studies have found decreased BDNF levels in the blood of depressive patients,[8-10] while antidepressant treatment seems to be able to normalize BDNF levels.[11,12] BDNF is thus an attractive candidate for current research in the pathophysiology of depression and the molecular mechanism of action of antidepressants.[13-16]

Herbal products have recently become the drugs of choice and investigated for the search of novel and better tolerated

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Correspondence: Amal Chandra Mondal, PhD
Department of Physiology, Raja Peary Mohan College, Uttarpara, Hooghly, West Bengal- 712258, India
Tel: +91-33-2663-4155, **Fax:** +91-33-2663-0191
E-mail: amal_mondal@rediffmail.com

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Bacopa

- "Preclinical results indicate that Bacopa monnieri extract administration modulates a BDNF effect that may underline its ability as an antidepressant and procognitive agent."

- "Bacopa Monnieri is associated with preventing beta-amyloid pigmentation build-up and may be a therapeutic approach to Alzheimer's."

- "Mechanism of memory enhancement appears to be related to either enhancing neuronal transmission (via enhancing dendritic proliferation) or through interactions with the serotonergic system (which then influence acetylcholinergic transmission)."

Botanicals as Modulators of Neuroplasticity: Focus on BDNF, Enrico Sangiovanni, Paola Brivio, Mario Dell'Agli, and Francesca Calabrese Department of Pharmacological and Biomolecular Sciences, Università degli Studi di Milano, Milan, Italy