Neurodynamics of Relapse Prevention: A Neuronutrient Approach to Outpatient DUI Offenders

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Abstract — The central nervous system rewarding properties of ethanol, cocaine, and heroin may activate a common catecholaminergic reward system in the mesolimbic circuitry of the brain. Driving-under-the-influence (DUI) offenders with either alcohol- or cocaine-related problems were studied. The neuronutrients SAAVE™ and Tropamine™ significantly reduced relapse rates and enhanced recovery in these DUI outpatient offenders over a 10-week period. Follow-up on both the SAAVE and Tropamine groups after 10 months revealed a 73% and a 53% overall recovery rate, respectively. These clinical results favor the use of these neuronutrients as adjuncts to psychological therapeutic modalities.

Keywords — alcohol, cocaine, DUI, neuropharmacology, SAAVE, Tropamine

During the past decade, considerable attention has been devoted to the investigation of the neurochemical and neuroanatomical systems that underlie chemical dependency. A review of the literature indicates that research on the neuropharmacological basis of dependence on alcohol, opioids, and cocaine points to the involvement of common biochemical mechanisms (Blum, Briggs & Trachtenberg 1989; Wise & Bozarth 1984). It appears that a limbic-accumbens-pallidal circuit is the critical substrate for the expression of drug reward (Koob & Bloom 1988). However, while each drug of abuse appears to act on this circuit at a different anatomical locus, the end result is the same: the release of dopamine, the primary chemical messenger of reward, at such reward sites as the nucleus accumbens and the hippocampus (Stein & Belluzzi 1986).

Alcohol activates the norepinephrine fibers of the mesolimbic circuitry through a cascade of events, including the interaction of serotonin, endogenous opioids, and dopamine (Blum 1989). In a more direct fashion, through the subsequent formation of the neuroamine condensation products tetrahydroisoquinolines (TIQs), alcohol may either interact with opioid receptors or directly with dopaminergic receptors to stimulate mesolimbic dopaminergic systems (Russell, Lanin & Taljaard 1988; Lucchi et al. 1982). Opioids are believed to interact with the reward circuits through opioid receptor-mediated activation of the mesolimbic dopamine systems, possibly at its origin in the ventral midbrain (Vaccarino, Bloom & Koob 1985). As an indirect agonist at catecholamine synapses, cocaine is believed to mediate reward at terminal regions of the mesolimbic dopaminergic systems, such as the nucleus accumbens and prefrontal cortex as well as CA_1 hippocampal cells (Stein & Belluzzi 1987; Dackis & Gold 1985).

A model describing the complex neuropharmacological and neuroanatomical substrates of the brain reward mechanisms, termed "the neuromodulator reward cascade," was recently proposed (Blum 1989; Blum, Briggs & Trachtenberg 1989). This model (see Figure 1) provides a comprehensible synthesis for understanding the numerous interactions required for achievement of normal reward and reinforcement. Neurochemical deficits occurring in this cascade, as a result of the abuse of psychoactive drugs, are thought to lead to uncontrollable craving behavior in both animals and humans (Blum & Kozlowski In press; Blum

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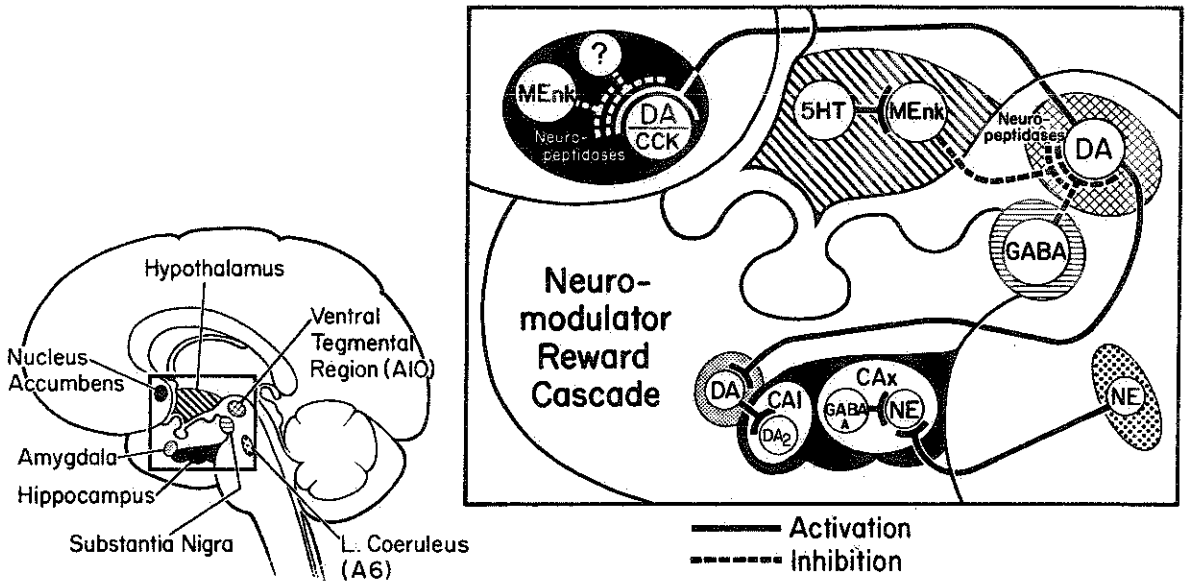

Figure 1. Serotonin (5HT) neurons in the hypothalamus project to met-enkephalin (MEnk) neurons, which inhibit mesencephalic projections of β-aminobutyric acid (GABA) neurons. These neurons in turn inhibit dopamine (DA) neurons, which project both rostrally to the nucleus accumbens and laterally to the DA neurons of the amygdala. The DA neurons of the amygdala project to the CA_2 area of the hippocampus. Norepinephrine (NE) neurons of the locus coeruleus (A6) also project to areas of the hippocampus (CA_x=several different areas) that also contain NE. $GABA_A$ neurons, projecting within the hippocampus, go to a variety of NE-containing CA_x sites. The neuropeptides regulate opioid peptides that affect subsequent activation of DA in the nucleus accumbens. It is proposed that MEnk inhibits an unknown inhibitory interneuron that, in turn, induces the corelease of DA and CCK_8 (Blum & Kozlowski In press).

TABLE I
OUTPATIENT DATA

	Age (Years)	Gender (M)	(F)	Race*		Drug Use (Years)	Drug Dependence (Years)	Family History** (Years)	
Alcohol Abusers									
SAAVE (n=15)	34.3	10	5	13 1 1	W H B	15.3	12.2	10+	DD
No SAAVE (n=15)	32.6	13	2	12 1 2	W H B	14.3	12.1	8+	DD
Cocaine Abusers									
Tropamine (n=15)	33.6	12	3	12 1 1 1	W H B A	5.5	3.8	10+	DD
No Tropamine (n=15)	34.6	13	2	13 1 1	W H B	6.1	4.1	10+	DD

*W=White; H=Hispanic; B=Black; A=Asian.
**DD=Drug dependence.

1989; Blum, Briggs & Trachtenberg 1989; Wise & Bozarth 1987).

There are numerous ways to alter the action of the reward cascade by pharmacological modification of neurotransmitter action: (1) dopaminergic agonists, such as bromocriptine (Tennant & Sagherian 1987); (2) mixed opioid agonists-antagonists, such as buprenorphine (Mello et al. 1989); (3) opioid antagonists, such as naltrexone (Volpicelli, Davis & Olgin 1986); (4) serotonergic reuptake inhibitors, such as Citalopram (Gill & Amit 1987; Naranjo, Sellers & Lawrin 1986); (5) catecholaminergic reuptake inhibitors, such as tricyclic antidepressants (Gawin & Kleber 1984; Chiolo & Antelman 1980); and (6) antianxiety agents with complex neurochemical action, such as buspirone (Collins & Myers 1987). Each of these drugs enhances neurotransmitter availability by acting at pre- or postsynaptic receptor sites or via reuptake mechanisms.

An alternate method to enhance neurotransmitter availability uses the principle of amino acid loading to naturally augment neurotransmitter synthesis and release (Hernandez & Hoevel 1988; Wurtman, Hefti & Melamed 1981). Certain amino acids have been reported to reduce craving behavior in rodents by virtue of their ability to inhibit opioid peptide-degrading enzymes (Blum et al. 1987).

Focusing on the approach of amino acid precursor loading and amino-acid-based enkephalinase inhibition, Blum and colleagues sought a nontoxic approach to restore brain neurotransmitter supply in patients recovering from the abuse of psychoactive drugs. The considerations that underlie this approach of using natural food-based materials are as follows: precursor amino acids increase both synthesis and release of neurotransmitters; specific neurotransmitters can be restored; responses to increased precursor availability are self-limited; excessive amino acid supply is metabolized; the compounds are nontoxic; and no known dependence occurs (Blum & Trachtenberg 1988).

In consideration of the different neurotransmitters involved in response to alcohol, opioids and cocaine, several distinct amino acid supplement approaches were devised. Two such amino acid supplements have been evaluated in open as well as double-blind, placebo-controlled inpatient clinical studies (Blum, Briggs & Trachtenberg 1989; Blum et al. 1988a, 1988b; Blum, Trachtenberg & Ramsey 1988; Blum et al. 1987). These studies, which have been conducted in inpatient settings, indicate (1) a reduction in the rate at which patients leave the program prematurely against medical advice (AMA), (2) reduced stress, and (3) more rapid and more complete participation in the therapy program.

In observations in an outpatient setting, Horne (1988) reported that the administration of these supplements improved client retention during the withdrawal and early recovery phases of treatment. However, there have been no systematic studies focusing on the long-term effects of these neuronutrient supplements in the recovery process and relapse prevention of outpatients. The purpose of the present study is to evaluate, over a period of one year, the utility of neurotransmitter precursor loading and enkephalinase inhibition with amino acid supplements in facilitating adjustment to a detoxified alcohol- and/or cocaine-free lifestyle in a self-selected outpatient population of persons convicted of driving under the influence (DUI).

METHODS

Patient Selection

A total of 60 patients were recruited from a population of persons convicted of DUI and were remanded to a DUI treatment program. Each alcohol abuser had been convicted of at least one DUI in the prior seven years, and each cocaine abuser had been convicted of at least two DUIs over a five-year period. These individuals are usually resistant to standard drug dependency treatment. During the educational phase of their DUI program, each person had received approximately two hours of classroom instruction on the neurochemical effects of drug dependency and the importance of neurotransmitter restoration in the recovery process. This information, in conjunction with the continued inability to stop using alcohol or cocaine, provided grounds for their volunteering for the study by enrolling, post-DUI, in the Cambridge Institute Freedom from Dependency Program. Each patient was required to have a physical exam before entering the program.

Demographic Data

An open-trial pilot study was carried out, with 30 alcohol abusers and 30 cocaine abusers. Each patient group was divided into experimental and control samples of 15 persons. The alcohol abusers reported being intoxicated at least two times weekly during the preceding 12 months; the cocaine abusers reported taking a minimum of one gram of cocaine per week over the previous 24 months. For all cocaine abusers, intranasal ingestion was the preferred route of administration. Table I details the demographic characteristics of the four study groups. There were no significant differences in years of use or of dependency for either the alcohol or cocaine groups.

Diagnosis

Each of the 30 alcohol abusers took the Michigan Alcoholism Screening Test, on which a score of 5 or more indicates alcoholism. Every patient scored between 10 and 20, with a mean value of 14. Each of the 30 cocaine abusers took the 800-Cocaine Addiction Screening Test,

on which a score of 10 points designates cocaine addiction. Each of the patients scored between 21 and 38 points, with a mean score of 25 points. The mean value for the alcohol experimental and control groups was 14.07 and 14.20, respectively, which did not differ statistically. Statistical analysis of the two cocaine groups also indicated that their mean scores of 24.80 and 25.70 were comparable.

Treatment

All patients were voluntary referrals who sought additional treatment after they had completed their DUI program. As mentioned above, during the educational phase of their DUI program, each person had received approximately two hours of classroom instruction on the neurochemical effects of drug dependency and the importance of neurotransmitter restoration in the recovery process.

The material presented to the control groups focused on the importance of abstinence, a well-balanced diet, daily supplements of vitamin B complex (50 mg) and vitamin C (300 mg), exercise, and stress management training as the essential elements of neurotransmitter restoration and the alleviation of white-knuckle sobriety. The material presented to the experimental groups reinforced these same components of the recovery process but also included a presentation on neurotransmitter precursor loading and enkephalinase inhibition with amino acid supplements.

The importance of receiving a physical examination and obtaining approval from a physician prior to taking nutritional supplements or embarking on an exercise program was emphasized in all classes. The DUI classroom students were very receptive to the topics of the neurochemical effects on drug dependency and the possibility of neurotransmitter restoration. The patients in this study were so intrigued and motivated by this information that they initiated contact with the instructor after they had completed their DUI program to request therapy that addressed these areas. They began therapy after receiving a physical examination.

Each patient in both the alcohol and cocaine groups was seen twice weekly in individual therapy sessions during the initial 10-week treatment. Follow-up sessions were conducted (for the experimental groups alone) at four-week intervals over an additional 10 months. The program required abstinence from all psychoactive drugs. The use of caffeine and nicotine was not permitted during therapy sessions. All patients were actively encouraged to adopt a nicotine- and caffeine-free lifestyle. All patients were able to reduce and/or eliminate caffeine and nicotine use during the course of their recovery. None of the patients were taking prescription psychoactive drugs.

Elements of the program advocated the following: establishment of sober relationships with people, places, and activities; consumption of a well-balanced diet; daily administration of supplements of vitamin B complex (50 mg) and vitamin C (300 mg); implementation of a prescribed exercise program, including progressive relaxation, mind clearing, deep breathing, and visualization exercises; development of spiritual growth; and regular attendance at 12-Step self-help meetings. In addition to this standard program, the experimental alcoholics received daily supplements of SAAVE™ (6 capsules), while the experimental cocaine addicts received daily supplements of Tropamine™ (6 capsules).

Measurements and Monitoring

Every patient in each group completed a daily inventory that consisted of three sections: section A measured the extent of stress, depression, irritability, paranoia, anger, anxiety, and drug craving; section B considered subjective feelings of energy, self-confidence in the ability to abstain from drugs, and feeling of well-being; and section C asked for compliance with components of the program, such as Did you take your vitamin supplements today? Descriptions in sections A and B used a five-point scale, while section C could be answered with a yes or no.

Answers to the questions in the self-report were rated in two ways: (1) Building up to relapse (BUR) — decreases in feelings of stress, depression, irritability, paranoia, anxiety, and drug craving; and (2) Recovery scores (RS) — improvements in energy, self-confidence, and feelings of well-being. A careful record was also made of continued participation in the program.

Relapse Criteria

For the first 10 weeks, relapse was defined as the use of any psychoactive drug. After the first 10 weeks, three degrees of relapse severity were recognized. Relapse A was defined as an isolated episode involving very little drug consumption (i.e., two drinks for alcoholics or less than 0.25 g for cocaine addicts), and the patient was able to stop drug use and remained open to reviewing the precipitating variables and taking corrective action. Relapse B was defined as more than one Relapse A incident but the patient remained open about the problem, demonstrated a strong motivation to explore the precipitating factors, and engaged in corrective actions. Relapse C was defined as the patient dropping out of therapy due to relapse, the apparent loss of motivation to continue with the recovery process or making no effort to reestablish contact.

Statistics

All time-dependent processes were analyzed using repeated-measure ANOVA. The survival curve data were assessed by the Kaplan-Meier estimate for survival function, and statistical analysis by the Mantel-Cox, Breslow test between groups (Dixon 1988).

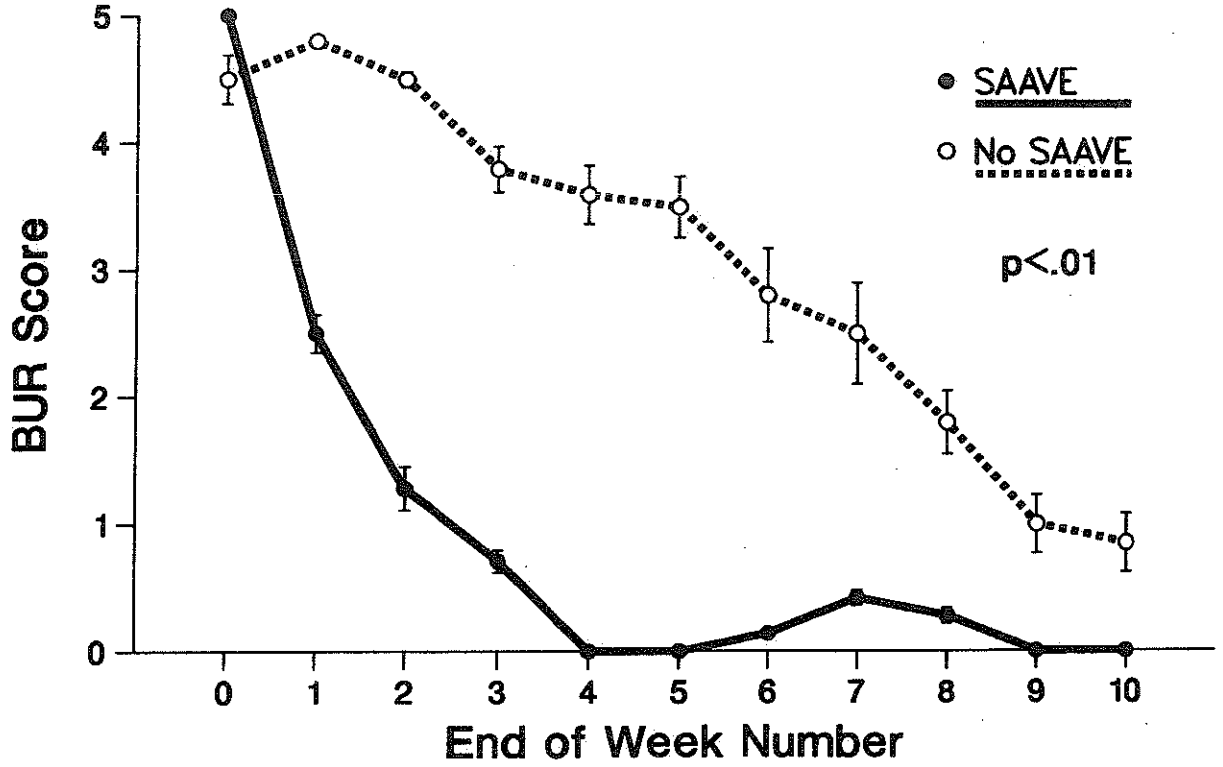

Figure 2. Graph represents a comparison of BUR scores between two groups of outpatient alcoholics, with or without SAAVE. BUR scores represent a daily average of variables, including stress, depression, irritability, paranoia, anger, and drug craving. A total of 30 patients (divided into 15 patients per group) was evaluated for a 10-week period. The BUR score for the SAAVE group was significantly less ($p<.01$) than that for the no-SAAVE group.

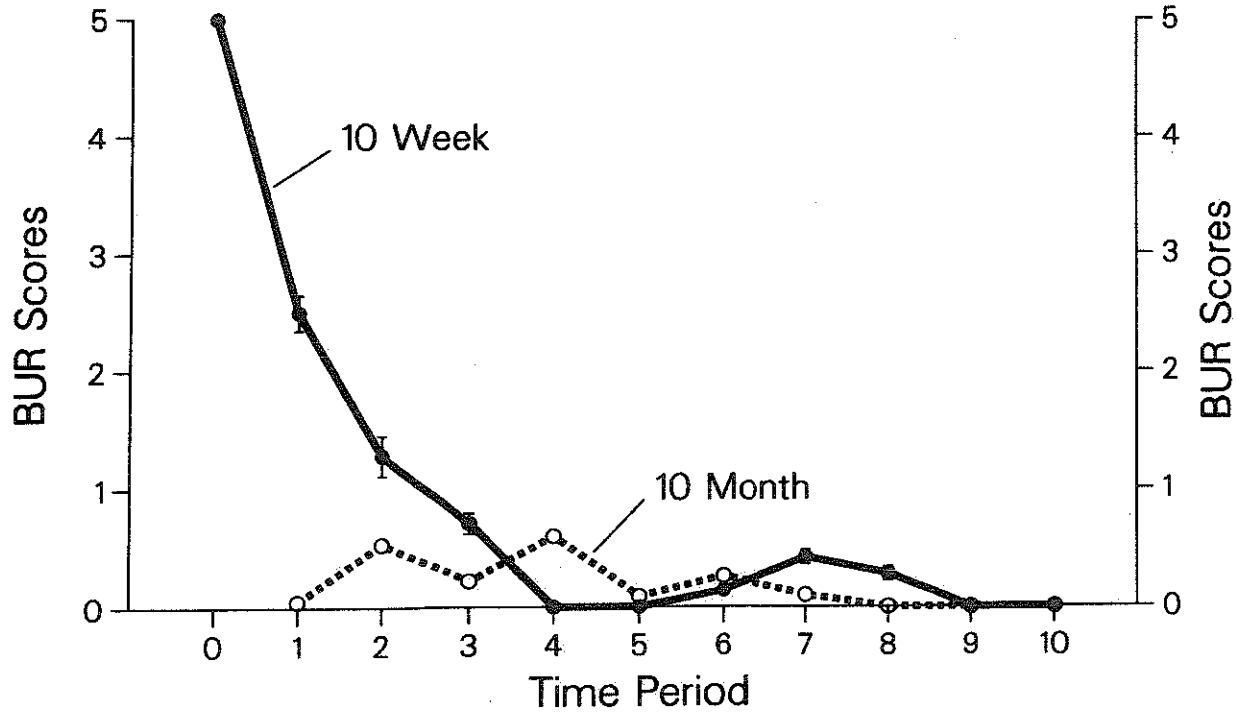

Figure 3. Comparison of BUR scores between 10-week and 10-month follow-ups of outpatient alcoholics receiving SAAVE. Maximal improvement was achieved by week four and continued for an additional 10 months.

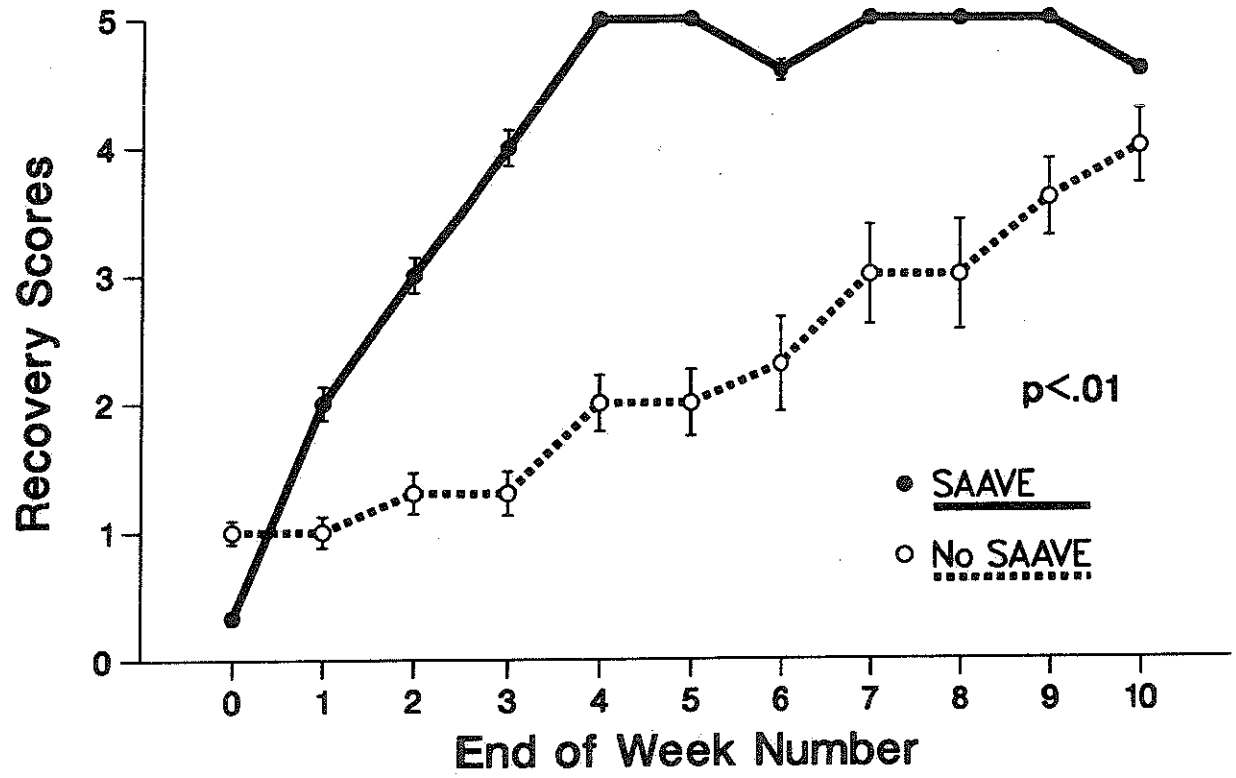

Figure 4. Graph illustrates a comparison of RS between two groups of outpatient alcoholics, with or without SAAVE. RS represent a daily average of variables, including energy, self-confidence, and feelings of well-being. A total of 30 patients (divided into 15 patients per group) was evaluated for a 10-week period. The RS for the SAAVE group was significantly greater ($p<.01$) than that for the no-SAAVE group.

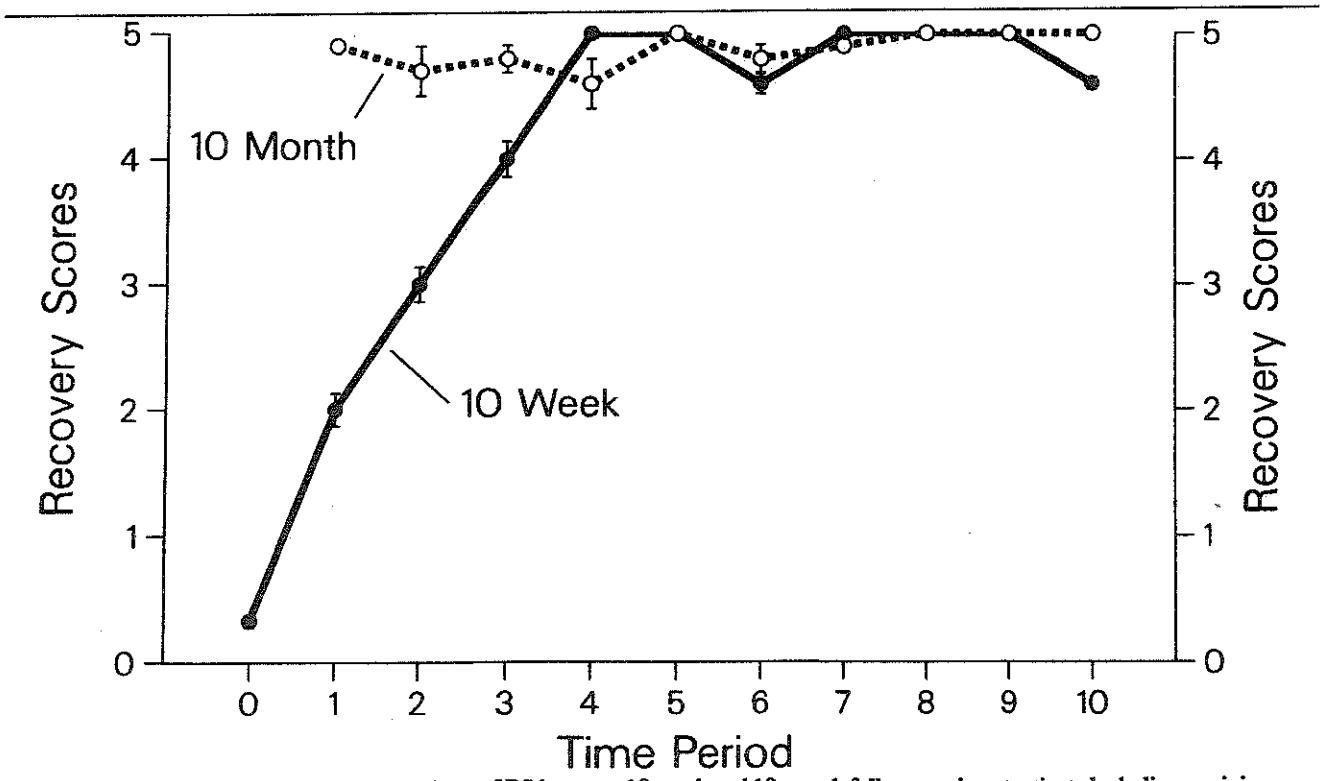

Figure 5. Graph illustrates a comparison of RS between 10-week and 10-month follow-ups in outpatient alcoholics receiving SAAVE. Maximal improvement was achieved by week four and continued for an additional 10 months.

RESULTS

Alcoholics

Figure 2 represents a comparison of BUR scores for the first 10-week period between the two groups of outpatient alcoholics, with or without the amino acid supplement SAAVE. BUR scores represent a daily average of the following variables: stress, depression, irritability, paranoia, anger, anxiety, and drug craving. Beginning at week one and continuing through week 10 there was a statistically significant difference between the two groups ($p<.01$). Continuing follow-up of the BUR for the experimental group showed that maximal improvement was achieved by week four and continued for an additional 10 months (see Figure 3).

The RS (see Figure 4) complement the BUR scores noted above, namely beginning week one and continuing for the entire 10-week period: the experimental group (receiving SAAVE) showed more dramatic and statistically different ($p<.01$) recovery, as assessed by energy, self-confidence, and feelings of well-being. As above, maximal improvement was achieved at week four (see Figure 5) and continued unchanged for the next 10 months.

Relapse rate comparison between the two groups of outpatient alcoholics, with or without amino acid supplements (see Figure 6), indicates a highly significant difference ($p<.001$). At the end of 10 weeks, only 13% of the patients receiving SAAVE dropped out. In contrast, 53% of the no-SAAVE patients were no longer participating in the study. The progressive relapse rates are shown in Figure 7. At the end of 10 weeks, 13 of the original 15 patients receiving SAAVE remained. Over the next 10 months, nine patients remained abstinent, two had type A relapses, one relapsed and returned to drinking (type C), and one left the program (type C). The relapse rate increased by only 7.7% (i.e., 84.6% of those continuing in treatment were still in recovery). Thus, at the end of 12.5 months, 11 of the original 15 patients were in recovery. This yields an overall recovery rate of 73%.

Cocaine Addicts

The BUR scores for cocaine addicts for the first 10 weeks are shown in Figure 8. For the entire period, beginning at week one, there was a statistically significant difference ($p<.027$) between the group that received Tropamine and the one that did not. This represents a dramatic decrease in stress, depression, irritability, paranoia, anger, anxiety, and drug craving. Continued follow-up of the experimental patients for an additional 10 months showed that the patients had maximally improved at week four, although there were slight increases in relapse measures at months two and four (see Figure 9).

Over the same 10-week period, the RS (see Figure 10) were also significantly better for the experimental than the control group ($p<.05$). Again, dramatic improvement in energy, self-confidence, and feelings of well-being were already evident at week one. Maximal RS were seen at week four and remained unchanged for the next 10 months (see Figure 11).

At the end of 10 weeks, 87% of the control group had left the program, while only 20% of the experimental group had dropped out (see Figure 12). This difference is significant at the $p<.001$ level. Figure 13 illustrates the progressive dropout rate, which is significant at the $p<.001$ level.

At the end of 10 weeks, 12 patients remained in the experimental group. During the following 10 months, seven patients remained abstinent, one had a type A relapse, and four had type C relapses. Thus, of the continuing group, almost 67% remained in recovery. Overall, eight of the original patients (i.e., 53%) remained cocaine-free.

Figure 14 illustrates a comparison of the percentage of patients remaining in the program between outpatient alcoholics, with or without SAAVE, and cocaine addicts, with or without Tropamine. A total of 60 patients (divided into 15 patients per group) was evaluated for a 10-week period. SAAVE patients signicantly remained in the program to a much greater percent ($p<.02$) than no-SAAVE alcoholics. Tropamine patients significantly remained in the program to a much greater percent ($p<.001$) than no-Tropamine cocaine addicts.

DISCUSSION

As patients proceed through recovery they experience both negative and positive feelings. Negative feelings are often characterized as anxiety, depression, anger, irritability and paranoia, all of which promote drug craving as a perceived solution. These feelings have been assayed and grouped under the heading BUR. Gorski and Miller (1986) and Marlatt (1978) have commented on the progressive stages that lead to relapse. These negative emotions and the attendant reinforcing behaviors are central to their concept.

Both the alcoholics and cocaine addicts in the experimental groups exhibited a dramatic decrease in such feelings, as compared with their control counterparts. The BUR scores of the experimental groups attained minimal values after only four weeks in the program. In contrast, the control groups did not achieve comparably low values by 10 weeks. Thus, individuals in the control groups remained significantly more at risk of relapse for a time period exceeding 2.5 times longer than that of the experimental subjects.

The converse of the BUR is the RS, a measure of positive, self-enhancing feelings. As with the BUR, the RS leveled off asymptotically for the experimental patients at four weeks, while it improved far more slowly for the

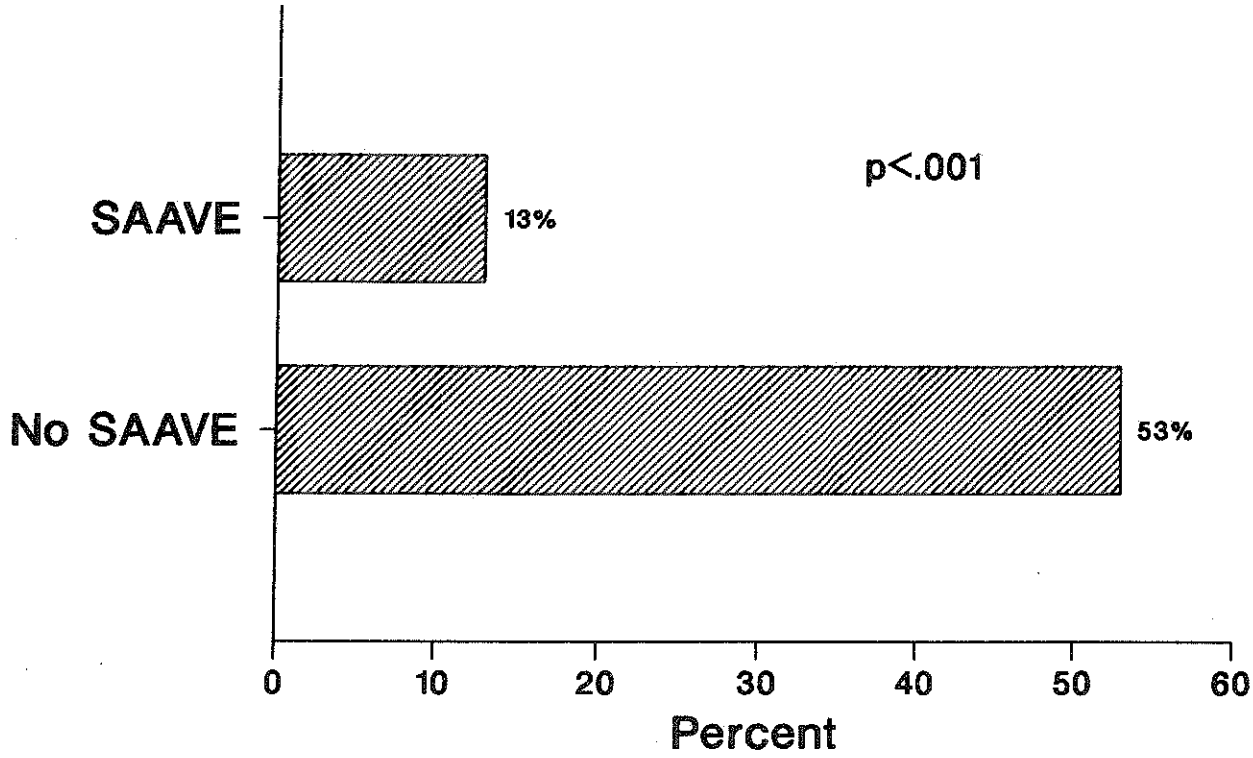

Figure 6. Relapse rate comparison between two groups of outpatient alcoholics, with or without SAAVE. Individuals who dropped out of the program were considered to be in relapse. A total of 30 patients (divided into 15 patients per group) was evaluated for a 10-week period. The relapse rate for the SAAVE group was only 13%, whereas without SAAVE the relapse rate was 53% ($p<.001$).

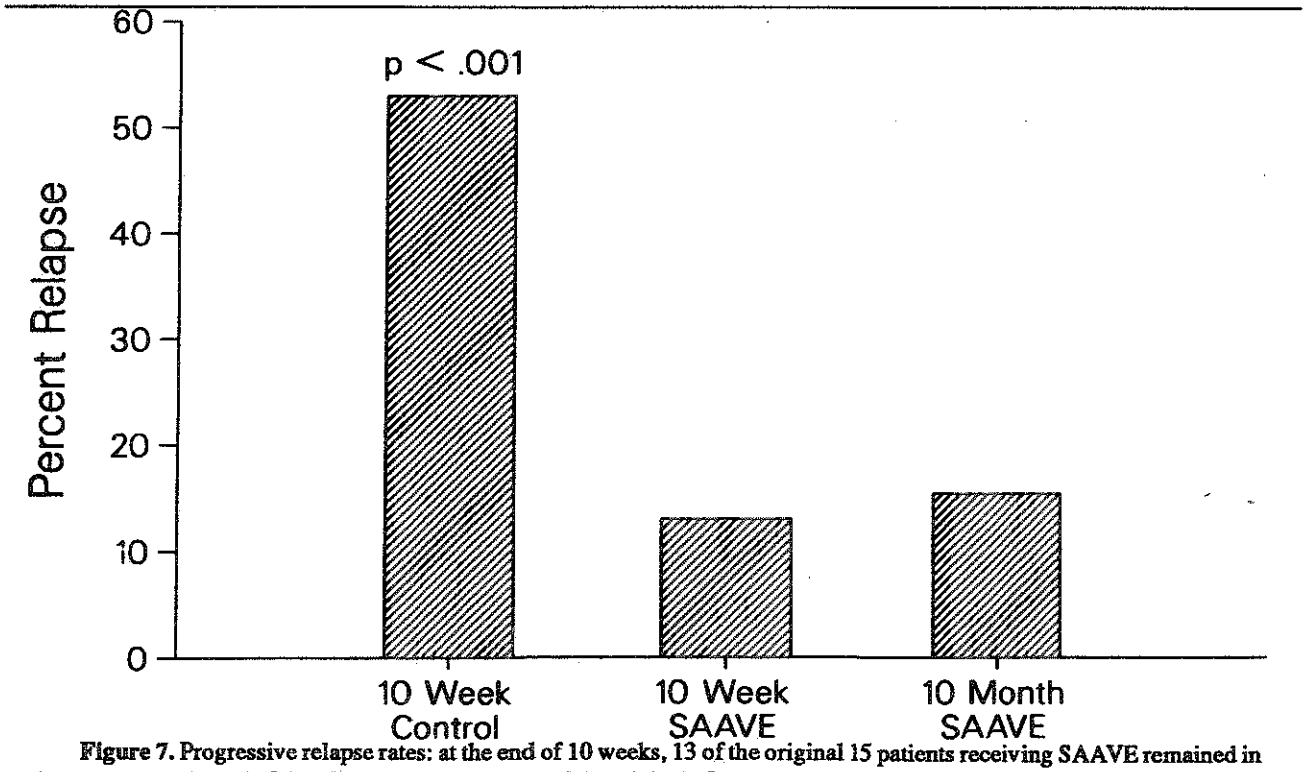

Figure 7. Progressive relapse rates: at the end of 10 weeks, 13 of the original 15 patients receiving SAAVE remained in the program; at the end of the 10-month follow-up, 11 of the original 15 patients were in recovery. This yields an overall recovery rate of 73%.

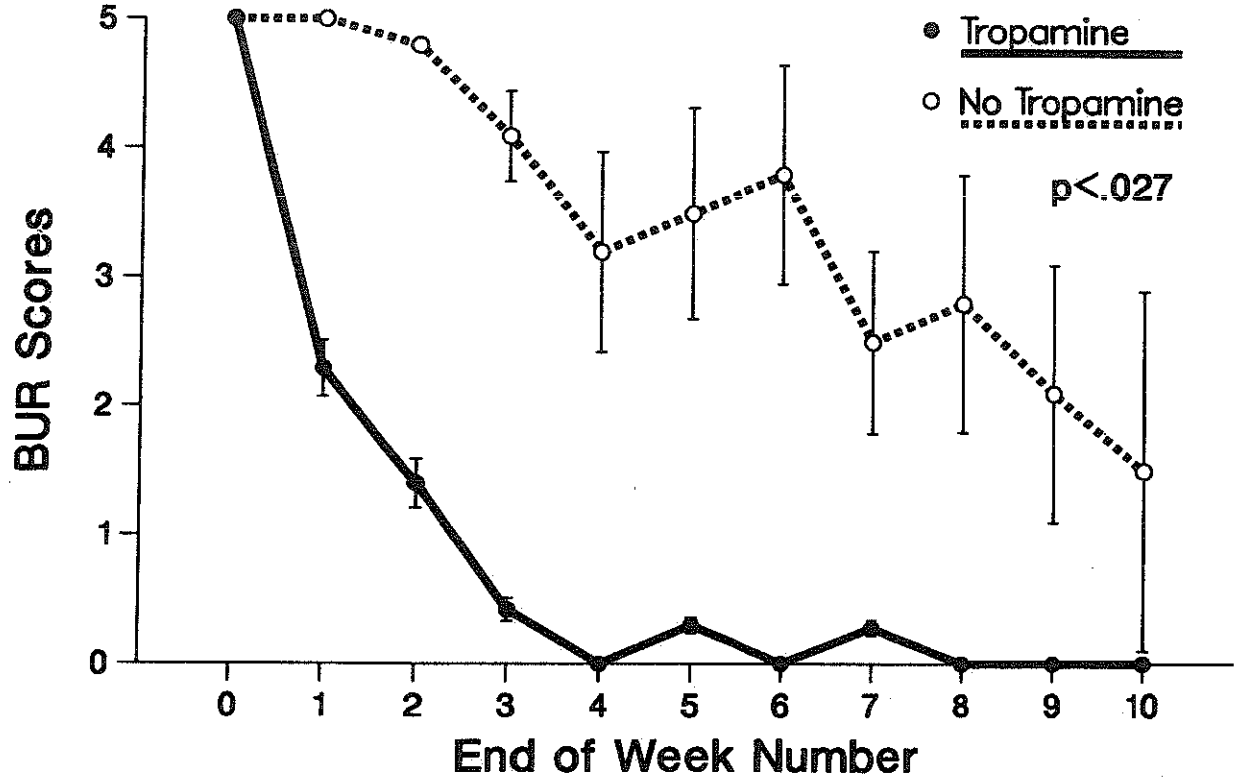

Figure 8. Graph illustrates a comparison of BUR scores between two groups of outpatient cocaine addicts, with or without Tropamine. BUR scores represent a daily average of variables, including stress, depression, irritability, paranoia, anger, and drug craving. A total of 30 patients (divided into 15 patients per group) was evaluated for a 10-week period. The BUR score for the Tropamine group was significantly less ($p<.027$) than that for the no-Tropamine group.

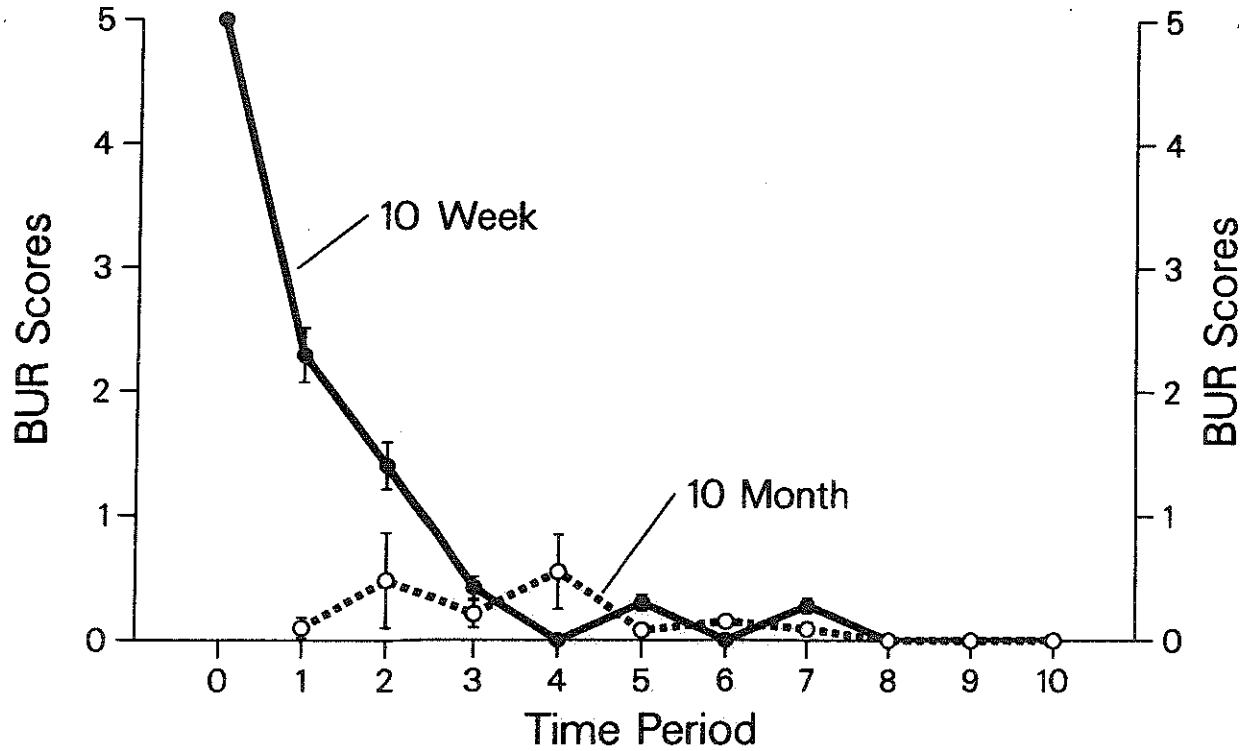

Figure 9. Graph illustrates a comparison of BUR scores between 10-week and 10-month follow-ups of outpatient cocaine addicts receiving Tropamine. Follow-up of this group showed that the patients had maximally improved at week four, with slight increases at months two and four.

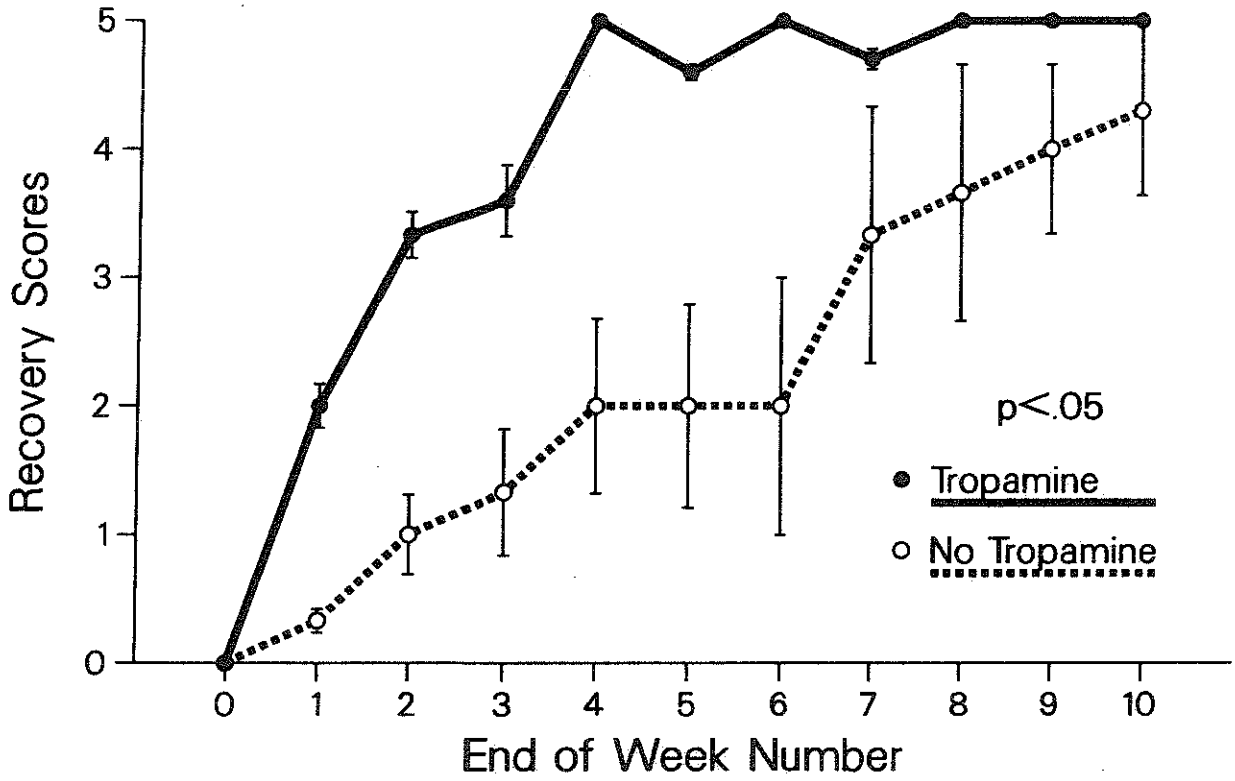

Figure 10. Graph illustrates a comparison of RS between two groups of outpatient cocaine addicts, with or without Tropamine. RS represent a daily average of variables, including energy, self-confidence, and feelings of well-being. A total of 30 patients (divided into 15 patients per group) was evaluated for a 10-week period. The RS for the Tropamine group was significantly greater ($p<.05$) than that for the no-Tropamine group.

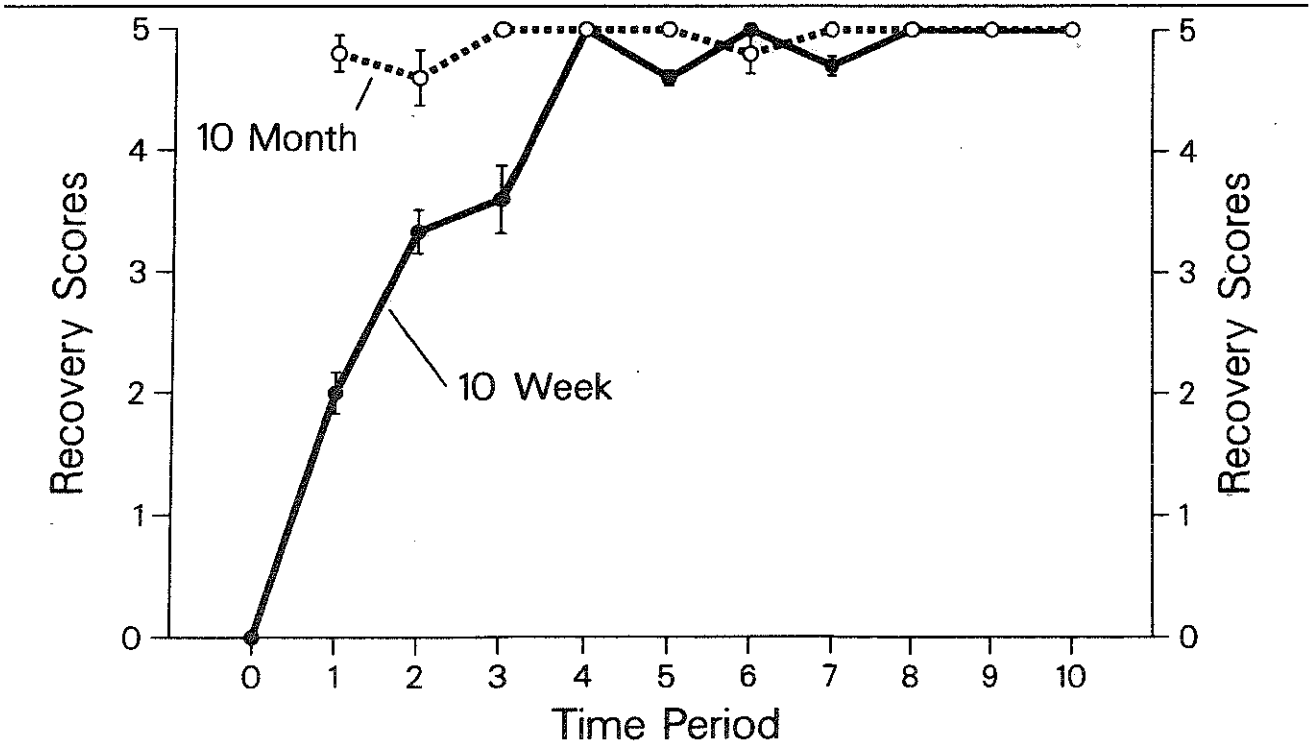

Figure 11. Comparison of RS between 10-week and 10-month follow-ups of outpatient cocaine addicts receiving Tropamine. Maximal RS are seen at week four and remained unchanged for the next 10 months.

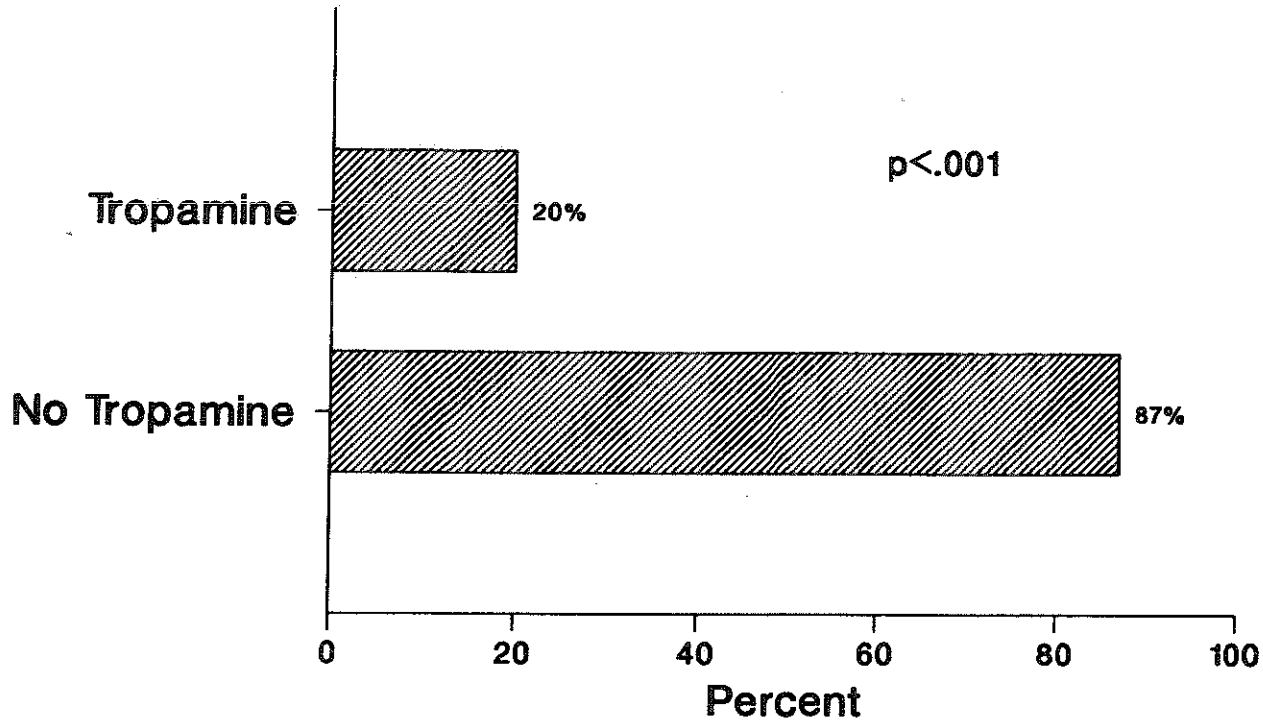

Figure 12. Relapse rate comparison between two groups of outpatient cocaine addicts, with or without Tropamine. Individuals who dropped out of the program were considered to be in relapse. A total of 30 patients (divided into 15 patients per group) was evaluated for a 10-week period. The relapse rate for the Tropamine group was only 20%, whereas without Tropamine the relapse rate was 87% ($p<.001$).

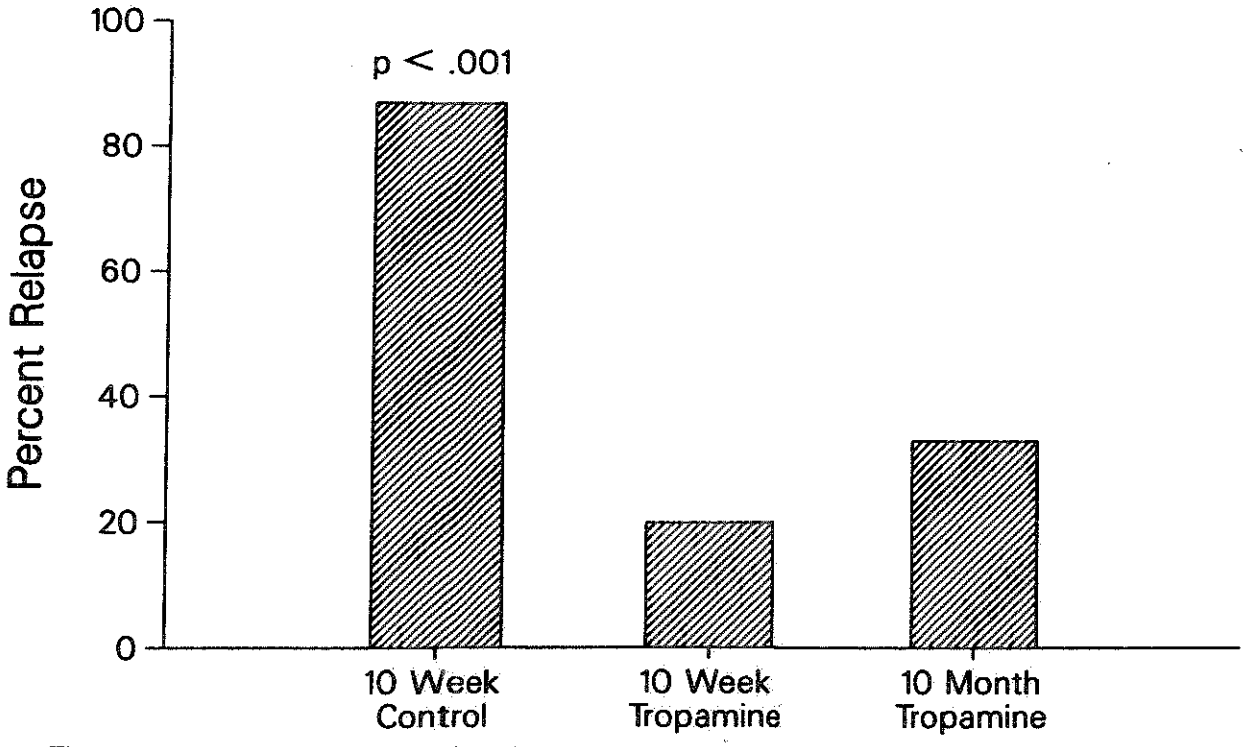

Figure 13. Progressive relapse rates: at the end of 10 weeks, 12 of the original 15 patients receiving Tropamine remained in the program (20% relapse rate); at the end of the 10-month follow-up, eight of the continuing group remained in recovery (33% relapse rate). The relapse rate for the control group, the 15 patients who did not receive Tropamine, was 87% after the first 10 weeks.

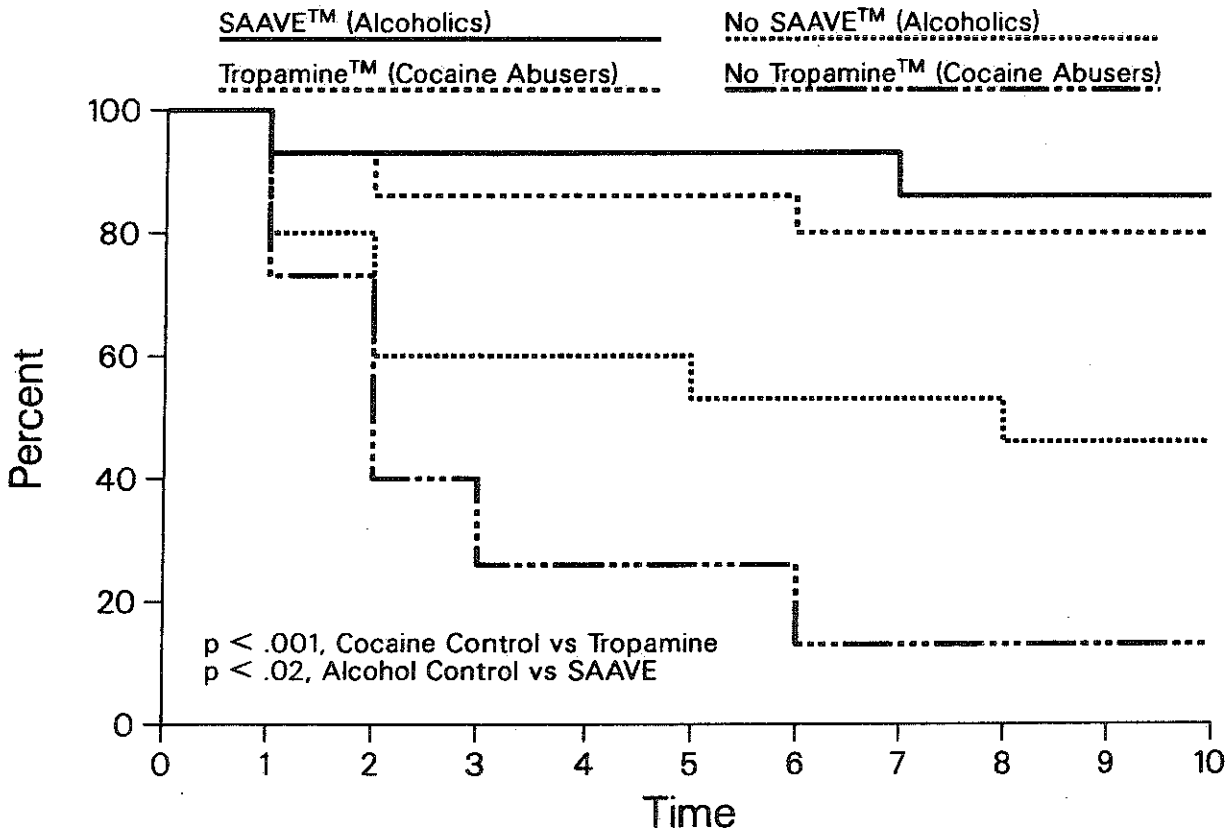

Figure 14. Graph illustrates a comparison of the percent of patients remaining in the program between outpatient alcoholics, with or without SAAVE, and cocaine addicts, with or without Tropamine.

TABLE II
TREATMENT OUTCOME PATH OF
CHEMICAL ABUSE TREATMENT OUTCOME REGISTRIES (CATOR)*

12-Step/Aftercare Program	One Year Sober (%)	(n)	Two Years Corrected (87%) (%)	(n)
Regular attendee	83	72	80	70
Occasional attendee	59	51	57	50
Nonattendee	59	51	48	42

*Modified from Harrison, P.A. & Hoffman, N.G. 1988. *CATOR Report: Adult Outpatient Treatment Perspective on Admission and Outcome*. St. Paul: St. Paul Ramsey Clinic.

control patients. Even at 10 weeks, the RS had not attained the same level as the control subjects. The rate at which patients dropped out of the program mirrors the rate of improvement seen in the BUR and RS values for these two groups of patients. Similarly, the number and type of relapse episodes exhibited by the patients in the experimental and control groups during the first 10 weeks are consistent with the patterns noted above.

The present study demonstrates that retention for the alcoholics at the end of 10 weeks was 87% for the experimental subjects but only 47% of the control patients. For the cocaine addicts, these numbers are 80% and 13%, respectively. These are dramatic differences. The recovery dropout pattern seen over the first 10 weeks continues in like manner over the next 10 months. Thus, over the succeeding 10 months, the experimental group of alcoholics

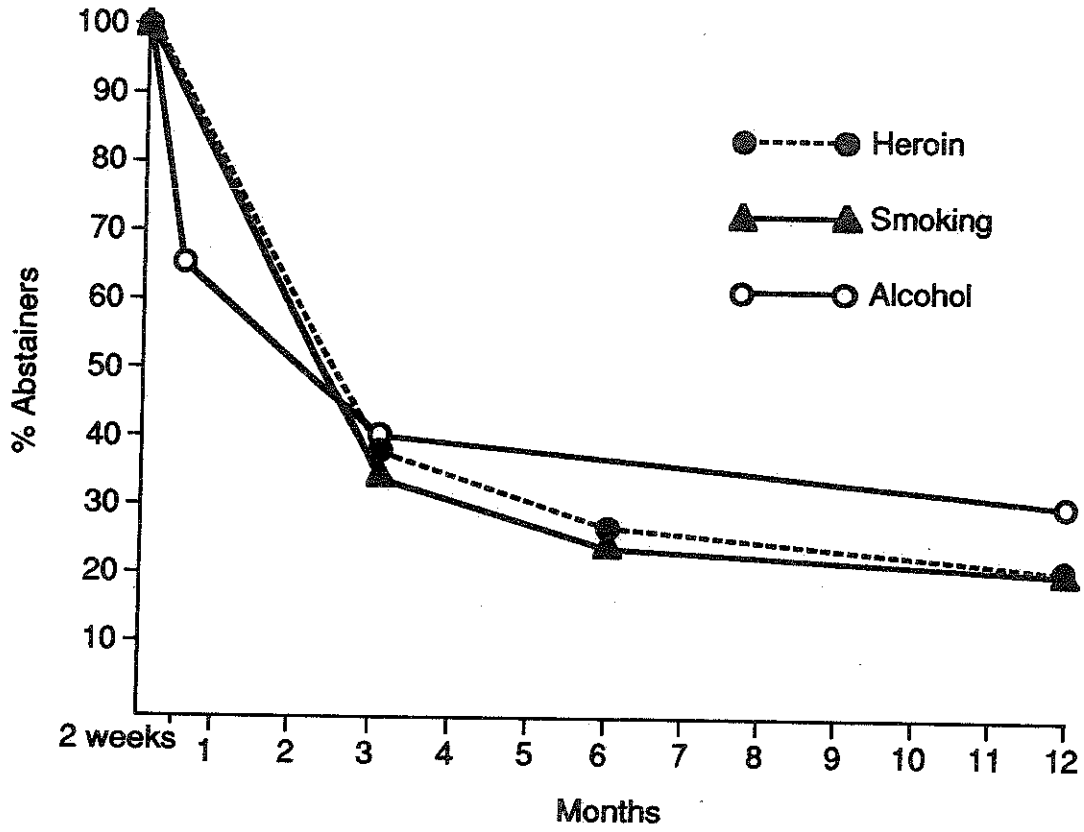

Figure 15. Relapse curves for individuals treated for heroin, smoking, and alcohol addiction. Reprinted with permission from: Hunt, W.A.; Barnett, L.W. & Branch, L.G. 1971. Relapse rates in addiction. In: Marlatt, G.A. & Gordon, J.R. (Eds.) 1985. *Relapse Prevention: Maintenance Strategies in the Treatment of Addictive Behaviors*, p. 34. New York: Guilford.

suffered only a further 7.7% patient loss. Similarly, after the first 10 weeks, the experimental group of cocaine patients lost an additional 14% over the next 10 months. Furthermore, the overall one-year recovery values of 73% for the alcoholics using SAAVE and 53% for the cocaine addicts using Tropamine in this outpatient setting compare favorably with the more intense intervention seen with inpatient treatment.

Hoffman, Harrison and Belille (1983) found that following a substantial initial dropout (perhaps 30%-50%), 73% of alcoholics who had attended Alcoholics Anonymous (AA) weekly for at least six months were still sober. In contrast, only 33% of nonattendees remained sober. These data indicate the necessity of ongoing 12-Step program attendance for continued sobriety. In contrast, the experimental subjects in the present study had comparably high relapse-free rates independent of AA attendance.

Due to the high dropout rate, it was not possible to follow up all of the control subjects for the entire 12.5 months; thus, data are presented only for the experimental subjects. While the present authors believe that the recovery rates for the control subjects are dramatically lower than those on the active product, extrapolation to undocumented areas is not warranted.

Table II presents data derived from a report by Harrison and Hoffman (1988) on adult outpatient treatment outcome. The group characteristics of this study included (1) persons treated in outpatient clinics; (2) persons who were not grouped according to type or drug used; (3) self-report used to answer direct questions; and (4) sample verification by significant others, with a reliability of about 87% for self-reports.

It should be noted that the subjects in the present study were resistant to the 12-Step program, in spite of continual encouragement from the staff. On this basis, after correction of 87% reliability, the outcome data of recovery of 53% to 73% is quite favorable and suggests that neuronutrient supplementation assists in the recovery process.

Further support for these findings can be derived from numerous studies on outcome data or outpatients that have been conducted over the past three decades. Figure 15 illustrates relapse curves for individuals treated for heroin, nicotine, and alcohol addiction. An average 12-month relapse percentage of 67% was obtained by Hunt, Barnett

and Branch (1971). Additionally, Bill (1965) found that 34.6% of AA members were abstinent at the end of one year. Ditman (1967) supported Bill's finding when he reported that AA members have a cure rate of 30% to 35%. Baekeland, Lundwall and Kissin (1975) reported that outpatient dropout rates for alcoholism treatment tend to be from 52% to 75% by the fourth session. Finally, Milkman and Sunderwirth (1987) stated that "approximately 75% of all those who attempt abstinence from alcohol reverse their habits between three and six months after beginning a program for recovery." The present findings of facilitated recovery, with both SAAVE for the alcoholics and Tropamine for the cocaine addicts, suggest that these neuronutrients — through possible chemical restoration — are important adjuncts in the treatment of drug dependency.

A limbic-accumbens-pallidal circuit appears to be a critical substrate for the expression of the drug reward, while defects or imbalance of the neurotransmitter-receptor interactions at the critical site induce uncontrollable drug-seeking behavior (Koob & Goeders 1988). Given the overall diversity of the drugs abused by humans (e.g., stimulants, opioids, ethanol, sedatives, hallucinogens, solvents), it is not likely that a single neurochemical system can account for all aspects of drug abuse and the psychopathology of addiction (Blum, Briggs & Trachtenberg 1989). Rather, a consensus of the literature suggests that drugs gain access at various levels to a complex but integrated circuit that may provide the endogenous substrate of reward. Persistent modulation of this circuit by psychoactive drugs and reinforcing behaviors may lead to addictive behavior.

The present authors believe that the final common pathway of reward involves activation of dopamine D_2 receptors in the nucleus accumbens and/or the hippocampus (Blum et al. 1990; Blum 1989; Stein & Belluzzi 1986). This involves both inhibition and excitation of neurotransmitter-receptor signal transduction. Because psychoactive drugs (e.g., cocaine, amphetamines, opioids, ethanol) initially activate dopaminergic pathways, it seems reasonable to speculate that all these substances compensate for one or more malfunctions in this reward circuit, leading to aberrant activity at dopamine D_2 receptor sites. Following long-term abuse of these drugs, there is a down-regulation of dopaminergic functions, leading to drug hunger.

The addictions field is shifting to briefer treatment models within the long-term process of recovery. The initial phase of short-term treatment is the logical time to address the biological aspects of recovery. The focus needs to be on restoring the pleasure-producing, calming, and energizing neurochemicals by establishing a well-balanced diet and taking the appropriate nutritional supplements. As the recovering person begins to experience internal calmness, pleasure, and increased energy, there is more enthusiasm and vitality to invest in the social, psychological, and spiritual dimensions of the recovery process. The success of long-term recovery hinges on the effectiveness of this initial stage of treatment.

It is the present authors' contention that improvement of inpatient treatment of alcoholics, cocaine abusers, and multiple drug abusers can be rapidly attained by utilization of both precursor amino acids (to enhance neurotransmitter activity of such biogenic amines as serotonin, dopamine, norepinephrine, and β-aminobutyric acid) and a carboxypeptidase A inhibitor (to potentially raise enkephalinergic activity). Parameters that have already been tested and have shown improvement include reduced craving; lowered requirement for benzodiazepine-type medications; reduced withdrawal tremors; reduced stress measured by skin conductance level; reduced AMA rate; and increased behavioral, emotional, social, spiritual, and physical scores (Blum et al. 1988a, 1988b; Blum, Trachtenberg & Ramsey 1988).

These studies have been extended to include data on a one-year follow-up study utilizing these neuronutrients with DUI offenders remanded to a drugfree AA-oriented outpatient program. The findings are compatible with an earlier proposal (Blum 1989) that along with solid therapeutic support systems (e.g., psychiatrist, counselors, 12-Step groups) both SAAVE and Tropamine may be useful as an adjunct to therapy when used in outpatient recovery, specifically to assist in reducing relapse. These results further suggest that the neuronutrient approach significantly reduces relapse of drug-dependent outpatients in recovery, when compared to utilization of vitamin B complex and vitamin C without amino acid precursor loading and enkephalinase inhibition. The present authors plan to systematically investigate the long-term benefits of these and other neuronutrient supplements in double-blind placebo-controlled studies in relapse prevention of motivated recovering drug-dependent outpatients involved in 12-Step programs.

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