QUALIA NOOTROPIC ENERGY SHOT

WHITE PAPER

INTRODUCTION

AUTHOR: **SARA ADÃES, PH.D.**

Neurohacker Collective developed **Qualia Nootropic Energy Shot** with the goal of creating a liquid nootropic supplement capable of producing a fast, noticeable, and durable enhancement of mental and physical energy to support peak performance. **Qualia Nootropic Energy Shot** was designed to boost performance in high-demand situations that require extra mental effort and energy, be it at work, school, a social gathering, or even an athletic event.

But what are the main cognitive challenges that demand extra effort and energy? What determines our ability to perform at our best? And how can we boost our performance?

In this paper, we explore these questions and share how the ingredients in **Qualia Nootropic Energy Shot** act—individually and in combination—to support mental performance. If you want to know more about the thought processes behind formulation design at Neurohacker Collective, you may also be interested in reading **Qualia: The Complex Intelligence Behind Its Formulation and Neurohacker Dosing Principles.**

OUR FORMULATION

The combination of Caffeine and L-Theanine is probably the most widely used stack for boosting mental energy. Caffeine and L-Theanine support cognitive performance on their own [1,2], but together they do it better. This synergy, well-known within the neurohacking community and supported by human studies [3–6], is outstanding because Caffeine and L-Theanine target multiple aspects of mental performance that add to and complement each other.

With Qualia Nootropic Energy Shot, we wanted to go beyond what Caffeine and L-Theanine can give us. We wanted to build a stack with a set of ingredients that would have multiple stand-alone actions, but also complementary, additive, and synergistic actions between them that would allow better support of neural and cognitive pathways and processes.

Qualia Nootropic Energy Shot was formulated by taking into account which brain functions, neurochemical systems, and physiological processes we could target to quickly boost cognitive performance. Our research led us to a formula containing nootropic compounds, vitamins, amino acids, choline donors, fruit extracts, and herbal extracts that we believe will work well together in supporting a fast enhancement in mental energy, focus, cognitive processing capacity, and productivity.

These are the ingredients in Qualia Nootropic Energy Shot:

- Alpha-glycerylphosphorylcholine (Alpha-GPC)
- EnXtra® *Alpinia galanga* Root Extract
- Cereboost™ American Ginseng Root Extract
- Inositol-enhanced Bonded Arginine Silicate (as NooLVL™)
- Organic Coffeeberry® (90 mg caffeine) Whole Coffee Fruit Extract
- *Celastrus paniculatus* Seed Extract
- L-Theanine
- L-Tryptophan
- N-Acetyl-L-Tyrosine (NALT)
- Saffron Stigma Extract
- Niacin (as niacinamide)
- Wild Blueberry Fruit Extract

Let's take a look at some of the most important aspects of mental performance and how our ingredients may support them.

AROUSAL, ALERTNESS AND VIGILANCE

Alertness and vigilance are determining factors of both mental and physical performance. In brain research, the physiological and psychological state of being alert and vigilant is called arousal, i.e., our level of wakefulness. Arousal determines the level of activation and excitability of physical and mental states and processes. It is a state of drive, interest, motivation, and active physiology, behavior, consciousness, cognition, and affect [7].

No matter what, we won't perform at our best if we're feeling drowsy. That's because arousal is a fundamental prerequisite for alertness and vigilance. When we are alert and vigilant, we are ready to receive and process information and to devise a quick response in accordance with the demands of the task in hand or the goals we want to achieve [7]. Arousal is a state of readiness for action and is essential for cognitive tasks that require attention, and higher-level active thinking and executive functions. That's why supporting it is so important.

Caffeine (included in our formulation as **Coffeeberry®**) is the most widely used central nervous system stimulant. That's because caffeine is one of the most researched substances for promoting wakefulness and alertness [8–10]. The need to feel fully awake in order to function at a peak level is what makes every coffee drinker reach for a cup first thing in the morning.

Caffeine acts as a stimulant by inhibiting the receptors for the neuromodulator adenosine [1,11], which has a key role in stimulating sleep [12]. **Caffeine** promotes wakefulness because it counters these sleep-inducing effects of adenosine.

L-Theanine is a great complement to **Caffeine's** stimulant actions because it promotes the alpha (α) brain waves associated with alertness, but which are also linked with relaxation and selective attention [2,13–17]. This means that **L-Theanine** helps support a state of calm flow and productivity (i.e., calm energy). **Caffeine** and **L-Theanine** are synergistic in supporting alertness, cognitive performance, and mood [5].

As additional alertness support, ***Alpinia galanga* root extract (as EnXtra®)** was also included in our formulation. ***Alpinia galanga*** is able to enhance alertness for up to 5 hours with and without caffeine [18]. But, importantly, ***Alpinia galanga*** is synergistic with caffeine in supporting alertness and sustained attention. ***Alpinia galanga*** prevents the caffeine crash and prolongs and enhances caffeine's actions, especially in supporting faster reaction times [18].

THINKING AND PROBLEM-SOLVING

When we perform a mental task, we recruit a set of cognitive tools that help us process information, solve problems, and orient our behavior. These cognitive processes work at two levels: the conscious and the unconscious [19].

Unconscious (or implicit) information processing is based on things we've learned, those that have become ingrained in our long-term memories and that we access without even noticing it. Implicit cognition is responsible for our ability to read or write in our native language, or to know that 1+1=2 with no effort. It is also responsible for those sudden insights—"a-ha!" moments—when a solution to a problem that's been on your mind suddenly reveals itself seemingly out of nowhere. Unconscious cognition is effortless, quick, involuntary, and automatic [19].

Explicit thinking and problem-solving, on the other hand, is the conscious, active process of thinking or reasoning, of consciously working through a problem or towards a goal. Explicit thinking requires that we voluntarily maintain sustained attention and keep information in our working memory while we process that information. It is what is recruited when we calculate 55 x 89 or when we try to read the German word viertausendachthundertfünfundneunzig (which is the solution to the multiplication problem). We need to focus and stop everything else we're doing because it is a complex and effortful process. And we can't keep doing it indefinitely because the effort will end up exhausting our "mental reserves" [19].

Our mental performance (and physical performance during exercise and sports) depends on the major brain processes that are at the core of conscious thinking: on our ability to sustain attention, on the capacity of our working memory, and on the efficacy of our executive functions.[19]

Let's take a closer look at these processes.

ATTENTION

What we pay attention to will be what enters our consciousness at any given time. Unless we invest some effort into it, our attention is usually generalized, involuntary, and unfocused. When we have a task to carry out, we'll perform it better if we focus our attention on what is relevant to that task and avoid being pulled away by distractions or irrelevant information. But this attentional focus comes with a cognitive cost; it takes mental effort and energy.

Selective attention is a state of conscious, voluntary mental effort in which we detect, prioritize, and isolate relevant information and integrate it into the thought process of the task in hand [7]. It is the ability to voluntarily focus and concentrate our conscious thinking on one of several inputs, objects, trains of thought, or actions. Simultaneously, the other possible inputs, objects, trains of thought, or actions are shut down or tuned out. What receives our attention becomes vivid in our mind, whereas everything else becomes dim.

Our capacity for selective attention determines our ability to allocate our attentional system to what's most relevant at a given moment and to ignore what's irrelevant or distracting [19]. This capacity is limited.

Qualia Nootropic Energy Shot contains a set of ingredients that have been shown to support sustained attention and focus in human studies, including **Alpha-GPC** [20,21], ***Alpinia galanga* Extract (as EnXtra®)** [22], **American Ginseng (Cereboost™)** [23], **Saffron Stigma Extract** [24], **Caffeine (as Coffeeberry®)** [9,10,25,26] and **L-Theanine** [2,27,28].

L-Theanine has been shown to support alpha (α) brain waves [2,13–16], which are associated with selective attention and suppression of distractions [17,29]. The combination of **Caffeine** and **L-Theanine** has been shown to support focus by decreasing mind wandering [30].

Choline signaling (i.e., the neurotransmitter acetylcholine) is involved in enhancing alertness when we wake up and mediating selective and sustained attention [31,32]. So, not surprisingly, higher dietary choline intake has been associated with more efficient neural processing during attention tasks [33]. Supplementation with choline supports attentional performance [34]. Combining choline with caffeine supports sustained attention and concentration [35]. We included **Alpha-GPC** since it (1) is, by weight, the richest source of choline and supports blood levels of choline more than other forms of choline [36], and (2) can cross the blood-brain barrier and get into the brain [37,38].

WORKING MEMORY

Working memory is a type of short-term memory that holds information that is being used in cognitive processing readily accessible in consciousness [39]. Working memory is what allows you to finish a sentence knowing how you started it. It's what sustains your train of thought.

The amount of information and the time it is held in working memory are limited in capacity [19]. Maintaining in memory several pieces of information to be processed simultaneously is effortful. The effort increases with the amount of information we try to hold.

Qualia Nootropic Energy Shot contains a set of ingredients that have been shown to support working memory in human studies, namely **American Ginseng (Cereboost™)** [23,40] and **N-Acetyl-L-Tyrosine** (NALT) [41–47].

EXECUTIVE FUNCTION

Executive function is the set of cognitive control processes, i.e., the set of functions that allow us to select adequate action and thoughts from the host of possibilities available to us at any given moment. Executive functions are in charge of sustained attention, working memory, goal-directed behavior, impulse control, response inhibition, cognitive flexibility, planning, judgment, and decision-making [31,48].

Executive control functions allow us to 1) set goals and subgoals and define tasks; 2) plan, organize, and regulate the flow of information processing; 3) select and focus on what is relevant to our task while ignoring and suppressing what is irrelevant or distracting; 4) switch our focus between subgoals or tasks in a coordinated way; 5) monitor the progress of our actions towards the intended outcome; 6) adjust a course of action in light of our progress and results.[19]

L-Theanine has been shown to support executive function [27]. It supports logical reasoning, mathematical processing [27,42], and convergent ("deep") thinking, which is a component of creativity [49]. **L-Theanine** also supports cognitive control through the inhibition of behavioral responses [50]. Likewise, **Caffeine (Coffeeberry®)** supports executive function and reasoning [25,51–53]. **Inositol-enhanced Bonded Arginine Silicate (NooLVL™)** was shown to support performance in complex cognitive tests requiring executive functioning [54].

COGNITIVE FLEXIBILITY

Executive functions underlie a very important aspect of mental performance: cognitive flexibility. Cognitive flexibility is our mental agility; it is our ability to quickly switch our attention between different tasks and quickly shift our cognitive set in response to new challenges, demands, or contingencies. It is the opposite of mental fixedness, i.e., being stuck in a way of looking at a problem that may not be the best.

Mental flexibility determines our ability to override habits and automatisms (i.e., the effortless processes of implicit cognition), allowing us to switch between different approaches or points of view on a problem. It determines our capacity to think and act in new and creative ways [55]. It is key to peak cognitive performance.

One of the mechanisms through which **Caffeine** supports cognitive performance is by supporting creative thinking [51]. Creativity is also supported by **L-Theanine** by stimulating convergent ("deep") thinking [49]. **Inositol-enhanced Bonded Arginine Silicate (NooLVL™)** supports performance in complex cognitive tests requiring mental flexibility [54]. Cognitive flexibility is also supported by **N-Acetyl-L-Tyrosine (NALT)** [56].

REACTION TIME AND PROCESSING SPEED

Reaction time is the measure of our cognitive processing speed, i.e., of how fast we process information, the time between stimulus and response, how long we take to carry out a mental process or operation. Our mental speed is another determinant of cognitive performance.

Inositol-enhanced Bonded Arginine Silicate (NooLVL™) supports performance in complex cognitive tests requiring processing speed [54]. **American Ginseng (Cereboost™)** was also shown to support reaction time accuracy [23]. **Caffeine (Coffeeberry®)** upregulates the rate of information processing [3,26,57] and supports faster reaction times [9,26,58,59], as does **L-Theanine** [2] and the combination of **Caffeine and L-Theanine** [30].

MENTAL EFFORT AND FATIGUE

By now you may have noticed that the word effort keeps coming up in this text. That's because all-important brain processes underlying productive conscious thinking—sustained attention [60], working memory [61], reasoning [62], task-switching [63], overcoming habits and automatisms [64]—are cognitively demanding and require mental effort.

Conscious, controlled thinking requires effortful mental work, particularly when we face demanding, complex, laborious, or intimidating tasks or contexts. But there is a limit to the amount of mental effort we can exert, i.e., our cognitive resources are exhaustible [29].

Conscious thinking is constrained by our limited capacity to maintain task-relevant information (goals, tasks, plans, instructions, intentions) in working memory. It is also constrained by our limited information-processing capacity due to bottlenecks created when different tasks compete for the use of the same set of mental representations

(for example, we can't carry out two mental arithmetic problems simultaneously). The effort of actively thinking and pushing those boundaries adds mental load to normal, baseline, cognition [29,65].

Active conscious thinking and what it entails—mental effort, sustained increased neural activity in the brain—can be quite burdensome if the problem or task in hand is new or particularly complex and requires high mental effort. That's why we feel mental fatigue after a period of intense cognitive activity. How well we cope with this effort, i.e., how resistant we are to mental fatigue, determines how well we perform in a demanding context [29,66].

Mental effort (not only cognitive, but also emotional) requires mental energy. We have a pool of mental energy that we exhaust when we engage in effortful tasks. This exhaustion (known as ego depletion) decreases our motivation and our performance in subsequent tasks. When we experience mental fatigue, we are, in a sense, feeling the result of a depletion of our mental energy resources [67].

In **Qualia Nootropic Energy,** we have a few ingredients that can help to support mental effort. These include **Caffeine**, which has been shown to protect from mental fatigue [3,10], **N-Acetyl-L-Tyrosine (NALT)**, shown to protect from performance decline during cognitively demanding tasks [68], and **Wild Blueberry Fruit Extract**, which supports task-related brain activation [69].

DOPAMINE SIGNALING

Brain dopamine pathways have a key role in many creative-productive capacities and states, including attention, focus, cognitive control, and emotional resilience. Dopamine signaling also determines our cognitive processing speed. Furthermore, dopaminergic activity in the medial prefrontal cortex mediates one of the most important aspects of executive function—cognitive flexibility in the form of task-switching and set-shifting. Higher levels of dopamine are associated with optimal performance of these cognitive processes.[31,70–72]

Dopamine supports another important aspect of performance: intrinsic motivation. Intrinsic motivation is the spontaneous tendency to be curious, interested, driven to learn, to seek out novelty and challenges, and to exercise and develop skills. It differs from extrinsic motivation in that people do not engage in an activity because of the possible consequences, rewards, or outcomes. Intrinsically motivated people find challenges appealing and satisfying. This is probably why intrinsic motivation is correlated with enhanced cognitive performance, cognitive flexibility, and creativity.[73]

Therefore, supporting dopamine signaling and dopaminergic pathways is one of the main goals of **Qualia Nootropic Energy Shot.**

Dopamine is synthesized in the brain from the precursor amino acids L-phenylalanine and L-tyrosine. In the dopamine synthesis pathway, L-phenylalanine is converted into L-tyrosine, which in turn is converted by the enzyme tyrosine hydroxylase (TH) into L-3,4-dihydroxyphenylalanine (L-DOPA), which is the direct precursor to dopamine. TH is the rate-limiting enzyme in the dopamine synthesis pathway, i.e., the slowest step, the bottleneck of the pathway.[74,75]

Insufficient levels of any precursor amino acid or in any cofactor in this pathway can impair the synthesis of

dopamine. And because dopamine is also the precursor to catecholamine neurotransmitters (i.e., epinephrine and norepinephrine), those insufficiencies end up impairing the synthesis of all three neurotransmitters.

Because L-Tyrosine is an important precursor in the dopamine synthesis pathway [76], we included **N-Acetyl-L-Tyrosine** in the formulation of **Qualia Nootropic Energy Shot. N-Acetyl-L-Tyrosine** is a more soluble form of this amino acid [77]; it is a better form of L-tyrosine to use in a liquid product. By enhancing the L-tyrosine pool, this amino acid can be recruited for dopamine synthesis whenever there's an increased demand for this neurotransmitter.

N-Acetyl-L-Tyrosine upregulates dopamine synthesis and release upon neuronal activation [78–83]. Similarly, it upregulates norepinephrine synthesis and release upon neuronal activation [83–85]. Furthermore, it protects from neurotransmitter (DA, NE) depletion due to increased brain activity [68].

Because TH requires tetrahydrobiopterin as a coenzyme, which is synthesized in a NADPH-dependent pathway [86], **Vitamin B3, as Niacinamide,** a precursor to NADPH [87], can support the activity of the rate-limiting enzyme of the dopamine synthesis pathway.

Within neurons, dopamine is degraded into inactive metabolites by monoamine oxidase (MAO) A and B. Studies in mice have shown that ***Alpinia galanga*** downregulates MAO A and B activity in the brain [88], suggesting that it may contribute to the maintenance of higher dopamine levels. ***Celastrus paniculatus*** **Seed Extract** was also shown to downregulate brain MAO-A levels in mice [89].

As a result of its antagonism of adenosine receptors, **Caffeine** also supports dopaminergic signaling. Since adenosine receptor activation reduces dopaminergic activity, inhibiting adenosine receptors can indirectly contribute to an enhanced dopaminergic signaling [11,57,90]. **Caffeine** has been shown to upregulate the release of dopamine, dopamine receptor levels, and dopamine signaling in the brain [91–93]. **Caffeine's** impact on adenosine receptors in dopamine-rich areas of brain contribute to supporting the attentional system, namely task-switching [94,95]. **L-Theanine** has also been shown to enhance brain dopamine levels in animal studies [96–103] and to protect against neurotoxicity from excess dopamine [104].

American Ginseng (Cereboost™) can support dopaminergic neurotransmission through the activity of its bioactive ginsenoside compounds [105–108]. The ginsenosides Rb1and Rg1 have been shown to regulate dopamine levels and the activity of dopamine receptors [105,109,110]. Rb1 has been shown to counter stress-induced changes in dopamine levels [111], having additive potential with caffeine on the regulation of dopamine in stress contexts [112].

Inositol-enhanced Bonded Arginine Silicate (NooLVL™) may support dopamine signaling, because of its ability to enhance L-arginine levels, and the role of L-arginine in producing nitric oxide (NO). L-arginine and NO participate in the regulation of dopaminergic neurotransmission, possibly through the dopamine transporter (DAT) [113–116] and D1 receptors [117]. L-arginine promotes dopamine release in vitro [118–120]. L-arginine has also enhanced dopamine in the preoptic area [121].

Saffron Extract upregulates brain dopamine levels [122,123] and **Blueberry Extract** supports dopamine release and dopaminergic neurotransmission [124–126]. ***Celastrus paniculatus*** **Seed Extract** interacts with dopamine-D2 receptors [89] and modulates the levels of monoamine neurotransmitters (dopamine, noradrenaline, and serotonin) and their metabolites in the brain [127]. **Alpha-GPC** has been shown to enhance dopamine release, dopamine levels in the frontal cortex and cerebellum areas of the brain, and dopamine plasma membrane transporter (DAT) [37,128].

ACETYLCHOLINE SIGNALING

Acetylcholine is a neurotransmitter that plays a key role in cognitive function. Although it is most recognized for its role in the neural mechanisms of memory and learning [129], the cholinergic system (cholinergic refers to neurons that use acetylcholine as their main neurotransmitter) also has important actions in other aspects of cognition.

Acetylcholine enhances alertness when we wake up and mediates selective and sustained attention [31,32]. The cholinergic system also regulates executive function, either by direct action, or by influencing other neurotransmitter systems (e.g., dopamine, norepinephrine, and serotonin signaling). For example, by promoting dopamine release in the prefrontal cortex, the cholinergic system supports task-shifting and attention [31,32].

Acetylcholine is synthesized from choline, an essential nutrient we must obtain from our diet. In the formulation of **Qualia Nootropic Energy Shot** we included one of the best supplement sources of choline, alpha-glycerophosphocholine **(Alpha-GPC). Alpha-GPC** is part of the CDP-choline (or Kennedy) pathway, which has a central role in choline homeostasis [130,131]. Through this metabolic pathway, **Alpha-GPC** upregulates plasma choline levels [132], and is a precursor for acetylcholine synthesis [133,134], being able to upregulate acetylcholine production and release [133–135]. **Alpha-GPC** has additional actions on the cholinergic system by upregulating the levels of the transporters that take up choline into neurons for acetylcholine synthesis (high affinity choline uptake transporters) [136] and of the transporters that load acetylcholine into vesicles to be released for neurotransmission (vesicular acetylcholine transporters) [135,136].

Acetylcholine is synthesized by the enzyme choline acetyltransferase (ChAT), which transfers the acetyl group from acetyl-coenzyme A (acetyl-CoA) to choline. ChAT is the rate-limiting enzyme step in acetylcholine synthesis [137]. The activity of ChAT is supported by **American Ginseng (Cereboost™)**, which upregulates ChAT expression [138].

Acetylcholine released into the synapse is inactivated (i.e., its signaling is terminated) by the enzyme acetylcholinesterase (AChE), yielding choline and acetate [137]. Slowing the activity of AChE is a strategy that can be used to enhance acetylcholine signaling by leaving more acetylcholine available to produce greater receptor stimulation. In **Qualia Nootropic Energy**, there are a few ingredients that downregulate AChE levels and/or activity in the brain, including ***Alpinia galanga*** **(EnXtra®)** [88,139], **American Ginseng (Cereboost™)** [138], ***Celastrus paniculatus*** **Seed Extract** [140], and **Saffron Stigma Extract** [123].

Additional upregulation of acetylcholine signaling is provided by **Caffeine (Coffeeberry®)** [1,141–143]. Due to its action as an adenosine receptor antagonist [57], **Caffeine** counters adenosine which otherwise can act to decrease the levels of acetylcholine [1,11]. **American Ginseng (Cereboost™)** also upregulates acetylcholine levels [138] and modulates cholinergic neurotransmission [138,144–147].

MOOD AND STRESS RESISTANCE AND RESILIENCE

In a cognitively demanding context, acute stress responses are usually adaptive. They increase heart rate, respiratory rate, blood pressure, pupil dilation, energy mobilization, and focused attention, a set of changes that are evolutionarily designed to increase our chances for survival, but that can be channeled to increase performance in any context. Only when stress responses cross the threshold from being adaptive to maladaptive does stress become problematic.

Stress resistance is not the absence of a stress response but rather a greater ability to endure stress exposure and maintain adaptive responses to stress before experiencing the negative effects of stress [148]. Stress resistance manifests as an ability to maintain a relaxed and positive mood that benefits performance. During cognitively demanding tasks, enhanced stress resistance is sometimes described as a calm feeling, as opposed to anxious or irritable feelings that can accompany stress when the ability to manage stress is low.

Stress resilience is a greater capacity to recover after experiencing the negative effects of stress. Stress (emotional) resilience can be thought of as the ability to bounce back from a stressful situation and not letting it affect our intrinsic motivation [148]. Both stress resistance and resilience are important characteristics in demanding contexts.

A central pathway in the regulation of stress responses and mood is the hypothalamic–pituitary–adrenal (HPA) axis, a complex network of interactions between the hypothalamus, the pituitary gland and the adrenal gland [149]. The HPA axis regulates the production of several important molecules that coordinate the adaptive stress response, such as the stress hormone cortisol, for example [150,151].

Qualia Nootropic Energy Shot contains a set of adaptogenic ingredients, i.e compounds that support mood, stress resistance and resilience, and resistance to fatigue. Adaptogens typically act by promoting homeostasis, exerting a normalizing or stabilizing impact on physiological processes [150].

One of the adaptogenic ingredients in our formulation is **American Ginseng (Cereboost™)** [145]. Its active constituents, called ginsenosides, are thought to be responsible for many of ginseng's adaptogenic and health-promoting properties [144]. **American Ginseng** downregulates HPA-axis activation and stress hormone levels, promotes calmness, and supports mood [23,144,152,153]. ***Celastrus paniculatus* Seed Extract** is another adaptogen that has been shown, in animal studies, to downregulate plasma stress hormone levels and to support a positive mood [89,154,155].

L-Theanine also modulates psychological and physiological stress responses [156] and protects from stress-induced cognitive impairments [157,158]. Most importantly, **L-Theanine** supports a relaxed mood [27,156,159–163], likely as a consequence of promoting the alpha brain waves associated with relaxation [2,13–16].

Augmenting L-tyrosine pools (supported in our formula with **N-Acetyl-L-Tyrosine (NALT)**) protects from the (1) negative effects of stress on cognitive performance [43–46,164], (2) adverse behavioral responses to environmental stress [165], (3) stress-induced declines in norepinephrine levels [166], and (4) stress-induced increases in blood pressure [43,164] L-tyrosine also supports global mood [167].

A positive and relaxed mood is also supported by **Caffeine (as Coffeeberry®)** [1,52,58,59,168], **Saffron Extract** [169–174], and **Wild Blueberry Fruit Extract** [175].

CEREBRAL METABOLISM AND CELL ENERGY

Neural activity, as all cellular activity, requires cell energy. The brain cannot do its work without energy. In fact, the brain has the highest metabolic rate of any organ in the human body, being the major consumer of glucose and responsible for the use of around 20% of our daily caloric intake [176–178].

All key aspects of conscious thinking require increased brain activity: 1) attentional networks are activated as you focus on what's relevant and ignore what's irrelevant and resist distractions; 2) working memory networks actively keep information in mind; and 3) executive control regions (in the prefrontal cortex) are active as you plan, act, and switch between tasks.

Effortful conscious thinking and problem-solving adds to the baseline energetic requirements of the brain. Sustained attention, reasoning, cognitive control, all draw on cell energy reserves to sustain the neuronal activity they require. Therefore, we may support our brain's ability to cope with mental effort by supporting cerebral metabolism and energy production.

Neurons' (and all other cells') "energy currency" is called adenosine triphosphate (ATP). The major process of ATP production is called oxidative phosphorylation (OXPHOS). OXPHOS uses the energy of electrons extracted from glucose and fatty acids in glycolysis, fatty acid oxidation, and the Krebs cycle to power the production of ATP. ATP production takes place in the electron transport chain (ETC) located in the inner membrane of mitochondria. In the ETC, electrons are transferred in a series of redox reactions to oxygen (O2). It's the energy of the electron transfer through the ETC that powers the synthesis of ATP from ADP [179].

The electrons that power ATP production are transported from glycolysis, fatty acid oxidation, and the Krebs cycle to the ETC by electron carrier molecules. The most important carrier is nicotinamide adenine dinucleotide (NAD+). NAD+ is converted into NADH upon receiving two electrons and a hydrogen ion; NADH delivers the electrons to the ETC and is converted back into NAD+, which becomes available to receive more electrons [180].

NADH is the main driver of ATP production. An adequate balance between NAD+ and NADH—the NAD+/NADH ratio—is critical for optimal energy metabolism and mitochondrial and cellular function. Supporting NAD+ production therefore provides an essential aid for cell energy production.

NAD+ can be produced from **Niacinamide (Vitamin B3)** in the **"Salvage Pathway"** [181] and from the amino acid L-Tryptophan via the **"De Novo Synthesis Pathway"** [182]. L-Tryptophan and Niacinamide are included in **Qualia Nootropic Energy Shot** to support NAD+ production, and consequently, support the breakdown of sugars and fats for energy and the mitochondrial production of ATP [183].

Because of its high metabolic rate, the brain is a big consumer of ATP. Optimal mitochondrial function is therefore fundamental for the production of ATP required to sustain neuronal activity. **Qualia Nootropic Energy Shot** provides additional support for mitochondrial function with **American Ginseng (Cereboost™)**, which upregulates mitochondrial enzyme complex activities [152], and **Saffron Stigma Extract** which also supports the activity of mitochondrial enzymes [123] and upregulates mitochondrial membrane potential [184].

Additionally, by supporting healthy cardiometabolic parameters [185–187], including healthy blood glucose levels [188–190], healthy insulin sensitivity [191], and healthy fat metabolism [185], **American Ginseng (Cereboost™)** provides an additional support for the optimization of metabolic function. **Caffeine** supports

energy production by upregulating the metabolic rate [192–194].

While sugars and fats can be used to produce ATP, glucose (blood sugar) is the brain's preferred energy source. Cognitively demanding tasks, especially when they are sustained, may cause local glucose depletion (i.e., the parts of the brain that are most active run low on glucose). This local deletion then acts as a limiting factor in sustaining cognitive performance [195]. Conversely, consuming sugar can improve performance in cognitively demanding tasks (but not simple ones). Glucose administration has been found to enhance attention, memory, auditory and visual processing, emotional regulation, mental flexibility, and performance in other cognitively demanding tasks. Single doses of sugar used to support cognitive performance are often based on body weight in scientific studies, with a commonly used amount being about 25 grams [196]. Non-sugar sweeteners don't provide this same nootropic energy benefit to the brain, because they are not a source of fuel. Because of this, we opted to sweeten the Qualia Nootropic Energy Shot with 4 grams of **Organic Coconut Sugar.**

CEREBRAL BLOOD FLOW

Brain activation is associated with increased cerebral blood flow. This increase in cerebral perfusion is fundamental for the proper delivery of oxygen and glucose. It is also essential for the removal of metabolic waste products that accumulate with neural activity. Optimal cerebral blood flow is therefore essential for optimal cognitive function.

One of the key molecules in the regulation of blood flow is nitric oxide (NO). NO is a biological messenger and signaling molecule. NO is used by endothelial cells—cells that line the interior surface of blood vessels—as a messenger that instructs the smooth muscle surrounding blood vessels to relax, causing the widening of blood vessels (vasodilation) and increasing blood flow. NO is produced from L-arginine by enzymes called nitric oxide synthases (endothelial NOS, eNOS, in the case of vascular NO) in a reaction that requires NADPH (vitamin B3-dependent) [197,198].

One of the goals of the formulation of **Qualia Nootropic Energy Shot** was to support NO production and thereby support endothelial function and healthy blood flow, including cerebral blood flow. Therefore, **Qualia Nootropic Energy Shot** provides two important ingredients in the NO synthesis pathway: **L-Arginine and Niacinamide.**

L-arginine is provided by **Inositol-enhanced Bonded Arginine Silicate (NooLVL™)**, which has been shown to upregulate the blood levels of arginine and NO [199]. Silicate upregulates endothelial NOS (eNOS) [200], also contributing to the support of NO production. Both arginine [201] and inositol [202,203] support healthy blood pressure. Through these mechanisms, **Inositol-enhanced Bonded Arginine Silicate (NooLVL™)** supports healthy vascular function [204].

Vitamin B3 as Niacinamide is the precursor to NADPH required for NO production [87]. **Niacinamide** has also been shown to support blood flow by increasing microvascular density and microcirculation [205,206].

Blood flow to metabolically active tissues, such as the brain, plays an important part in supporting peak performance. Accordingly, **Inositol-enhanced Bonded Arginine Silicate (NooLVL™)** has been shown to support brain performance [54,207,208].

Wild Blueberry Fruit Extract provides additional blood flow support. It also upregulates eNOS activity [209] and supports healthy blood pressure [210–214], vascular function [215], and brain perfusion [69].

MOTOR AND PHYSICAL PERFORMANCE

Just as brain performance is supported by a healthy blood flow, so is physical performance. And the same is true for cell energy production. Active muscles require the blood to supply nutrients and oxygen, and good cellular metabolic capacity in order to perform their functions at a high level. Therefore, all ingredients in **Qualia Nootropic Energy Shot** that support healthy vascular function, healthy metabolism, and mitochondrial function also support physical performance.

Accordingly, **L-Arginine**, from which NO is produced, has been shown to support exercise performance, delay time to exhaustion, and delay muscle fatigue [216,217]. Likewise, by supporting muscle blood flow, **Inositol-enhanced Bonded Arginine Silicate (NooLVL™)** enhances exercise performance and post-exercise recovery, while protecting muscles from damage [218].

But beyond blood flow and cell energy production, the ingredients included in **Qualia Nootropic Energy Shot** have shown other ergogenic features (i.e., enhancing physical performance).

American Ginseng (Cereboost™) supports high-intensity endurance performance [219,220] and protects from exercise-induced muscle damage [219–221]. **Alpha-GPC** supports isometric force production [222] and maximum power and velocity in jump movements [223]. **Caffeine** reduces perceived exhaustion, supports muscle endurance and strength, and enhances speed, power, and agility during intense exercise [9]; it thereby protects from physical fatigue [25,59,224,225]. **L-Tryptophan** supports power output and delays time to exertion [226,227]. **Saffron Extract** enhances reaction times, supports muscle strength [228], and prevents muscle soreness [229]. **Wild Blueberry Fruit Extract** supports exercise performance [230] and supports recovery from muscle damage [231].

An additional aspect of physical performance that **Qualia Nootropic Energy Shot** also addresses is locomotor activity and motor coordination, which is supported by *Alpinia galanga* [232]. **L-Theanine** also supports perceptual-motor task performance [43,164]. **Alpha-GPC** is a precursor in the biosynthesis of acetylcholine, which participates in the neuronal activation of muscles; therefore, it may also support neural aspects of muscle performance.

SOCIAL COGNITION

Social cognition can be defined as the brain processes that manage social behavior and interactions, i.e., the reception of social stimuli (e.g. reading facial expressions), social reasoning and decision-making (e.g., deciding whether or not to trust someone), and social responses (e.g., making facial expressions) [233,234].

Social cognition is an important aspect of our performance because, more often than not, we perform our tasks while interacting with other people, either because we want to or because we have to. The goals of our actions become social goals, in the sense that they are shared goals involving two or more people. These joint actions require communication and being able to read social cues, for example [233]. Social cognition is the collection of all cognitive skills that underlie these abilities.

Social cognition is built on the ability to recognize emotions, to infer, read, and understand other people's feelings, intentions, and motivations, and to anticipate other people's reactions. Social cognition involves empathy, theory of mind, cooperation, and social feedback-based learning. Importantly, it also involves reciprocity: being able to perceive and understand social cues, while also being able to transmit appropriate signals and reactions.[235]

Social cognition is a key skill in any type of social context, be it work, school, or a party. Supporting social cognition can contribute to a better performance in social interactions.

Social cognition support was one of the main reasons why we included the essential amino-acid **L-Tryptophan** in the formulation of **Qualia Nootropic Energy Shot.**

L-Tryptophan is the precursor to the neurotransmitter serotonin [236]. **L-Tryptophan** administration supports the synthesis of serotonin in the brain [237,238]. Increased serotonin levels have been linked to enhanced processing of social emotional information with a bias towards positive information (e.g., towards happy faces, away from negative words), which is linked to more positive social behaviors [239]. Accordingly, increased serotonin levels in the brain have been linked to an increased sensitivity to social factors, leading to increased prosocial behaviors such as cooperation [240,241].

Thus, through its support on serotonin production, **L-Tryptophan** may promote the serotonin signaling system's role in social behavior. And indeed, **L-Tryptophan** has been shown to promote prosocial behavior [242,243] and support healthier social interactions [244–246]. **L-Tryptophan** has even been shown to promote charitable behaviors [247]. Through this action, **L-Tryptophan** may enhance social functioning and facilitate social interactions [242].

Saffron Extracts have been researched in a variety of areas, most of which fall into caregories of cognition, vision, sex drive, and emotional health. One mechanism involved in the emotional health area may be related to serotonin signaling [248].

VISION

For sighted individuals, vision is one of the major sources of input for most tasks, be it to read, to watch a presentation, to drive, to observe other people's reactions, to follow the trajectory of a ball... Visual acuity and visual health in general are therefore fundamental for the ability to pay attention and react to visual stimuli.

Therefore, **Qualia Nootropic Energy Shot** also includes a few ingredients that support vision. **Saffron Extract** is particularly helpful in this respect as it has been shown to protect retinal cells against damage and degeneration [184,249–253], including light-induced damage [250,254–256], and to support healthy intraocular pressure [257]. **Saffron Stigma Extract** also enhances retinal function [258] and visual acuity [252,259].

Wild Blueberry Fruit Extract also contributes to the support of vision. **Blueberry Extract** has been shown to protect retinal photoreceptor cells from blue LED light-induced damage [260,261] and to protect against screen-induced ocular fatigue [262,263]. **L-Theanine** and **Caffeine** also support visual reaction time [264].

PERFORMANCE BOOST IN A SHOT

As we have seen, optimal mental performance requires the capacity to plan, organize, focus, sustain attention, and avoid distractions. It also requires the ability to shift attention between two or more relevant tasks, to process information and react quickly, to adjust to changing circumstances and new demands, to change our mind or point of view, to hold information in short term memory as we use it, to use logical reasoning to see patterns and solve problems, all while managing emotions and behaviors. This requires mental energy to support the mental effort.

We believe we have developed a product that can boost mental energy while also supporting other aspects of performance: arousal, focus, motivation, cognitive control, emotional control, and physical energy.

Qualia Nootropic Energy Shot was designed and optimized to help you meet these outcomes, feel a fast boost in mental and physical energy, feel sustained focus, and feel more drive to get things done. All with no pills, just a liquid shot.

These statements have not been evaluated by the Food and Drug Administration (FDA). This product is not intended to diagnose, treat, cure, or prevent any disease.

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