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Case Report

Hypothesizing Enhanced Brain Activity as A Function of Dopamine Homeostasis as Observed with KB220 in A Male with Delayed Cognitive Performance

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Abstract

Background: Quantitative electroencephalography (qEEG) has proven invaluable in assessing the neuropsychological impact of various substances, providing insight into their effects on brain activity and cognitive functions. KB220, a nutraceutical neuroadaptogen, has shown promise in modifying the dopaminergic system to enhance cognitive and neurological functions without dependency risks.

Case Presentation: A 26-year-old male with a history of multiple neuropsychiatric diagnoses, including ADHD, PTSD, and sensory integration disorder, underwent qEEG analysis to explore the effects of KB220 on brain function. The patient's EEG was recorded before and 60 minutes after oral administration of KB220, observing changes in various frequency bands indicative of cognitive and alertness states.

Methods: Baseline and post-administration EEG recordings were analyzed to assess changes in Delta, Theta, Alpha, and Beta wave activities, which correlate with alertness, memory processing, and cognitive engagement. The study utilized a 19-channel EEG with a consistent setup to ensure accurate comparative results.

Results: Significant alterations were observed in the patient's EEG post-KB220 administration. There was a notable reduction in Delta activity, suggesting increased alertness. Theta and Alpha activities increased, indicating enhanced working memory and neuronal synchrony. Beta activity changes suggested improved focus and cognitive processing. These shifts point towards restoring dopamine homeostasis, potentially enhancing brain activity and cognitive functions.

Conclusion: The case highlights the potential of KB220 to significantly impact brain function and cognitive performance through modulation of the dopaminergic system. These findings support further research into KB220 as a beneficial treatment for cognitive delays and neuropsychiatric conditions beyond traditional applications in addiction and reward deficiency syndrome. The data suggest a broader utility for KB220 in improving cognitive outcomes in patients with complex neuropsychiatric profiles.

Keywords: Hypothesizing; Brain; Dopamine; KB220; Cognitive

Introduction

EEG was first recorded by a British physician, Richard Caton, in 1875. He recorded the brain's electrical impulses in rabbits and monkeys. After that, some researchers published the results of recording the brain's electrical impulses in other mammals. In 1929, Hans Berger, a German physiologist and psychiatrist, reported the electrical activity of the human brain during sleep. Ten years later, EEG recordings were used to document the first aspects of epileptic attacks [1].

The brain's electrical charge is maintained through ion exchange along the membrane of billions of neurons, resulting in electrical potentials. Thus, an EEG is the summation of the activity of billions of neurons laid close to each other. EEG seems to be produced by pyramidal cells of the brain cortex (Table 1).

EEG has contributed extensively to understanding the relationship of brain oscillations in different frequency ranges with brain states and cognitive processes. Frequency-specific oscillations incur local alterations in amplitude and synchrony with characteristic spatial and chronologic distributions depending on the cognitive requirements of a given task [2]). There is a plethora of published works that highlight the prominent role of the electrical activity of the brain measured by EEG for each specific frequency in terms of mechanism and cognitive processing: Theta rhythm [3]), Alpha rhythm [4]), Beta rhythm [5]), Gamma rhythm [6]).

EEG can provide evidence of underlying diffuse or focal cerebral dysfunction by demonstrating background slowing. The two main types of slowing are focal and generalized.

Band	Frequency (Hz)	Location	Normally	Pathologically
Delta	< 4	Frontally in adults, posteriorly in children; high-amplitude waves	Adult slow-wave sleep In babies Has been found during some continuous-attention tasks	Subcortical lesions Diffuse lesions Metabolic encephalopathy hydrocephalus Deep midline lesions
Theta	4-7	Found in locations not related to the task at hand	Higher in young children Drowsiness in adults and teens Idling Associated with inhibition of elicited responses (has been found to spike when a person actively tries to repress a response or action).	Focal subcortical lesions Metabolic encephalopathy Deep midline disorders Some instances of hydrocephalus
Alpha	8-15	Posterior regions of the head, both sides, higher in amplitude on the dominant side. Central sites (c3-c4) at rest	Relaxed/reflecting Closing the eyes Also associated with inhibition control, seemingly for timing inhibitory activity in different locations across the brain.	Coma
Beta	16-31	Both sides have symmetrical distribution, most evident frontally; low-amplitude waves	Range span: active calm -> intense - > stressed -> mild obsessive Active thinking, focus, high alert, anxious	Benzodiazepines

Table 1: Cerebral Functions Related to Different EEG Frequencies [5,7].

Generalized background slowing in the Theta and Delta frequency ranges is a normal finding on the EEG of developing children, adolescents, and some young adults or in states of drowsiness and sleep. However, and importantly, intermittent or persistent focal slowing consistently over one head region, or persistent, unvarying, unreactive focal or generalized slow wave activity in a vigilant adult patient, should be considered pathologic and indicate corresponding focal or generalized cerebral dysfunction or both [8]. Abnormal, generalized background slowing indicates diffuse cerebral dysfunction, which, similar to focal slowing, is also not specific as to cause. Several different etiologies may elicit generalized background slowing [7]. Slow brain waves are also seen in conditions such as sleep, coma, brain death, depression, autism, brain tumors, obsessive-compulsive disorder (OCD), attention deficit hyperactivity disorder (ADHD), and encephalitis. Conversely, rapid waves are generally reported in conditions such as epilepsy, anxiety, post-traumatic stress disorder (PTSD), and drug abuse [9].

PRO-Dopamine Regulation with Kb220 Variants

KB220 and its variants are a nutraceutical neuroadaptogen [10]). The most recent variant of KB220Z (powdered form) used in the present study is comprised of the following ingredients: Thiamine, 15 mg (1033% of Daily Value); Vitamin B6, 10 mg (500%); Chromium poly nicotinate 200 mcg (166%) and a fixed dose of Synaptose. Synaptose is a combination of amino acids and herbs that contains DL-Phenylalanine, L-Tyrosine, Passion Flower Extract; a Complex containing Arabinogalactans, N-Acetylglucosamine, Astragalus, Aloe Vera, Frankincense Resin, White Pine Bark Extract, and Spirulina; Rhodiola; L-Glutamine; 5-Hydroxytryptophan (5-HTP); Thiamine Hydrochloride; Pyroxidal-5-phosphate and Pyridoxine HCl [11]. The powder

was manufactured by Cephram, Inc. (New Jersey), distributed by Victory Nutrition International (Pennsylvania), and sold under the brand 'Brain Reward'.

Historically, KB220 has been used mainly in treating patients with various addictions, including alcohol, cocaine, heroin, and certain non-substance addictions (e.g., gambling, hypersexuality, etc.). One study by Miller., *et al.* pointed out emerging evidence whereby the potential of utilizing a natural, non-addicting, safe, putative D2 agonist may find its place in recovery from Reward Deficiency Syndrome (RDS) in patients addicted to psychoactive chemicals [12]. Utilizing quantitative electroencephalography (qEEG) as an imaging tool, the authors demonstrated the impact of Complex Variant KB220 as a putative activator of the mesolimbic system. Specifically, they showed for the first time that its intravenous administration could reduce or "normalize" aberrant electrophysiological parameters of the reward circuitry site. This work is further supported by a clinical trial on Synaptamine Complex Variant KB220™ using intravenous administration in > 600 alcoholic patients, resulting in significant reductions in RDS behaviors [13]. In support of the hypodopaminergic hypothesis of addiction and neuropsychiatric abnormalities, Willuhn., *et al*. reported that as dopaminergic function is reduced, cocaine use and non-substance-related addictive behaviors increase [14]. Chronic cocaine exposure has been associated with decreases in D2/D3 receptors and was also associated with lower activation of cues in the occipital cortex and cerebellum in a recent PET study [15]. Therefore, treatment strategies, like dopamine agonist therapy, that might conserve dopamine function may offer alternative approaches to relapse prevention in psychoactive drug and behavioral addictions.

To this aim, Blum analyzed the effect of KB220Z on the reward circuitry of 10 people with a heroin addiction undergoing protracted abstinence – an average of 16.9 months [16]. In a randomized placebo-controlled crossover study of KB220Z, five subjects completed a triple-blinded experiment in which the subject, the person administering the treatment, and the person evaluating the response to treatment were blinded to the treatment that any particular subject was receiving. The study also found preliminary evidence that KB220Z increases Blood Oxygenation Level Dependent (BOLD) imaging in the caudate-accumbens-dopaminergic pathways compared to placebo 1-hour after *stat* administration. Furthermore, KB220Z also reduced resting-state activity in the cerebellum of abstinent heroin addicts. In the second phase of this pilot study of all ten abstinent heroin-dependent subjects, they observed that three brain regions of interest were significantly activated from resting state by KB220Z compared to placebo ($p < 0.05$). Increased functional connectivity was observed in a putative network that included the dorsal anterior cingulate, medial frontal gyrus, nucleus accumbens, posterior cingulate, occipital cortical areas, and cerebellum.

In psychostimulant and polydrug abusers, a randomized, triple-blind, placebo-controlled crossover study with KB220Z revealed positive outcomes using quantitative electroencephalographic (qEEG) imaging [17]. Using t-statistics, significant differences were observed with KB220Z compared to placebo after one week of daily administration. The findings included increased Alpha waves and low Beta wave activity in the parietal brain region. Positive changes were also particularly noteworthy in the frontal brain regions, with improvements in the formerly dysregulated electrical activity of these people with a substance use disorder. The results included a phase change from low amplitude or low power in the brain to a more regulated state by increasing an average of 6.169 mV across the prefrontal cortical region. The changes persisted in a second measurement after two weeks of taking KB220.

These positive effects of KB220 variants on substance abusers have suggested there may be potential benefits of using KB220 in normal individuals as well as certain non-addictive neuropsychiatric conditions. Preliminary evidence supports this hypothesis. For instance, our laboratory has shown that daily ingestion of KB220 in normal subjects raises cognitive event-related potentials (ERPs) associated with performance. These normal young adult volunteers served as their own controls before and after 28-30 of daily intake. Cognitive ERPs were generated by two computerized visual attention tasks: the Spatial Orientation Task (SOT) and the Contingent Continuous Performance Task (CCPT). Statistically significant amplitude enhancement of the P300 component of the ERPs was seen after KB220 for both tasks, as well as improvement with respect to cognitive processing speeds [18].

RDS is not only associated with addiction. Several psychoneurological conditions share similar hypofunction and dysregulation of the dopaminergic system, including Attention Deficit Hyperactivity Disorder (ADHD), Tourette's- Syndrome, and Posttraumatic Stress Disorder. To date, there are at least 35

clinical trials with KB220 variants for a number of RDS addictive behaviors – both substance and non-substance-related [19]. We cite herein just several papers showing attenuation of shopping and hoarding, repetitive paraphilia, and ADHD. Improved focus, long-term memory, and other positive clinical metrics were also reported [11,20-22].

Patients with RDS often report Lucid Dreams, which may be pleasant, unpleasant, or terrifying. During Lucid Dreams, the dreamer is aware, experiences the dream as if fully awake, and may control the dream content. The dreamer can start, stop, and restart dreaming, depending on the nature and pleasantness of the dream. For patients with Reward Deficiency Syndrome (RDS) behaviors, like PTSD, the dream content is often unpleasant and even terrifying. In a sample of psychiatric center patients identified as having RDS a coincidental improvement in pleasant lucid dreaming was reported after taking KB220. Notably, the frequency of terrifying dreams was reduced. These reports motivated the study of eight clinical cases with known histories of substance abuse, childhood abuse, and PTSD. The administration of KB200Z eliminated unpleasant or terrifying lucid dreams in seven of the eight subjects. Subsequently, other published cases have further established the possibility of the long-term elimination of terrifying dreams in PTSD and ADHD patients [11,20-24]).

The subject of this case study suffers from a wide range of psychoneurological disturbances treated with various psychopharmaceuticals with only partial success. The most disruptive behavioral features have been attenuated but without improvements in function. No structural abnormalities have been identified. Based on the experience with quantitative EEG analysis and the effects of KB220, we hypothesized that enhanced brain activity, as a function of dopamine homeostasis, might be helpful.

Case Presentation

Mr. KB is a 26-year-old male with a history of multiple neuropsychiatric diagnoses, some of which have yet to be confirmed. These include Obsessive Compulsive Disorder and Attention Deficit Disorder. What adds to the complexity (and is a confounding factor in terms of a definitive diagnosis) is an underlying Autism Spectrum Disorder. In addition, there are elements of Depression, Post Traumatic Stress, and Sensory Integration Disorders. The complexity of the case prompted an EEG assessment to assist in identifying the electrophysiological abnormalities and to rather use these patterns of dysfunction than a diagnostic categorical approach for relief of his functional challenges. KB's most troublesome symptoms included (1) mental inattentiveness; (2) hypersensitivity to light and sound; (3) general social anxiety and agoraphobia; (4) difficulty in maintaining the cadence of ordinary conversation with unusually wordy responses; (5) difficulty in interpreting and transmitting non-verbal cues appropriately; (6) uncoordinated movements affecting his body in the form of general clumsiness, and unusual eye movements; (7) possible self-stimulatory behaviors (stims); (8) obsessive ideation; (9) dermatillomania (excoriation disorder); (10) anger outbursts; (11) poor perception of time; (12) difficulty in establishing and maintaining relationships; (13) lack of motivation; (14) procrastination; (15) poor self-esteem; and (16) complex domestic relationships. His treatment over the past year has included Amitriptyline (Elavil), Quetiapine (Seroquel), Aripiprazole (Abilify), and Clomipramine (Anafranil).

Methods and Materials

The patient was seen while off his medication for 72 hours and fasting for 8 hours. A 19-channel EEG was performed using a Nihon Kohden Electroencephalograph (Nihon Kohden, Japan). The recordings included 10 minutes with eyes open, 10 minutes with eyes closed, 5 minutes performing mental math, and 5 minutes moving his dominant hand. After finishing the EEG, the patient was given the contents of three "Brain Reward" KB220 capsules by opening the capsules directly on his tongue to optimize absorption. The patient remained sitting in the same position, with the EEG electrodes in place. The same EEG sequence was repeated 60 minutes after the administration of KB220. The EEG tracings were converted into European Data Plus (EDF+) format and opened in Mitzar WinEEG (Mitzar, St Petersburg) for EEG and Quantitative EEG analysis. EEG artifacts were removed using 60 Hz electrical interference filters; others were manually excluded based on annotations made by the EEG technician (e.g., the patient moved or yawned) or tracings related to eye or muscle movements. Abnormal waveforms were coded by one of the co-authors, highly experienced in analyzing EEGs. Fast Fourier Analysis was made for 1-30 Hz frequency bands.

Results

Findings comparing the baseline to the features 1 hour after ingesting KB220 revealed the following: When comparing the uV^2 (i.e., the electrical potentials per surface area) to the baseline value before taking KB220, the average uV^2 in the Delta range was reduced by 23.5%. The Theta uV^2 increased by 10.5%. The Alpha uV^2 increased by 25%. Beta 1 saw an increase of 11% in uV^2.

When comparing the Hz peak of BL 3 with KB220, the Delta peak was unchanged. However, the Theta peak increased by 12.9% one hour after the administration of KB220. The Alpha in the KB220 condition had a 1.3% drop, which was not significant. However, the KB220 condition had a frequency distribution of 1 (9.03) compared with 2 frequencies in BL 3 (9.03, 9.28), and prior to the administration of KB220. This suggests that the brain had become fully synchronous with one predominant peak. Lastly, we found a 3.5% decrease in the Beta 1 frequency with the administration of KB220 (Table 2, Figure 1).

	Delta	Theta	Alpha	Beta1
	uV^2	uV^2	uV^2	uV^2
BL 1	3.9	1.9	2.7	0.9
BL 2	1.4	3.1	3.4	0.6
BL 3	3.4	1.7	2.7	0.8
KB220	2.6	1.9	3.6	0.9
	Hz	Hz	Hz	Hz
BL 1	1.6	4.8	9.3 (2)	14.9
BL 2	1.6	7.8	8.1 (2)	13.7
BL 3	1.5	5.4	9.1 (2)	16.2
KB220	1.5	6.2	9.0 (1)	15.8

Table 2: KB220 Study Comparison of the Average uV^2 and Hz.

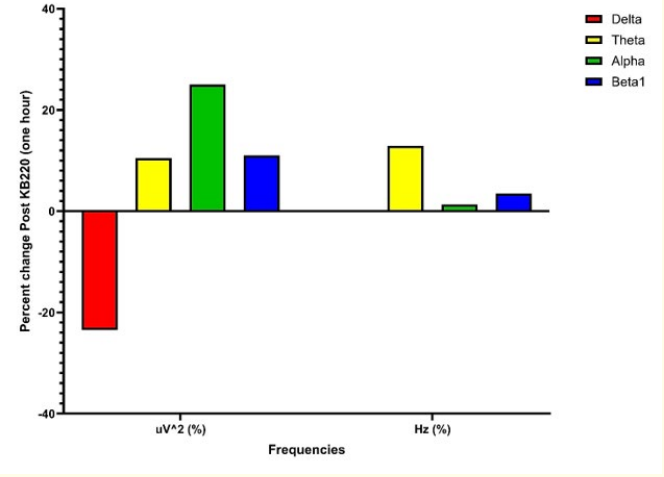

Figure 1: Illustrates the impact of the administration of KB220 within 60 minutes of administration. The figure plots the uV^2 (%) and Hz (%) following one hour post KB220 treatment. The Y-axis represents the percent change up or down, whereas the X-axis represents frequencies.

Discussion

This case study illustrates the value of using EEG to identify psychoneurological disorders as well as the significant impact of the administration of KB220 within 60 minutes of administration. The findings also support the premise that KB220 restores dopamine homeostasis without untoward side effects [10].

Specifically, findings comparing the baseline to the features 1 hour after ingesting KB220 revealed the following: when comparing the uV^2 (i.e., the electrical potentials per surface area) to the baseline value before taking KB220, the average uV^2 in the Delta range was reduced by 23.5%, suggesting more alertness with a single dose of KB220 within one hour of ingestion [25]. The Theta uV^2 increased by 10.5% of unknown significance. The Alpha uV^2 increased by 25%, which correlates with an increase in neuronal synchrony [26]. Beta 1 saw an increase of 11% in uV^2, suggesting an increase in focus, attention, short-term memory, and cognitive functioning [27].

When comparing the Hz peak of BL 3 with KB220, the Delta peak was unchanged. However, the Theta peak increased by 12.9% one hour after the administration of KB220, which may correlate with better working memory [28]. Lastly, we found a 3.5% decrease in the Beta 1 frequency with the administration of KB220. Beta 1 range is normally 12-15 Hz. The administration of KB220 almost normalized the Beta 1 peak at 15.8 Hz. The patient has difficulty with self-reporting, so the changes could not be correlated to any significant subjective neurocognitive changes 1-hour after ingesting KB220.

Conclusion

KB220 appears to have greater utility than is the predominant current use of addressing traditional RDS manifestations attributed to substance and non-substance addictive behavior. Indeed, based on at least 36 clinical trials, including this case study, it seems parsimonious to encourage additional larger trials in people with cognitive impairment to further confirm this encouraging EEG result.

Conflicts of Interest

Kenneth Blum, PhD, is the inventor of KB220Z, and his company Synaptamine holds a number of US and Foreign patents that have been licensed to Victory Nutrition International.

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