The Effect of Nootropics on Brain Activity

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Abstract:

This research aims to compare Apoaequorin and Piracetam, focusing on their respective benefits and side effects, and analyze how these cognitive enhancers (CEs) affect non-impaired and impaired brain activity. CEs, also known as smart drugs and nootropics, have been developed over the past fifty years and enhance memory performance. Cognitive enhancement is the "amplification or extension of the core capacity of the mind by improving the internal and external information processing systems" (Sharif, 2021). Apoaequorin is a calcium-binding protein that is derived from jellyfish. In the racetams group, Piracetam is a cyclic derivative of gamma-aminobutyric acid (GABA) obtained after losing one water molecule and ring formation. We examine the efficacies of drugs without head-to-head clinical trial data by understanding the outcome of taking CEs and their impact on a healthy human brain compared to a brain that suffers from a neurovascular condition.

Keywords: Apoaequorin, Piracetam, cognitive enhancers, gamma-aminobutyric acid

The Effect of Cognitive Enhancers on Brain Activity:

Cognitive enhancers have been used by healthy people and people with mental illnesses. CEs improve memory and learning by acting as Ca-channel blockers, AChEI, glycine antagonists, antioxidants, serotonergic, dopaminergic, and glutamic acid receptors antagonists (Chiroma, 2019). Among different CEs, there are distinctions between other aspects. For example, the processing speed (the cognitive processing assessments that require rapid performances of tasks that range from basic to advanced) and executive functioning (mental processes that enable subjects to plan, focus attention, and multitask).

CEs are primarily taken to fight against diseases that affect the neurovascular system. Individuals with a history of mental or substance use disorders are particularly vulnerable to their adverse effects compared to healthy individuals. Specifically, using CEs by users with memory or learning deficits can result in paradoxical short and long-term cognitive decline, decreased potential for plastic learning, and addictive behavior.

In contrast, CEs have significantly increased among healthy university students and professionals who want to improve their academic or competitive professional practices. For instance, Cambridge, Oxford, and Imperial College London universities shipped modafinil to students who wanted to perform their best on upcoming exams. Many students noticed an improvement in their concentration, motivation, accuracy, productivity, alertness, creativity, and academic performance.

Piracetam:

Piracetam was initially marketed by UCB Pharma in 1971, becoming the first CE to modulate cognitive function without causing sedation or stimulation. With neuroprotective and anticonvulsant properties reported to improve neural plasticity, Piracetam’s efficacy has been

documented in many mental disorders such as dementia, vertigo, and dyslexia. Moreover, dyslexic children improved their reading comprehension and accuracy. Also, it has improved alertness, socialization, and IQ in elderly psychiatric patients. Also, Piracetam has treated alcoholism.

Part of the racetam's group with the chemical name 2-oxo-1-pyrrolidine acetamide (Figure 1), Piracetam shares the same 2-oxo-pyrrolidone base structure with pyroglutamic acid (amino acid formed enzymatically or non-enzymatically, participating as a biological intermediate with unique pharmacodynamics). In 1991, Paula Barbosa and colleagues discovered that one year of alcohol-feeding to rats increased lipofuscin (age-related waste pigment) formation in brain cells. After intaking high doses of piracetam, the alcohol-fed rats reduced their lipofuscin levels below control levels. Confirming this experiment, in 1997, piracetam was established to have reduced neuronal loss following chronic alcohol consumption. Piracetam's pharmacological properties were reported almost fifty years ago; however, its uses for unknown for a long time.

In the 2000s, tests began under the "central nystagmus" model, sensitive to only anticholinergic and antihistaminic drugs. Piracetam is reported to have mild side effects. Initially, its side effects were anxiety, insomnia, agitation, irritability, and tremor. These are identical to the symptoms of excessive acetylcholine/glutamate neuroactivity. Despite these effects, piracetam is not generally considered a significant agonist/inhibitor of the synaptic action of most neurotransmitters.

Apoaequorin:

Found in Aequorea Victoria jellyfish, Apoaequorin is a calcium-binding protein that has been used as a calcium sensor in research for the past decade (Figure 2). Apoaequorin is a crucial

ingredient in many over-the-counter (OTC) medications for improving memory and verbal learning. When conjugated with coelenterazine, the natural form of apoaequorin has natural bioluminescence because of exposure to calcium. Apoaequorin has calcium-binding characteristics resembling calmodulin, an intracellular protein complex that plays a significant role in memory. Because of this phenomenon, recombinant apoaequorin, after undergoing the regulation of calcium flux, has been developed for research studies to improve memory.

A trial of oral apoaequorin in patients with memory problems found no differences in changes in measures of verbal learning but reported improvements in a subset of patients with typical cognitive test values as a baseline. These findings were questioned because of the lack of evidence that apoaequorin can be taken orally or cross the blood-brain barrier (BBB). Nevertheless, apoaequorin is marketed as a dietary supplement that supports brain health and helps with aging-related memory loss.

Furthermore, it has been used off-label (unapproved use of an approved drug) in patients with amyotrophic lateral sclerosis and multiple sclerosis, both of which are both neurodegenerative diseases that attack both the brain and spinal cord.

Conclusion:

This is the first attempt to compare the first CE, Piracetam, with a newer CE, Apoaequorin. Many authors have closely observed the effects of both CEs, but only some have commented on how they fare comparatively in an uncontrolled setting. Indeed, both CEs have their pros and cons, but after closely understanding how each one operates, Apoaequorin has shown better results.

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Appendix

Figure 1: Piracetam Molecular Structure

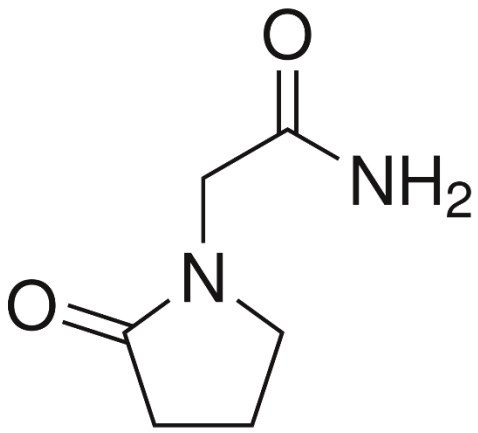

Figure 2: Apoaequorin Molecular Structure