

DRAFT DOCUMENT

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RESEARCH REPORT

INCREASE IN THE EFFECTIVENESS OF THE DIETARY SUPPLEMENT, beCALM'd™, CAUSED BY THE MODIFICATION OF AMINO ACID RATIOS AND THE ADDITION OF FOLIC ACID

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ABSTRACT

beCALM'd™, an amino acid, vitamin, and mineral formulation, was designed to restore catecholaminergic, opioidergic, GABAergic, and serotonergic deficits observed in individuals suffering from (1) addiction to certain abusable substances, (2) from long-term, moderate-to-high emotional stressors, and (3) from attention deficit hyperactivity disorders. Several clinical studies proved the original beCALM'd to be very effective as adjuncts to therapy for these disorders through. Its formulation's success was shown able to raise the dopamine, GABA, norepinephrine, epinephrine, and serotonin neurotransmitter levels through precursor loading. It raised the opioid neurotransmitter, enkephalin, levels through enkephalinase inhibition using the amino acid, d-phenylalanine. This was effective. However, it was found that the addition of folic acid, a reduction in the d/l-phenylalanine could be achieved. . . .(Patents 5,189,064 & 5,922,361) The slightly modified formula was tried on patients suffering from the above three disorders. The four week test followed a base line establishment using the original formula. Measurements during the study included AAP response, counselor assessment, and sobriety maintenance for the abusable substance disorder measurements. The stress portion of the study used perceived stress and systolic blood pressure. The ADHD used counselor appraisal of attention span and hyperactivity. During the experimental phase of the study, these indicators were very significantly improved. The results thus show, that through the use of this formulation modification, the clinical success achieved by the original beCALM'd formula is significantly improved.

INTRODUCTION

Many well documented studies, such as those by K. Blum, B. Ferrell, and T. Neher, have shown that the hypothalamus and hippocampus neurotransmitters dopamine, enkephalin, GABA, norepinephrine, and serotonin have very important effects on emotional response. A brief discussion of these follows. A graphic list is given in table 1.

The hypothalamus and hippocampus are those portions of the brain which apply in the case of stress, AD/HD, and certain addictive diseases. The neurotransmitter “subsystems” within these areas are an essential part of man and have been used over the millennia to produce (among others) the psychophysiological mechanisms necessary for human fight or flee(self defense) reactions. It is seen from the following and Figure 1 (on page 9), that the interrelationship among the systems form a loop and thus each ultimately effects the others. This system is triggered by the three disorder classes being studied here:

- (1) Stress causes the opioids to go down and norepinephrine to go up.
- (2) Addictive diseases are often the result of a genetically or toxically caused shortage of the opioids.
- (3) Attention deficit, hyperactivity disorder is often caused by a shortage of the opioids, GABA, dopamine and serotonin. When any combination of these are at abnormal levels, all become affected.

Thus, if stress holds the opioid level low frequently, or over a long period of time, the "signal" goes from the opioids to Dopamine and GABA to Norepinephrine to Serotonin to Opioids to, etc. and a loop occurs. Each time around the loop, each of the neurotransmitter levels are placed in an even lower supply condition. The individual first becomes irritable, easily angered and finds himself or herself suffering from easy loss of temper, sleeplessness etc., as shown in the table. Many find relief in the artificial opioid produced by alcohol, THIQ (tetrahydroisoquinoline), and thus become alcohol dependent. Others find relief in carbohydrate bingeing. A few turn to opiates such as heroin, morphine, etc.

The loop and the following, then explain the problems mentioned:

* Lower opioids levels create a sense of urgency. This sense of urgency is usually expressed as the need to respond to certain physical demands, (including cravings.) As soon as the body's need has been taken care of, the sense of urgency goes away. According to National Institute of Health studies, one in every 18 in the United States abuses alcohol and is thus predicted to have genetically caused low opioid levels. This means that from birth they have a sense of urgency that does not relate to environmental causes.

* When external factors (such as stress) force a lowering of the opioids there results an increase in dopamine and norepinephrin levels and a decrease in GABA levels. This produces a combination of alertness and anxiety (a part of the fight or flee response.) The so called adrenaline rush is in large part the feeling of exhilaration caused by the norepinephrin and dopamine release. Continual extra dopamine release causes emotional fatigue which can become debilitating. The dopamine conversion to norepinephrin can also lead to anhedonia, in which case, one can no longer enjoy beauty, music, or even love, in the extreme case. Continuously low GABA usually causes anxiety and can lead to feelings of inadequacy. In the long term it can manifest as panic attacks with no apparent cause.

* The lowering of the GABA levels causes the norepinephrine levels to increase and serotonin levels to decrease.

* The increase in norepinephrine causes adrenaline to be released. The adrenaline presence induces the essential (internal) organs to return their captured oxygen and energy packets to the blood

stream. It also produces a faster and more powerful heart beat to get the packets to the muscles thus enabling better defense. If this is continued over long periods of time the heart triggering mechanisms often take the new rates as their set points and hypertension frequently results. Unfortunately, this condition may not be reversible. In the extreme case, this condition can cause strokes and damage to a number of pressure sensitive organs and passages. It can also cause damage to the heart. Further, it usually causes the internal organs to become diseased.

* The reduction of serotonin makes sleep difficult to impossible for without serotonin, melatonin cannot induce sleep. It is important to note that serotonin enables sleep. It does not induce it. Once the serotonin becomes available, the body demands the sleep it now badly needs. When this has been done the person feels rested and “fully refreshed.” However, if it is not done and the stress continues, the lack of sleep can cause a great deal of damage to the body.

* The increased norepinephrine encourages a quick, emotional response (e.g. anger) and discourages slower, deliberate (logical) thinking. The anger, thus indirectly released by the lack of the opioids, is triggered more rapidly in the presence of the norepinephrine.

* The serotonin reduction further modulates the opioids downward. The cycle therefore repeats with continually increasing intensity as long as the opioid reduction cause (e.g. stress) continues.

THE SOLUTION: The last 20 years of research by many notable scientists such as Dr. Kenneth Blum, Dr. Gerald Kozlowski, Dr. Terry Neher, and Dr. M. L. Barbaccia, found that the depleted neurotransmitters can be replaced from normal diet, but only very slowly. They further found that the slowness was **not due to a “lack of production cells” but rather a “lack of precursors (raw materials).”** While the quantities required vary from one individual to another, getting these additional nutrients from food is generally difficult. The average person would require several pounds of exotic fish, two quarts of milk, and a variety of other high cholesterol and high fat content foods daily. Condensed supplementation is thus the preferred method of replacement. This can be done by taking each of the necessary supplements individually or by taking a single capsule containing all of them. Quantities of each are interrelated.

Various formulae have been tried. For example, experiments in Russia showed that good success could be achieved using 2 kilograms of d-phenylalanine (d-Phe) per day. The d-Ph, cost, \$250 per kilo’, makes this infeasible. Similar experiments with GABA, or its precursor l-glutamine, yielded similar results. It was later discovered and patented that a combination of d-Phe, l-Phe, l-glutamine, and l-tryptophan (or catalysts for its more efficient production of serotonin) required only a small amount of each. In its newest form, that used in this study, it was found that by adding folic acid, the quantities of d/l-Phe could be reduced even further. This new formulation was demonstrated by the clinical trial, reported upon here-in, to be superior to the previous formulation.

Particular emphasis must be made that in the previous formulation, trade named “beCALM'd”, as much as two grams per day of d-phenylalanine was used to inhibit the opioid destruction enzyme, enkephalinase. This was done as the principal opioid precursors were so expensive as to be very cost prohibitive. A new discovery (patent pending) found that a small amount of d/l-Phenylalanine combined with requisite amounts of folic acid provide the precursors necessary to increase the opioid supply. Thus, the opioid shortage is normalized by body function rather than controlled by patient demand (PRN.)

Inspection of The Stress Cycle(See Figure 1, p. 9) shows how such action stops the “loop from recycling.” That is, enhancement of the opioids, GABA, and serotonin each reduce the amplitude of the signal that is passed on from the opioid system to the dopamine and GABA systems, etc. This having been done, the human is able to function normally. That is he or she can be himself or herself rather than like someone suffering constant “agitation.”

CONCLUSION: Today’s preferred treatment of these related diseases is not a new miracle drug or even significant life-style changes. (The latter often cause more problems than they cure.) It is nutritional supplementation with common items we all consume every day. . .but not in large enough quantities. It is found in fish and algae, in fish liver oil, carrots, liver, eggs, and dairy products. It is found in many fruits and nuts, in milk, cheese, ham, and turkey. If one were to eat the quantities of the above foods that are required to handle modern continual stress, AD/HD, or predilections to addiction, he would become obese in very short order and would probably have cholesterol and triglyceride counts that would be life threatening.

The concentrated nutritional supplementation is generally water soluble and to take too much is a practical impossibility. That is, the highest recommended dosages of the new beCALM’d formula is 6 capsules per day. An average 180 pound man would be likely to require 5,000 capsules a day before he noticed the first untoward effect, slight euphoria. Thus, this nutritional supplementation is perhaps the most safe, practical means of managing three of this century’s most important disorders.

Contempt prior to investigation on this issue may do more than keep man in ignorance, it may be fatal.

Table 1
THE FORMULATION
(Patent # 4,761,429 & Others Pending)

Ingredients/capsule	Administration	Amount	%USRDA
Vitamin A	beta carotene	1000 IU	20%
Vitamin B ₆	pyridoxine HCL	1 mg	50%
d/l-Phenylalanine		150 mg	*
l-Glutamine		300 mg	*
Calcium	chelate, carbonate	50 mg	6%
Magnesium	Chelate, oxide	25 mg	6%
Folic Acid		0.1 mg	25%
Chromium picolinate	(Patent #4,315,927)	0.01 mg	8%

* U.S. Recommended Daily Allowance has not been established

Table 2 Neurotransmitter Functions & Requirements

NEURO TRANSMITTER	FUNCTIONS IN:	DEFICIENCIES RESULT IT:	SUPPLEMENT REQUIRED:	FOODS IN WHICH FOUND:
Serotonin	Emotional stability	Lack of rational emotion; Feelings of irritability; Sudden unexplained tears; Sleep problems	l-tryptophan from food Calcium & Magnesium Chromium Vitamin A	Turkey; Ham; Milk; Cheese
GABA	Staying calm	Free floating anxiety; Fearful, insecure feelings; Feelings that things are closing in around you; Unexplained panic	l-glutamine Vitamin B ₆	Fish, especially mackerel; Wheat bran
Enkephalins	Psychological pain relief	Feelings of incompleteness; Lack of fulfillment; Feelings of inferiority; Feelings of inadequacy; Never feels "Equal"	d-phenylalanine Vitamin B ₆ Folic Acid	Fish and algae; Wheat germ Green leafy veg. Egg yolk Tortula yeast
Dopamine	Pleasure, reward; Good feelings toward others; Maternal/ Paternal love	Anhedonia - no pleasure in life; World looks colorless; Inability to "love" No remorse about personal behavior	l-phenylalanine Vitamin B ₆	Fish and algae; Blackstrap molasses
Norepinephrine	Arousal; Energy; Drive	Lack of ambition; Lack of all drive; Lack of energy; Depression	l-phenylalanine Vitamin B ₆	Fish and algae; Beef liver or kidney

SUBJECTS AND METHOD

To test the formula, measurements were chosen to be as close as possible to the those used to test the original beCALM'd formula as discribed in the Research Reports on its first three clinical trials. This formulation is discribed in detail in the first of these reports. Copies of the reports may be obtained from the Authors by writing them at P.O. Box 1111, Seabrook, TX 77586.

Group Selection and Dosage Regimen

The twenty-four subjects of this clinical trial were tested without either formula for a one week period, to establish a base line. They were then given the original ("Old") formula for 10 days. The study was then completed by giving the "new" formula for 15 days. The subjects were chosen at randum from people who were then regularly taking either five or six capsules per day of the original beCALM'd formula and had a clinical history of their performance before taking that formula. In each case the dosage had been established through clinical observation of at least two months. The group included eight who were taking the product for stress related reasons, twelve were recovering alcoholics, and four were AD/HD students.

Test Measurements

The time of day for taking measurements was left to the individual. The one provision was that it must be taken at the same time each day.

Cardiovascular Measurements: Standard systolic and diastolic blood pressure measurements were taken by the participants, using a BMS model 11-780 Oscillometric Unit, and recorded daily throughout the study.

Perceived Stress Level: Participants were asked to record their percieved stress level by responding to the question "On a scale of 1 to 10, with 1 being no stress and 10 being the most stress you have ever experienced, how would you rate your stress level today?" Each was then asked to circle their response on a 1 to 10 scale on that day's data sheet.

AAP Behavioral Test:

AAP Scores are subjective measurements applied to each patient during the entire period of the test and the baseline establishment time before the test. The AAP is a nonstandardized evaluation tool developed by Dr. Neher. It includes key measures of clinically important psychological and behavioral performance. During the course of the study, changes were noted by Dr. Neher and

his staff.

On admittance each patient was assigned a baseline value of 0. Each day improvement or regression was noted with a range of improvement from 0 to +5, and a range of regression from 0 to -5: 0 indicated no change from admittance status.

These subjective measures quantify the clinical judgment of experienced professionals. Averaging the judgements of the participating professionals provided a profile that the staff agreed accurately represented their response to each individual in the study.

AD/HD Evaluation Test:

This test is one that has been used for a number of years by numerous CHADD groups. Each teacher during the day keeps a log of the child's performance in comparison with his "normal" classmates. Behavior more active than the norm is scored as a 1 point for HD and behavior less active (e.g., lack of attention) than the norm is scored as a 1 point for ADD. Behavior roughly the same as the norm is scored as "0" points.

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RESULTS

GENERAL

Table 3, below, gives a synopsis of the experimental data. An interpretation follows the table.

TABLE 3
TABULAR SYNOPSIS "F" SCORE & MEAN DATA

	Systolic		Diastolic		Perceived Stress		AAP Relation		ADD/HD Compare To Norm'	
	"F" Mean	Mean	"F" Mean	Mean	"F" Mean	Mean	"F" Mean	Mean	"F" Mean	Mean
Alcoholic Control		133		95				0.11		
to Old Formula:	2.04	112	2.02	97			2.30	-2.55		
Old Formula to New Formula:	1.19	113	1.15	78			1.24	-2.44		
General Stress Control		133		85		3.18				
to Old Formula:	2.04	112	2.02	97	2.17	2.84				
Old Formula to New Formula:	1.19	113	1.15	78	0.99	2.97				
ADD/HD Control										3.60
to Old Formula:									5.96	1.93
Old Formula to New Formula:									1.59	0.87

"F" Scores: 1.0 indicates no difference in population (between tested formulas), 1.84 indicates a 95% probability it is two different populations and 2.39 indicates a 99% probability it is two different populations. (95% is generally regarded as sufficient to prove a treatment is effective.)

Mean indicates whether the difference in population is represents a change in the "average" or a reduction in variation between data points..

Separate statistical analysis was done for blood pressure data of the recovering alcoholics and the general stress population. However, as there was little difference it was regarded as statistically better to combine the recovering alcoholic groups and the general stress groups to give a wider population basis. The blood pressures of the children and adolescents of the AD/HD group were not taken as it was a) not considered significant to this test, and b) not logistically practical.

The reduction in blood pressure swings between the base line and Old formula data (2.04)

represented a significant improvement. This is important as the swings generally represent spikes that often are the cause of various forms of cardiovascular disease and stroke incidents. This is made even more dramatic in that the mean systolic levels were lowered more than 20 points, an indication that norepinephrine levels dropped.

In the comparison of the Old formula to the New, portion of the test, the “F” Scores and the systolic means indicate little difference between the results. The 9 point drop in diastolic measurements might indicate more consistent serotonin levels, however, the change is considered statistically insignificant.

The perceived stress “F” Score for no formula to Old formula indicates a well above 95% correlation figure. Given the previous studies and experience with this formula, these high improvement results were expected. The perceived stress “F” Score for the Old formula to New formula comparison show little difference in results between the formulae. The measurements’ means are of little significance as it is the perceived variance that indicates formula success. The perceived “normal” level varies from person to person and has little to do with changes.

Dr. Neher’s HNL Relation scores, though subjective, are based on professional evaluation. Day 1 is by definition “0”. During the week while each subject was without either formula shows the wide variance that is to be expected of the sober alcoholic. The fact that all of them had been using the Old formula prior to this time, generally explains the fact that the scores got worse just after the no formula period began. The dramatic increase to an “F” score of approaching 3 standard deviations is commensurate with past findings of Dr. Neher and his staff in the use of the Old formula with similar patients and clients.

The comparison between the “F” scores shows that the New formula is a little more effective than the Old formula in this use. The difference is, however, not statistically significant, nor is the comparison of the means.

The AD/HD population is quite small. However, the “F” score of 5.96 is so high that even with the low “n”, the comparison to non formula is statistically very significant. The “F” score comparison between the formulae is not statistically significant. Nevertheless, the combination of the “F” score of 1.59 and the nearly 2 to 1 drop in the mean do indicate very favorably in favor of the New Formula.

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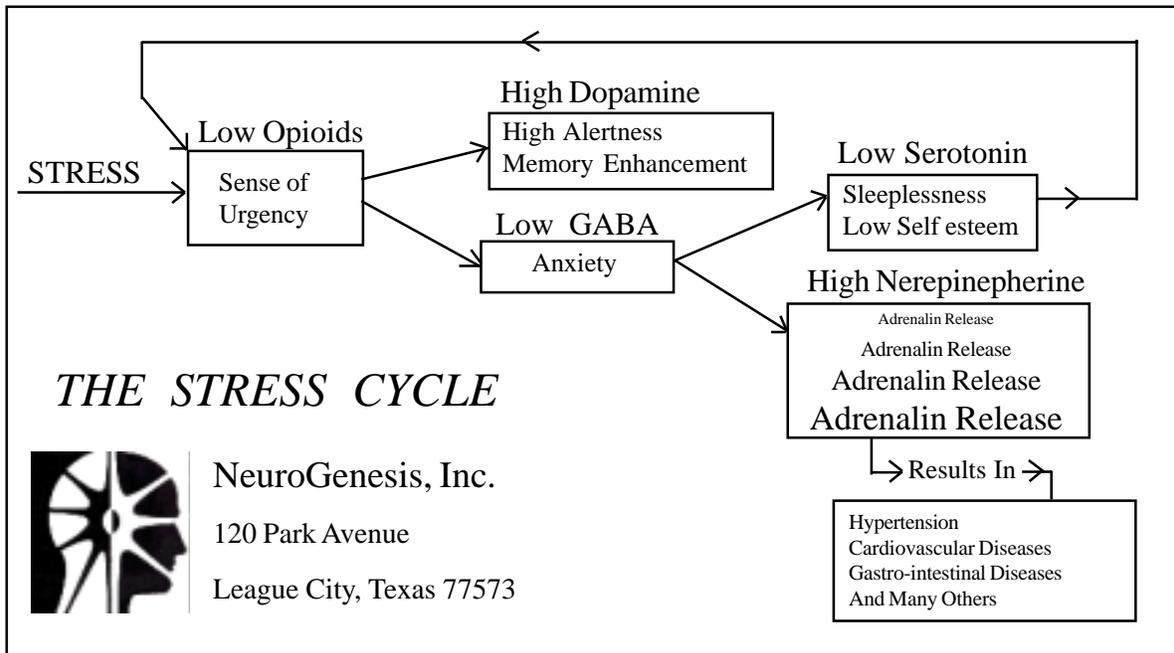


Figure 1

Notes:

