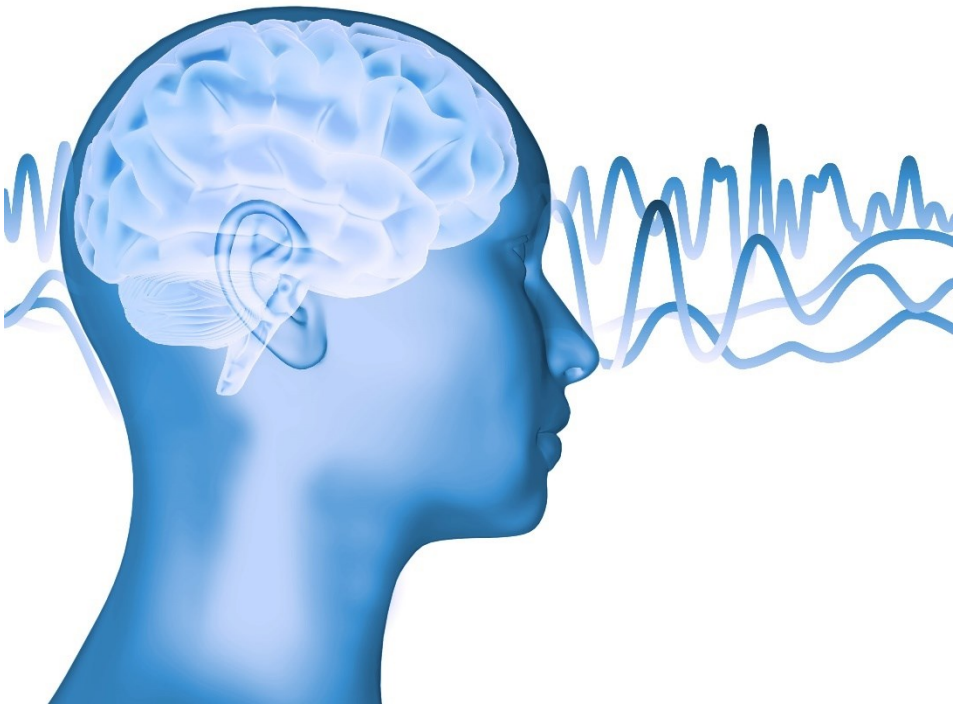
PROTEIN ACTIVITY, COGNITIVE FUNCTION & HOW TO IMPROVE THEM

Authored by Eng3 Corporation



Educational e-book www.eng3corp.com/AD

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INTRODUCTION

Almost any discussion of Alzheimer's Disease includes misfolded proteins and the plaques and tangles they create. While dysfunctional proteins are a big part of things, they are not the whole story. And your proteins are certainly not the villains they may appear to be when discussing the causes of Alzheimer's.

This e-book explores proteins and starts by giving you a basic overview of how they work, including protein folding. Then we dive into the role proteins play in Alzheimer's Disease, both in terms of misfolding and repairing oxidative stress damage. Finally, we offer information about what can be done to improve protein folding and function.

There are many diet and lifestyle factors that affect proteins and reduce cellular damage. These are well covered elsewhere and are not discussed here. Instead, this e-book will introduce a novel technology called NanoVi®, that improves protein folding. If you are already curious, the video on this page will give you a better idea of how NanoVi works: www.eng3corp.com/AD

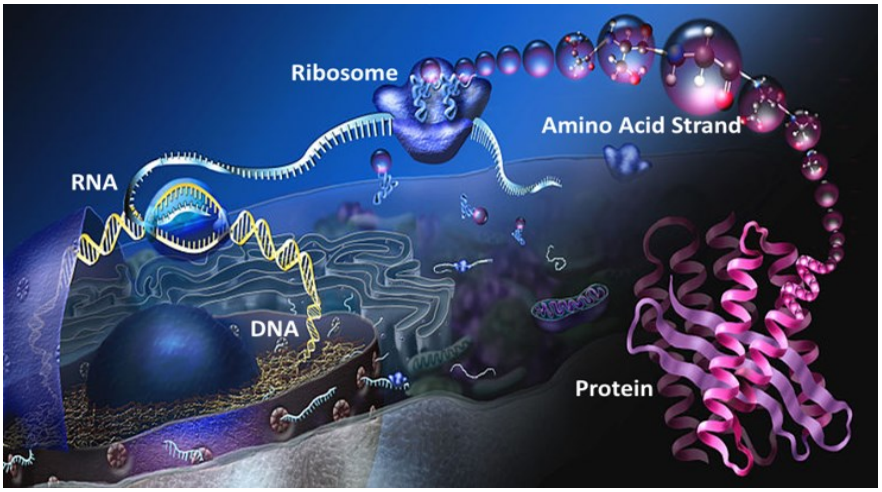
UNDERSTANDING PROTEINS

FROM DNA TO PROTEINS

Let's start at the beginning. Did you know that the reason you have DNA is to serve as the blueprint for proteins? With so much emphasis on DNA and genes, their whole purpose (to make proteins) can be somewhat overlooked. Although we won't get into the cellular machinery that builds proteins in the discussion, the simplest chain of events goes like this:

1. *DNA is 'read' and copied into messenger RNA (mRNA).*

2. *Ribosomes work like factories to produce strands of amino acids.*
3. *Amino acid chains fold into complex 3D structures that are the functional proteins needed to operate your body.*



Starting with the DNA and ending in a 3D folded structure, creating a protein is a complex process.

We hear a lot about the genetic aspect of early onset Alzheimer's; perhaps you or someone you love has already had genetic testing to evaluate your risk. While genetics are certainly a factor, they are not the whole story. Whether a genetic disadvantage exerts its impact or not, depends on many other factors - primary among them is oxidative stress. And unlike genetics, there are things you can do to prevent oxidative stress and reduce its damage. For this reason, we will focus on oxidative stress rather than genetics in this discussion.

PROTEINS (ALMOST) DO IT ALL

A quick overview of proteins

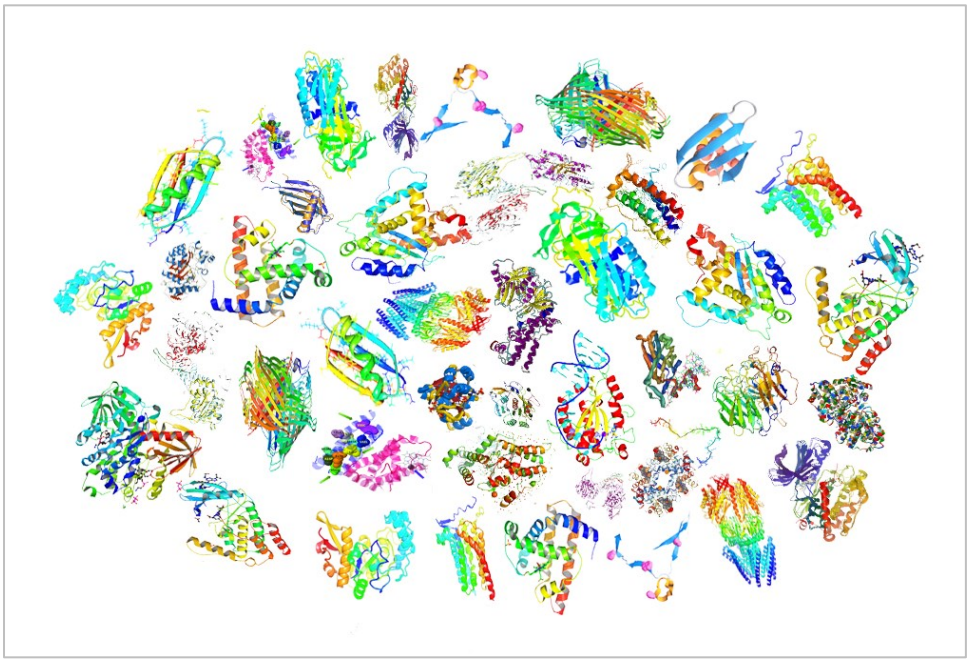
Proteins not only make up the structure of the body, they do most of the work as well. There are two long-standing clichés related to proteins, so let's get them out of the way:

1. *Proteins are "the workhorses of the body".*

2. *Amino acids are "the building blocks of life".*

Essentially, proteins do all the work and are built out of amino acids.

Scientists estimate that we could have close to a million different proteins in our bodies, and there are thousands (possibly tens of thousands) in each cell. Only a small percentage of all proteins have even been identified.



A protein's function depends on its folded structure, there are endless possibilities for the shapes that can be formed.

You may already be familiar with some types of proteins, like antibodies, enzymes, or hormones. Some individual proteins are also well known; say collagen, hemoglobin, or the hormone insulin. Related to Alzheimer's, Amyloid Precursor Protein (APP) is the one we often hear about[1].

What work do the protein workhorses do?

The proteins you have heard of, and hundreds of thousands of other proteins, are responsible for every function in your body from breathing, circulating blood, or digestion, to orchestrating your whole immune system. The body itself is made up of proteins. Proteins are also responsible for every movement you make; from blinking your eye to walking or lifting a book. All activities in the body, and all the repair and regeneration that gets done, are done by proteins.

Below are 9 common protein groups; their names will give you an idea of the work they do for you:

1. *Structural proteins*
2. *Transportation proteins*
3. *Receptor proteins*
4. *Enzymes (catalysts for biochemical reactions)*
5. *Storage proteins*
6. *Signal proteins*
7. *Gene regulatory proteins*
8. *Motor proteins*
9. *Special purpose proteins*

Because proteins do just about everything in the body, they have earned their title as the workhorses of the cell.

FROM AMINO ACID BUILDING BLOCKS TO PROTEINS

The actual blocks

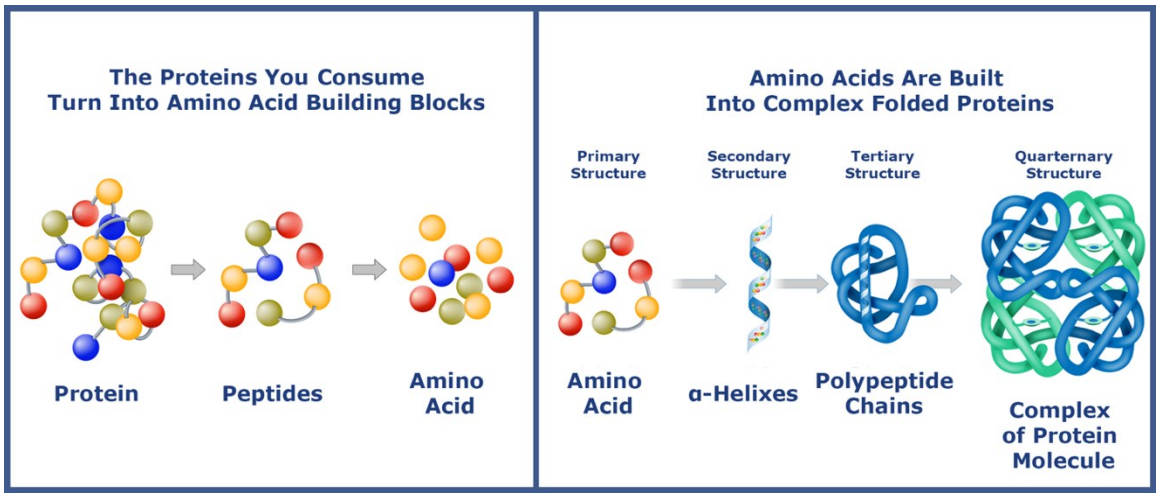
We know of 22 amino acids, only 20 are used to build humans and most of the rest of life on this planet. Each protein is some combination of only 20 different amino acids[2]. Half of these amino

acids must come from the food we eat, and the other half are produced by the body or are "endogenous".

To make each type of protein you must have a precise number of amino acids of the right type arranged in the correct order. About 200 amino acids are typical for most proteins but some, like collagen, use far more. To make collagen, which is the most abundant protein in the body, you need 1,055 amino acids. Every one of them must be the correct type in precisely the right order.

Where the protein you eat fits in

You hear a lot about the protein you consume. Of course, it is important because the body needs the right raw materials to create functional proteins. Below is an illustration of how food is broken down to create the amino acid building blocks that are rebuilt into proteins inside your body.



The process of turning the protein you eat into working proteins in the body.

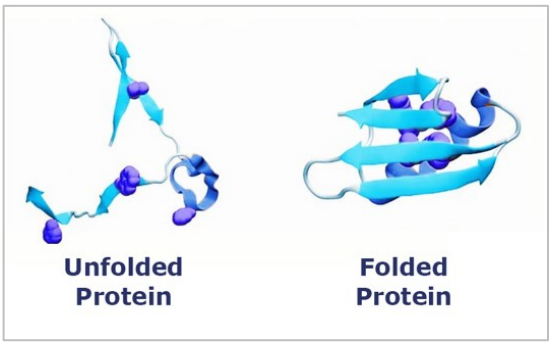
Now that we have the amino acids as building blocks, a protein can be made (to the specifications of the DNA blueprint). This process starts with the chain of amino acids mentioned earlier – called the primary

structure. But lining up the amino acids is not the hard part, it's what comes next that is truly phenomenal.

Protein folding

The amino acid chain then connects to itself at various points to form increasingly complex shapes called; secondary, tertiary, and quaternary structures.

To get to a functioning protein, the precise chain of amino acids must fold into its complex 3-D structure (shown to the right side of the diagram above). There can be rotation, kinks, and bends between any two amino acids in the chain. This means any part of the chain can head off in any direction at any angle. The possible shapes that could be formed by the chain of amino acids are virtually unlimited.



To function, proteins must fold into precise 3D structures.

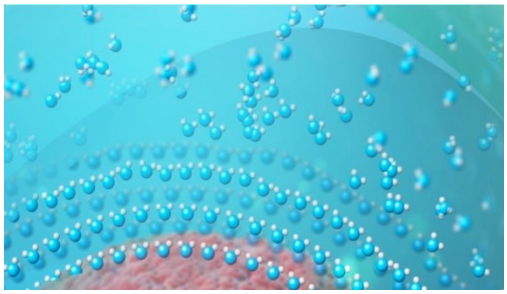
Chemical bonds support the protein's folded shape to create a structure that is highly precise and complex[3]. This "chemical origami" is truly a work of art and, as mentioned earlier, is also the workhorse of the cell.

THE ESSENTIAL ROLE OF WATER IN PROTEIN ACTIVITIES

The amino acids, proteins, and other cell components are immersed in water, which makes up 99% of the molecules in the body and 55-70% of the weight of a healthy adult. This water plays an essential role in building proteins out of amino acids.

Proteins get energy they need to fold from the cellular water. In this case, the energy is a transfer of entropy[4], meaning the water goes from being 'ordered' to being 'disordered' while the protein does the opposite - it snaps into an ordered or folded shape.

Influencing the cellular water to improve protein folding is the whole purpose of Eng3's technology. What makes us unique is that we have created *scientifically validated* technology specifically designed to promote cellular activities and improve protein functions by influencing the cellular water.

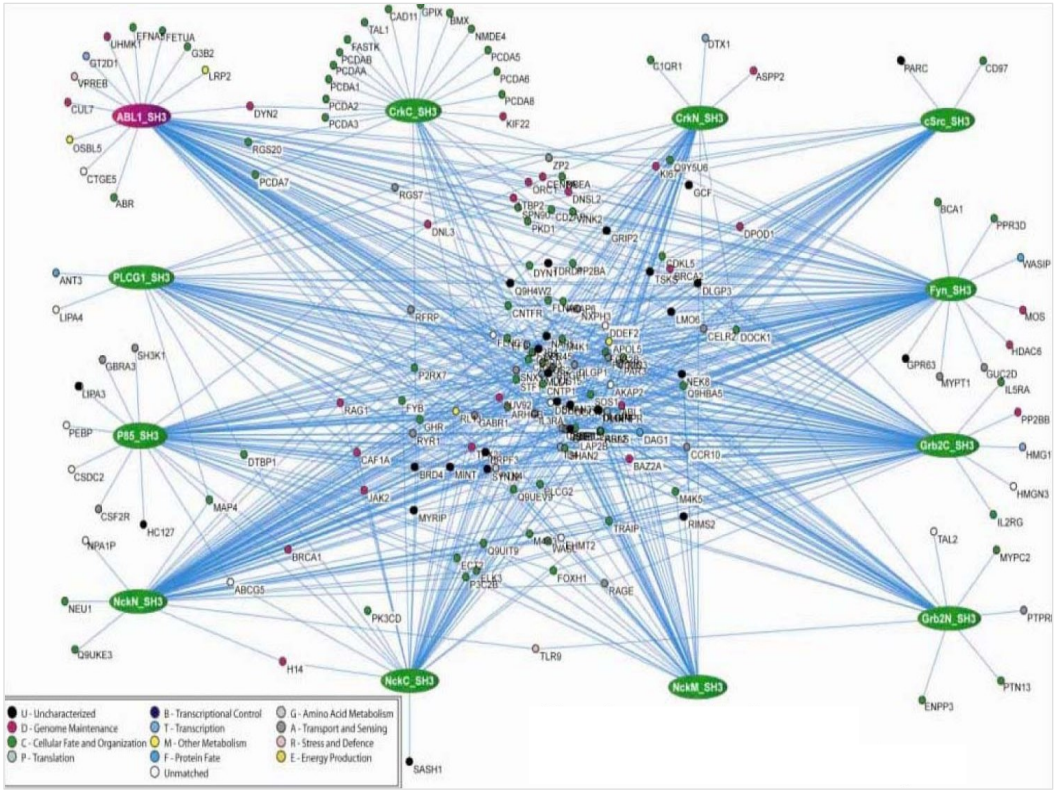


Ordered water surrounding proteins contributes to their folding process.

The fastest way to wrap your head around how NanoVi repairs and protects proteins is by watching this short 3D video on how the technology works: www.eng3corp.com/AD

PROTEIN INTERACTIONS ARE PROFOUNDLY COMPLEX

Now it really gets complicated. Proteins are constantly interacting; one can influence others in ways that we may never understand. To think of all these proteins as nodes in a network, rather than independent operators, is nothing less than mindboggling. The National Institute of Health mapped the known interactions of a small handful of proteins and created the diagram below, which only hints at the level of complexity.



Plotting a network of proteins shows the complex interactions between a small number of proteins.
Source: National Institute of Environmental Health Sciences, NIH.

Since we can't even name about 95% of the estimated number of different proteins in the human body, figuring out what each one does is almost inconceivable. Add to this the almost unlimited interactions between protein that are possible, and the mindboggling complexity of the human body starts to come into focus.

THE ROLE OF PROTEINS IN COGNITIVE PERFORMANCE AND ALZHEIMER'S

We don't have to understand the complexities of protein interactions, how they work, or even be able name proteins to find ways to improve their function. This is fortunate because proteins have a lot of work to do to support cognitive function and Alzheimer's Disease. In the

following pages, we will shift our focus to investigate the biggest villains, protein misfolding (which is directly associated with Alzheimer's Disease and results from oxidative stress) and oxidative stress itself.

PROTEIN MISFOLDING

The incidence of AD increases significantly with age. This is because as we grow older the sensitive balance between building proteins, folding them, and getting rid of degraded proteins is disrupted. This leads to the formation, accumulation, and aggregation of misfolded proteins. Proteins function properly when their constituent amino acids fold correctly[5], however, misfolded proteins assemble into insoluble aggregates that stick to other proteins and can be toxic for the cells[6].

Amyloid aggregates

The aggregation of the β-amyloid peptide in brain tissue is a distinguishing feature of Alzheimer's[7]. These amyloid aggregates are extremely immune to degradation[8]. This makes it difficult or impossible for your cellular machinery to break them down and get rid of them. Moreover, the amyloid aggregate is highly stable thermodynamically, making it even harder for the body to get rid of them. This is because the amyloid aggregates form sheets with large surfaces of contact between the protein chains. Think of it like pieces of sticky paper unable to slide past each other. The thermodynamic stability of amyloid aggregates also contributes to their ability to convert additional proteins into amyloid forms, creating additional damage[9].

Protein misfolding happens all the time

In fact, cells normally face continuously misfolded proteins. They are caused by errors in biosynthesis, DNA mutations, physiological stressors, and increased oxidative damage. However, cells handle issues arising from misfolded proteins by refolding, or degrading them, or even isolating them in special compartments formed between the cells[10]. When misfolded proteins are not taken care of, larger aggregates of misfolded proteins produce synaptic dysfunction and loss and, ultimately, nerve cell death[11]. This means your neuron (or nerve cell) may not be able to pass an electrical or chemical signal to another neuron so communication within your brain is disrupted.

Misfolding and oxidative stress

Researchers actively investigate the causes of Alzheimer's Disease. Experimental data showed that the aggregation of β-amyloid is caused by oxidative stress. Hence, it is obvious that oxidative stress has a significant impact on the formation of insoluble β-amyloid. Moreover, there has long been a common understanding that oxidative stress plays an important role as a cause of Alzheimer's disease[12]. Below is a closer look at oxidative stress and the workings of your brain.

OXIDATIVE STRESS AND COGNITIVE FUNCTION

What is oxidative stress?

Our cognition, like the cogs in a rusty machine, is downgraded by oxidative damage.

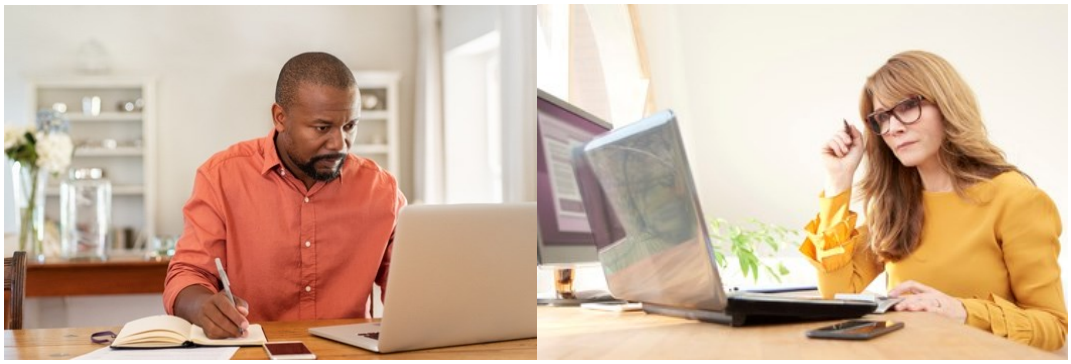
Oxidative stress is a phenomenon that occurs when the production of a group of molecules known as reactive oxygen species (ROS) overcomes our cells' natural ability to keep ROS in balance[13]. Members of one particularly potent subset of ROS are the infamous "free radicals"[14]. While ROS—in moderation—are important parts of our natural biology, an excess of them is dangerous. They damage our bodies by attacking critical parts of our cells such as proteins, DNA, and lipids (which make up the cell membranes)[15],[16]. Unfortunately, the brain is largely made up of lipids that are especially susceptible to oxidative stress damage.

In high enough abundance, oxidative stress can lead directly to cell death[17]. Proteins are the most abundant cell component, so they are likely targets for ROS. Ideally, ROS damage is repaired quickly, and it is proteins that do the repair work. When the proteins responsible for repairing oxidative stress damage are themselves damaged, it can lead to a dangerous downward spiral.

Where does oxidative stress come from?

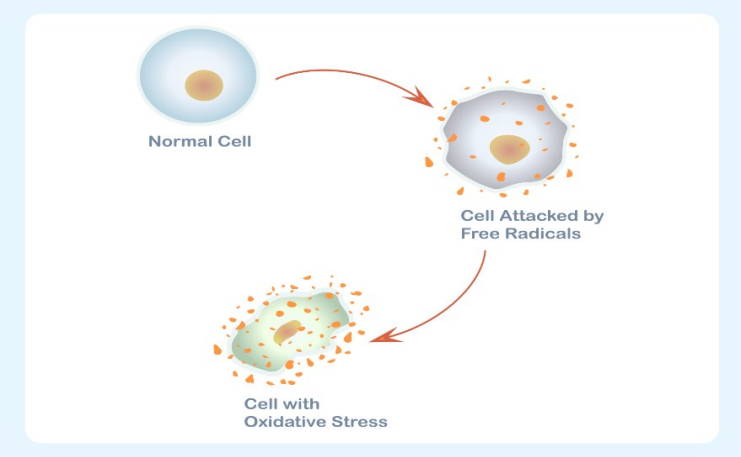
ROS have long been known to be byproducts of aerobic metabolism,[18],[19],[20],[21], which is when our cells use oxygen to help create energy. Consequently, ROS formation is unavoidable, especially in our brains where massive amounts of energy are required for optimal function[22]. This energy demand greatly increases during the

neuronal activity involved in performing mental tasks, which exposes our brains to increased levels of ROS and oxidative damage[23]. While our neurons have developed to rely on moderate fluctuations in ROS levels as a way of sending internal signals[24], they are also—quite ironically—particularly vulnerable to oxidative damage[25],[26]. This is in part because neurons have a reduced set of defenses against ROS, compared to other types of cells[27].



Concentration and decision making require massive amounts of energy and produces oxidative stress in the brain. This shows up as brain fog, mental fatigue, and ultimately lower performance.

How oxidative stress undermines mental function



Once oxidative stress accumulates, it can exceed the cell's capacity for repair.

Unfortunately, the resulting impacts of oxidative stress on mental health and performance can be devastating. Researchers at Emory University and University College London have linked oxidative stress in the brain to a decrease in executive function (the cognitive capacity to perform mentally

challenging tasks and control thoughts, emotions, and actions) and verbal fluency[28],[29]. Oxidative stress in certain parts of the brain diminishes the ability to learn[30], and has been strongly linked to memory impairments[31],[32],[33]. Appropriately, the administration of treatments and therapies reducing oxidative stress have demonstrated a powerful ability to recover not only memory function[34],[35],[36], but also broader cognitive performance and brain health[37].

Moreover, research exists to support a link between oxidative stress and reduced mental endurance. Scientists have found that an increase in oxidation in a part of the brain regulating sleep causes sleep induction[38]. To put it another way, it appears that oxidative stress may be a major promoter of mental tiredness and acute cognitive exhaustion. This oxidative mechanism of sleep induction may very well play a role in the development of decision fatigue.

Long-term effects of oxidative stress on the brain

Yet oxidative stress does not stop at tiredness and reduced performance—it can lead to much more serious and long-term detriments as well. It is linked to a vast range of psychiatric disorders and neurodegenerative illnesses, where an increased level of oxidative stress in brain cells is correlated with worsening disease[39],[40],[41].

Oxidative stress is a primary cause of damage to the brain.

With such sobering scientific evidence backing the danger of oxidative damage in our brains, it becomes clear that our ability to combat oxidative stress not only decides mental performance and endurance,

but helps to preserve the general, long-term health of our brains as well.

AN INNOVATIVE WAY TO IMPROVE CELLULAR PROTEIN FUNCTION

So, how do we fight the deleterious impact of oxidative stress on our cognitive system? What can be done to reduce protein misfolding or the buildup of unfolded proteins? This is where the powerful technology called NanoVi® steps in.

NanoVi® technology

IMPROVING THE WATER PROTEINS RELY ON TO FOLD

The NanoVi device is uniquely designed to increase the build-up of something called ordered or exclusion zone (EZ) water in cells throughout the body. An increase in ordered water helps to support the necessary protein folding. As discussed earlier, proteins are the true workforce of the cell, responsible for creating most of your body and undertaking its vast array of functions. Since a protein's function is dependent on it folding into the correct shape, increasing the rate of proper protein folding improves the function of your protein workforce, and, consequently, the adaptability, health, and well-being of your cells.

NanoVi is an easy way to increase ordered water in your cells to support protein folding and function.

HOW NANOVI® HELPS ADDRESS OXIDATIVE DAMAGE

The benefits of NanoVi for brain function can be thought of in two ways. The first is general. Improving protein function throughout the brain improves the ability of our neurons to meet the daunting demands of optimal brain function, from neurotransmitter release to membrane voltage regulation. The second way is intimately linked to the oxidative stress that so often arises from intense periods of high neuronal activity associated with focus and concentration.

SCIENTIFIC VERIFICATION OF NANOVI®

Use NanoVi while concentrating to exercise your brain and assist it at the same time.

NanoVi has been shown by scientific research to increase biological mechanisms of resistance to oxidative damage. One report shows that the administration of NanoVi to proteins that have suffered from oxidative damage significantly improves their ability to recover and refold into their appropriate, functional conformations[42]. Moreover, this same research team showed that people given NanoVi sessions produce significantly higher amounts of several critical antioxidant proteins known to scavenge and eliminate high levels of ROS in humans, likely helping to reduce oxidative stress in the first place. Such findings strongly suggest NanoVi may be a powerful way to regain ground lost to oxidative stress. This is especially important in the realm of mental performance where the production of oxidative damage is both so high and so consequential.

FINAL TAKE-AWAY: ANY BRAIN CAN BENEFIT FROM NANOVI® SESSIONS

Whatever your reason for seeking an improvement in cognitive function, every advantage is meaningful. Using NanoVi to improve protein activities and repair damage is one of the best things you can do for your brain (and your body). Research verifies that NanoVi helps improve cellular activities and the repair of oxidative stress damage. This makes it a robust tool for promoting mental endurance, acuity, and wellness. Combating the oxidative toll of mental exertion improves all aspects of brain function. NanoVi is a safe, easy-to-use technology supported by science and endorsed by users the world over.

If you'd like to learn more about the NanoVi device, its proven benefits, and the price, give us a call at **206 525-0227** or sign into the form on this page: www.eng3corp.com/AD

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