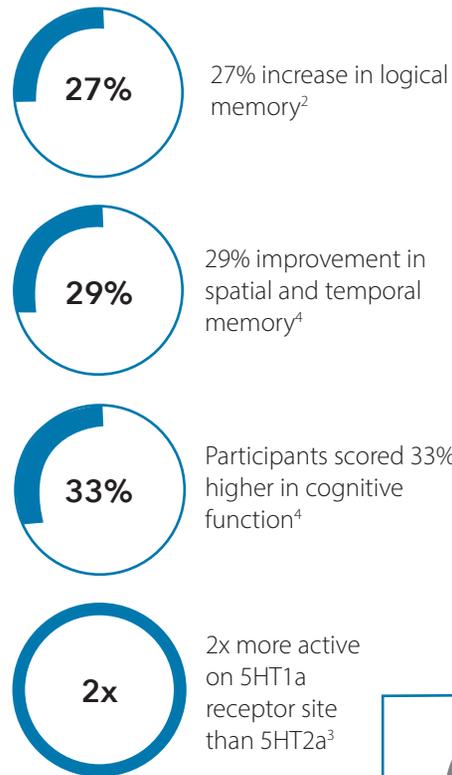


# COGNITIVE COMPLEX FOR COMPLETE NEURAL HEALTH

## BACOGNIZE®

*Bacopa monnieri* extract, supporting cognitive vitality through stress management, memory, attention, focus, recall, emotional balance and mood.\*

### CLINICAL RESEARCH SHOWS:



Improved acute & chronic cognitive function



Improved concentration & attention



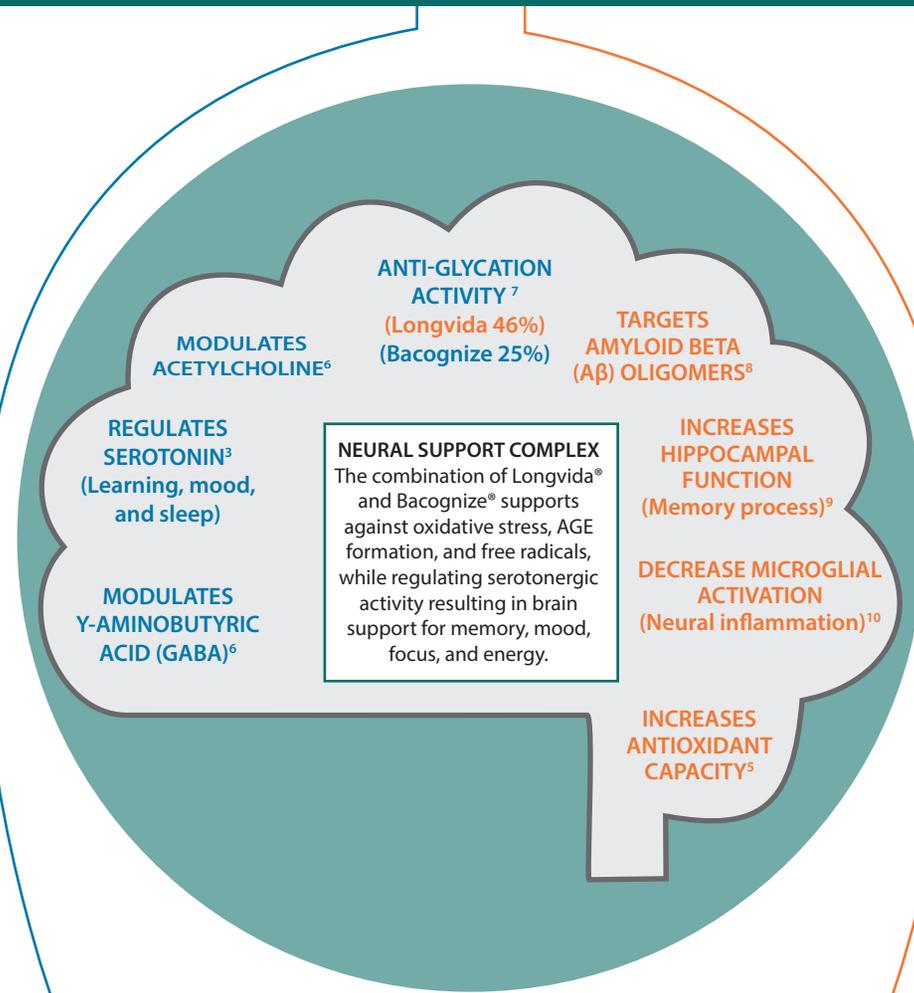
Improved working memory



Decrease in fatigue



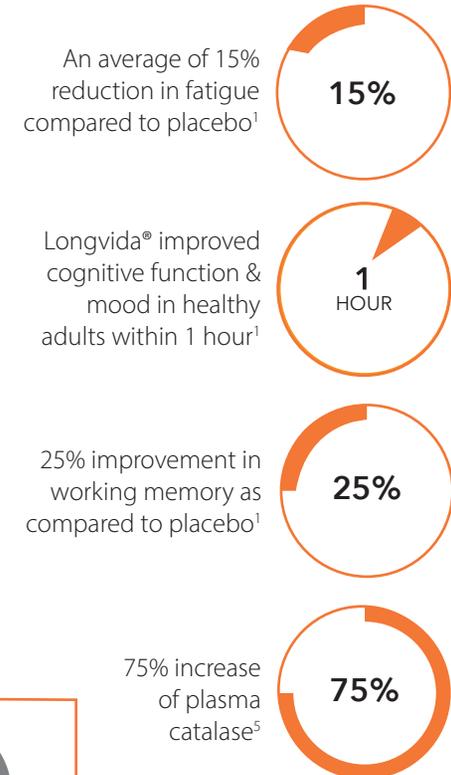
Improved mood /decreased irritability



## LONGVIDA®

*Curcuma longa* extract for balanced cognitive wellness, supporting cognitive function by targeting memory, mood, fatigue, and key biomarkers known to impact the brain.\*

### CLINICAL RESEARCH SHOWS:



1 - Cox KH et al. J Psychopharmacol. 2014 Oct. 20(5): 642-651.  
 2 - Kumar N et al. Evid Based Complement Alternat Med. 2016;2016:4103423.  
 3 - Hall et al. Am Soc Pharmacog Absts. 2005. 83-85.  
 4 - Goswami S et al. Int J Collab Research Internat Med. 2011 May 10. 3(4): 285-293.  
 5 - DiSilvestro et al. Nutr J. 2012 Sep 26. 11(79).  
 6 - Kollmani et al. Evidence-Based Complementary and Alternative Medicine, vol. 2015.

7 - Liu W et al. Neurochem Int. 2016 Sep 29. 100: 164-177.  
 8 - Karonyo Y et al. JCI Insight. 2017. 2(16).  
 9 - Scholey et al. 13th European Nutrition Conference: European Perspectives (FENS): Dublin, Ireland; 2019:P3-01-02  
 10 - Gyengesi et al. In: Neuroscience. Chicago, IL; 2019:9909.

\*\*Not an exhaustive list of references or clinical trials.



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\*These statements have not been evaluated by the Food and Drug Administration. These products are not intended to diagnose, treat, cure, or prevent any disease.

\*Please note that the physiological activity of the ingredient(s) described herein is supported by the referenced clinical trial report(s). Marketers of finished products containing the ingredient(s) described herein are responsible for determining whether claims made for such products are lawful and in compliance with the laws of the country in which they will market the products.

# COGNITIVE COMPLEX FOR COMPLETE NEURAL HEALTH

## BY THE NUMBERS:

People aged 45+ experience subjective cognitive decline<sup>1</sup>

1 in 9

20 yrs

Cognitive decline can begin 20 years before symptoms begin<sup>9</sup>

The brain can start showing signs of cognitive decline as a person enters their early 20's<sup>5</sup>

20's

Serotonin helps regulate your mood naturally. When your serotonin levels are normal, you feel happier, calmer, more focused, less anxious, and more emotionally stable.<sup>1-3</sup>

## FUNCTIONS OF NEUROTRANSMITTERS:



Dopamine (Reward)



Adrenaline (Alertness)



Serotonin (Happiness)



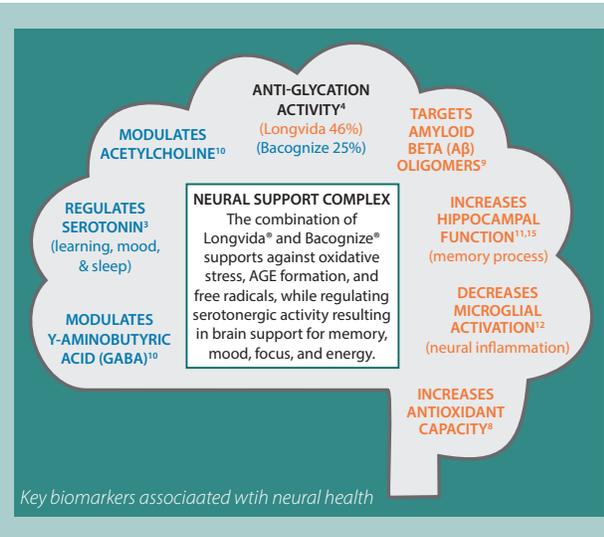
Oxytocin (Love)

Serotonin is considered a natural mood stabilizer. Well over 90 percent of the serotonin in our body is made in our gut. Since serotonin can't cross the blood brain barrier, it has to be synthesized in the brain from scratch. However, what does cross the blood brain barrier is tryptophan, the fundamental building block of serotonin. Within the neuron, enzymes turn tryptophan into 5-HT, which is the chemical name for serotonin. When serotonin binds to the receptors of the postsynaptic neuron, each receptor sends a signal to the cell body of the neuron. After it has activated a receptor it may get (a) taken back up into the presynaptic neuron; (b) taken up by a neighboring glial cell (glial cells are the most abundant cells in the brain—they don't transmit signals, but they do help keep everything neat and tidy); or (c) diffused away from the synaptic cleft via extracellular fluid. Any remaining serotonin gets broken down by the enzyme MAO (monoamine oxidase) and excreted from the cell as the metabolite 5-HIAA (5-Hydroxyindoleacetic acid). The brain can't produce large quantities of serotonin at once; therefore, it doesn't release large quantities of serotonin at once either. In fact, serotonergic neurons have multiple ways of up and down regulating their serotonin response in order to maintain balance and protect themselves from overstimulation.<sup>1</sup>

"We have more than 100 different types of neurotransmitters in our brain and their job is facilitating the communication between neurons."<sup>1</sup> In fact, "[y]ou have probably heard of the neurotransmitters dopamine, serotonin, adrenaline and oxytocin. A simplistic view: dopamine = reward, adrenaline = alertness, serotonin = happiness, and oxytocin = love."<sup>1</sup>

The communication of these neurons, through neurotransmitters, makes up the serotonergic system; in humans, this system originates in the brainstem and forms a network that spans every corner of the brain and plays a role in influencing nearly all aspects of the human body.<sup>1</sup> "It plays a key role in regulating mood, aggression, impulsivity, cognitive function, appetite, pain, thermoregulation, circadian rhythm, sleep and memory."<sup>1</sup> One way to look at the mechanism of this, from the perspective of *Bacopa monnieri*, is to consider cyclic AMP: cAMP (cyclic AMP), activates protein kinase which can open ion channels (non-selective channels that are activated by serotonin), which in turn mediate neurotransmitters and hormones.<sup>2</sup> Experts agree that "to properly regulate serotonin, proper regulation of cyclic AMP (cAMP) is also necessary," specifying that "[i]n many cases a decrease in [cAMP] is needed to maintain normal function of the serotonin system [also called the serotonergic system]."<sup>3</sup> Therefore, decreases in cAMP result in increases of serotonin (5HT) circulating in the synapse, or space between neurons. Bacognize<sup>®</sup> "reduced the amount of cAMP by half compared to control."<sup>3</sup> This allows the serotonin to circulate and be active longer in the system than it might otherwise, which may promote healthy sleep cycles, regulate mood, improve working memory, maintain focus, and reduce distractibility. Further, 5HT1a does not signal an overabundance of serotonin and overall mood increases.

Apart from short-term working memory, longer-term cognitive health goals are also paramount to the overall promotion of wellbeing, memory, and mood.



## BACOGNIZE

27%

27% increase in logical memory<sup>13</sup>

29% improvement in spatial and temporal memory<sup>14</sup>

29%

33%

Participants scored 33% higher in cognitive function<sup>14</sup>

2x more active on 5HT1a receptor site than 5HT2a<sup>3</sup>

2x

## LONGVIDA®

15%

Healthy adults noticed an average of 15% reduction in fatigue compared to placebo<sup>11,15</sup>

Longvida® improved cognitive function & mood in healthy adults within 1 hour<sup>14</sup>

1 hr

25%

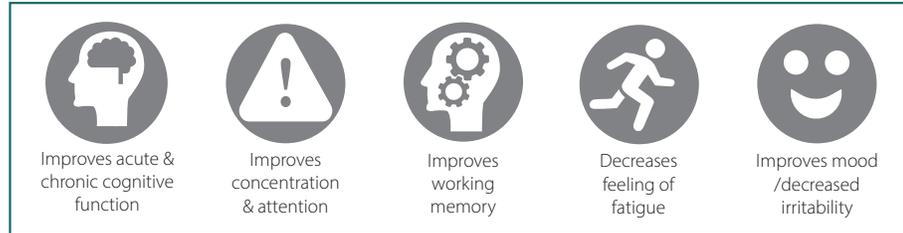
25% improvement in working memory as compared to placebo<sup>11,15</sup>

75% increase of plasma catalase<sup>8</sup>

75%

Several biomarkers associated with cognitive acuity including oxidative stress, amyloid beta (A $\beta$ ) fibrillation, carbonyl stress, protein glycation, and neuroinflammation—all of which are indicators of and contributors to cognitive and brain health—are shown to be impacted by both bacopa glycosides and by curcumin, as Longvida® Optimized Curcumin<sup>®4</sup>.

Longvida mediates oxidative stress by scavenging free radicals and acting as a natural antioxidant.<sup>4,6-7</sup>



Aside from

scavenging free radicals, curcumin has been shown to impact carbonyl stress and the formation of advanced glycation end products (AGEs), which result from protein glycation. When proteins and sugars combine (called glycation), AGEs are formed.<sup>5</sup> AGEs are associated with cognitive health for several reasons. Researchers explain that “AGEs bind to the transmembrane receptor for AGEs (RAGE), upregulate RAGE expression, and activate RAGE-mediated neuronal dysfunction and neuron damages. RAGE then inhibits the transportation of beta amyloid (A $\beta$ ) across the blood brain barrier (BBB). Therefore, the activation of RAGE by AGEs can cause A $\beta$  accumulation in the brain. During glycation and AGE formation, ROS (reactive oxygen species) and reactive carbonyl species (RCS) are generated as byproducts which, in turn, promote AGE formation and cause neurotoxicity.<sup>4</sup> Consequently, the contributing factors in this positive feedback loop are all considered targets for cognitive health.<sup>4</sup>

Amyloid plaque accumulation is another hallmark of cognitive decline. Amyloid is a general term for protein fragments that are produced naturally in the body. In particular, beta amyloid (A $\beta$ ) is a protein fragment that is broken down and eliminated in a healthy brain; however, A $\beta$  fragments may form hard, insoluble plaques in a brain in cognitive decline. Furthermore, “fibrillated A $\beta$  can induce neurotoxicity by enhancing neuronal oxidative stress and neuroinflammation.”<sup>4</sup>

Balancing availability of serotonin and maintaining its circulation without overstimulation naturally regulates mood and short-term working memory, improves focus and may even promote healthy sleep cycles; but cognitive health should focus on both the short-term and the long-term goals of a person. In addition to Bacopa targeting a natural solution to the short-term, curcumin from Longvida® may be a synergistic opportunity to offer a complete solution for both short- and long-term cognitive wellbeing.

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