### **CURRICULUM VITAE:**

### STEPHEN D. REIMERS, P.E.

**EDUCATION:** 

MS and BS, Mechanical Engineering, MIT 1969 (simultaneous)

Professional of Naval Science Award (Academics), 1969

**OTHER TRAINING:** 

US Navy Qualified as Salvage Diving Officer & Saturation Diving Officer Navy Qualified in SCUBA, Hardhat Diving Dress and Mark 10 Closed

Circuit Underwater Breathing Apparatus

Numerous medical meetings regarding clinical hyperbarics

PROFEESSIONAL REGISTRATION: Professional Engineer, Virginia No. 7275

#### **PROFESSIONAL COMMITTEES:**

ASME Committee on Pressure Vessels for Human Occupancy; Member (30+ years) and past Vice Chairman of Main Committee; Chairman (12 years) of Sub-Committee on Piping ANSI Z-135 Committee for Consensus Standards for Commercial Diving; Participated for approx. 3 years as alternate for W. F. Searle, Jr.

NFPA Technical Committee on Hyperbaric and Hypobaric Facilities; Member (>20 years)

UHMS Safety Committee: Member (>20 years) and past Chairman

#### **TEACHING:**

Senior lecturer: Technical Aspects of Hyperbaric Chamber Safety Course, 1997 to present

Senior lecturer: Hyperbaric Chamber Safety Director's Course, 2001 to present

#### **SOCIETIES & ASSOCATIONS:**

Undersea and Hyperbaric Medical Society (member since 1974)
International Congress on Hyperbaric Medicine (life member)
International Hyperbaric Medical Association

American Society of Mechanical Engineers; National Fire Protection Association.

#### **EXPERIENCE SUMMARY:**

Four years as Projects Officer for US Navy Experimental Diving Unit. Performed equipment evaluations on over 12 diving helmets (both air and mixed gas), numerous SCUBA regulators, several closed and semi-closed circuit underwater breathing apparatus, several types of deep diving breathing apparatus and two one-man portable recompression chambers.

33 years experience as President/Owner of Reimers Consultants, Reimers Engineering, Inc., Reimers Systems, Inc., and Hyperbaric Clearinghouse, Inc. Responsible for the design of over \$40,000,000 of currently installed clinical hyperbaric facilities. Typical projects have included:

AE design for the following major hyperbaric oxygen (HBO) therapy facilities:

- 10 place facility at Southwest Texas Methodist Hospital, San Antonio, TX
- 28 place facilities at Wright Patterson Air Force Base, Ohio and Travis Air Force Base, California
- 20 place facility at Portsmouth Naval Hospital, Portsmouth, VA

#### Turnkey construction for:

- 8 place HBO facility, Armed Forces Institute of Pathology, Walter Reed Army Med. Center
- 12 place HBO facility at Medical Center Hospital in Conroe, TX
- Environmental and life safety systems for Hyperbaric Swim Flume, US Olympic Swim Team
- Numerous multiple monoplace hyperbaric facilities
- Containerized 2 place HBO facility including on-board oxygen generation
- 18 place, Segmented, 3 lock, multiplace chamber system for Virginia Mason Medical Center
- Two, 8 place Mobile HBO Chamber Systems, RSI Model 9008E-Tr

#### Numerous other projects including:

- Safety inspections of major hyperbaric oxygen therapy facilities
- Reconstruction and expert witness services for several diving accidents
- Performance testing of breathing apparatus intended for use by miners, firefighters and divers
- Manufacture of over a dozen breathing simulators

**PUBLICATIONS:** Over 50 published test reports and journal articles and 3 textbook chapters

## **HBOT for Brain Injury: History & Safety**



Stephen D. Reimers, PE
President, Reimers Systems, Inc.
Reimers Systems, Inc.
Lorton, VA

## **HBOT** for Brain Injury is NOT New

- Standard treatment for neurologic decompression sickness (DCS) since the 1930s
- Originally thought to be treating ONLY bubbles. Now understood to be treating bubbles AND the endothelial damage created by their passage.
- Substantial history of use in Russia for treating addictions to alcohol, opiates and benzodiazapines.
   Reduces the length of the withdrawal period and in alcohol addictions the long term physiological damage.

# **HBOT for Brain Injury is NOT New**

- At least three centers have been treating stoke patients with good success for 20+ years. Many more such centers are currently operating.
- In the past few years researchers have been able to postulate mechanisms by which the observed clinical gains might be happening. No claims yet of "proof". However, the result from what we have seen, is a "sea-change" in attitudes toward the use of HBOT for neurological applications what the former "naysayers" largely quieted.

## **HBOT** is VERY Safe

- Approx 10,000 patient treatments in the U.S. every day in over 800 centers.
- · Exceptionally low complication rates
  - Rate of aborted treatments = approx. 83/10,000 Tx
  - Rate of interrupted treatments = approx. 27/10,000 Tx
- Due to diving experiences, the hazards are WELL known and readily managed
- One of the lowest malpractice rates of all medical subspecialties
- We know of no serious injury to a patient in the U.S. -- EVER

# Our Proposal

Combine three therapies, each shown separately to be effective:

- 1. Nutritional supplements
- 2. Effective substance detox, when applicable
- 3. HBOT to repair the brain damage/congitive defects that either led to an addition or resulted from it.

### North Dakota Commission on Alternatives to Incarceration

Testimony of Stephen D. Reimers, PE

April 21, 2008

Hyperbaric Oxygen Therapy (HBOT) as a treatment for brain injury is NOT new, but there are significant new developments.

- HBOT to treat neurologic decompression sickness (DCS) since the 1930s. It is accepted worldwide as the standard of care in that situation. What IS new, is the realization, starting around 1990, that neurologic DCS was caused by both bubbles AND the endothelial damage they did on the way through. The implications of that realization are huge. It means that the enormous history of successfully treating neurologic DCS with HBOT does have a significant degree of transferability to general healthcare whereas if all one was doing is treating bubbles there would logically be no such transfer. This realization is only now beginning to be appreciated.
- The Russians have a substantial history of using HBOT to both decrease the duration of withdrawal from alcohol and other addictions and to decrease the severity of the permanent impairments resulting from the addiction. One Russian abstract and the full text of one Russian paper on this topic are in the handouts. However, no-one outside Russia seems to have picked up on the Russian work and its potential implications. This can be partially explained by the highly dismissive attitude by many Western researchers towards the quality of Russian research. The Russian papers I have read would certainly not pass muster for what we call "evidence". However, its also unlikely that they just "made it up".
- Dr. Richard Neubauer (FL) and Dr. David Steenblock (CA) have been treating stroke patients with a high degree of success for over 20 years. Ischemic (blockage type) strokes have origins similar to neurological DCS. In recent years many more clinics specializing in using HBOT to treat stroke and other neurologic disorders have opened. What IS new is that within only the past few years, the researchers have begun to propose plausible mechanisms why the observed clinical gains might be occurring. I have not seen yet any claims of "proof". However, the simple fact that there are now in respected literature plausible explanations of why what the clinicians are seeing could be happening has silenced most of the nay-sayers. I can tell you that within the UHMS of which I have been a member since 1973, there has been a "sea-change" in attitudes in this area within just the past two years.
- There are now 13 indications where HBOT is considered "mainstream medicine" and is being widely used. The most common applications are the healing of

problem wounds in areas of poor perfusion, typically ulcers on diabetic feet and wounds (such as a tooth extraction) in tissue damaged from radiation therapy for cancer.

#### HBO as a medical treatment is VERY safe

- There are well approximately 10,000 patient treatments in the U.S. every day in the close to 800 centers that we know about with an exceptionally low complication rate (rate of aborted treatments = 83/10,000 treatments, rate of temporarily interrupted treatments = 27/10,000 treatments)
- Due to the long use of elevated oxygen levels by the world's diving communities
  for both treating decompression sickness and shortening decompression times, the
  risks associated with elevated oxygen levels, both short term and long term are
  VERY well known.
- HBOT centers enjoy one of the lowest malpractice rates of all medical subspecialties.
- To my knowledge, there has not been a serious injury to a patient from medical HBO therapy in the US, ever.

What we are proposing to do here is to combine the following therapies:

- Nutritional supplements that have been shown to reduce tendencies toward violent behavior
- An effective substance detox program
- HBOT to repair the brain damage/cognitive defects that either led to the addiction or resulted from it, thus reducing the changes of relapse.

[Hyperbaric oxygenation in the treatment of patients with drug addiction, narcotic addiction and alcoholism in the post-intoxication and abstinence periods]

[Article in Russian]

#### Epifanova NM.

Hyperbaric oxygenation was used in the treatment of 340 patients with narcomania, toxicomania, and alcoholism in the post-intoxication and abstinence periods; 223 of these were alcoholics, 68 toxicomaniacs, and 49 opium narcomaniacs. A group of 185 patients administered drug therapy alone were controls. Exposure to hyperbaric oxygenation had a favorable effect on the patient's status during sessions and persisted for some time after them. Patients with different premorbid symptoms and initial status experienced tranquilizing or bioenergizing effects of hyperbaric oxygen. A comparative clinical and psychopathological examination of patients in both groups showed accelerated reduction of psychoneurological and somatovegetative disorders, this bringing about an approximately twofold decrease of treatment duration and preventing the development of complications. The parameters of central hemodynamics normalized and myocardial status improved, which helped prevent the development of cardiovascular decompensation. Such a favorable time course of events appears to be due to the antihypoxic detoxifying and bioenergetic effects of hyperbaric oxygen.

PMID: 7653862 [PubMed - indexed for MEDLINE]

S282 P.5 Addiction

according to both Hamilton and Zung depression scales. Nimodipine also brought about a statistically significant decreasing of the level of state anxiety according to Spielberger test, while nifedipine did not. The only side-effect noted in the groups of patients treated with nimodipine and nifedipine was an insignificant decreasing of blood pressure.

Conclusion: The results of this study testify that calcium channel antagonists are effective in the treatment of affective disorders associated with alcoholism in abstinent alcoholic patients.

## P.5.003 Alcoholism treatment with antidepressant

N. Ivanets. Research Institute on Addictions, Moscow, Russia

The goal of this work was to study the anticraving efficacy of mianserin, in comparison with that of amitryptyline and relanium, in the treatment of alcohol withdrawal and postwithdrawal syndromes. In addition, the influence of mianserin on the biogenic amine neurotransmitter metabolism was studied and the clinico-biological correlations were found. Sixty patients with alcohol dependence syndrome (DSM-IV) were included in the study. 30 patients were given mianserin (60 mg, during 30 days), 15 amitryptyline (50 mg, during 30 days) and 15 - relanium (10 mg, during 7 days). Psychotherapy also was included in the therapeutic program. The catamnestic examination of all patients was made in 3 months. The results have prompted us a conclusion that mianserin has a pronounced anticraving, anxiolytic, antidepressive, hypnotic, sedative, and vegetocorrective action. Positive clinico-biochemical correlations were found. All said above permit us to recommend mianserin as an anticraving drug that may be given alcoholic patients to achieve stable remission and to prevent relapses of the disease.

#### P.5.004 Alcohol abuse and deviant social behaviour

J. Liappas, E. Peppas, V. Pomini, P. Papavasiliou, G.N. Christodoulou. Athens University Medical School, Department of Psychiatry, Eginition Hospital, Greece

Objective: The aim of this study is to investigate the deviant social behaviour in a sample of Greek alcohol abusers.

Material-Method: 127 alcoholics recruited from the specialized drug free outpatient drug addiction clinic at Eginition Hospital, fulfilling the DSM-III-R criteria for alcohol abuse/dependence. The subjects were treated on an inpatient or outpatient basis. Sociodemographic, psychological, behavioural and alcohol using characteristics were assessed by a structured interview.

Results: The mean age of the subjects was  $42.2 \pm 11.9$  years and 86.6% of the users were males. The mean duration of alcohol consumption was  $21.4 \pm 11.7$  years; mean duration of alcohol abuse with coexistent somatic problems was  $10.3 \pm 9.5$  years. 28.3% of the sample reported various types of traffic accidents; 22.8% and 8.7% of the individuals had been arrested and convicted at least once during their lifetime respectively. From a total number of 38 reported arrests, 3.2% were related to drugs, 10.2% to crimes of violence, 3.1% to offenses against property and 13.4% related to other offences (percentages refer to the total sample of alcohol abusers). From the total number of reported convictions (N = 16), 0.6% were related to drugs, 5.5% related to crimes of violence, 0.8% to offences against property and 5.5% to other offences (percentages refer to the total sample of alcohol abusers).

Conclusion: The above findings suggest that the behaviour of alcohol users is associated with an increased likelihood of traffic accidents and crimes of violence too.

## P.5.005 Comparison of criminality between drug and alcohol users: Preliminary report

J. Liappas, E. Peppas, T. Paparrigopoulos, V. Pomini, G.N. Christodoulou. Athens University Medical School, Department of Psychiatry, Eginition Hospital, Greece

Criminality consists a major issue in the field of substance misuse worldwide, urging for concerted measures, carefully planned policies and diverse treatment interventions.

Objective: The aim of the present study was to compare criminality between alcohol and drug abusers.

Material-Method: The sample comprised of 289 drug abusers and 127 alcoholics recruited from the specialized drug free outpatient drug addiction clinic at Eginition Hospital, in Athens-Greece, over a decade (1988–1997). All subjects fulfilled the DSM-III-R criteria for psychoactive drug or alcohol abuse/dependence. Sociodemographic, psychological, and behavioural characteristics, as well as the substance or alcohol abusing pattern were assessed by a structured interview, which also covered numerous criminality issues i.e. number of offences, arrests, convictions, type of crime, legal status and other related topics. For the statistical analysis the x<sup>2</sup> and Mann-Whitney U Test were used.

Results: The mean age of drug/alcohol abusers was 27.7  $\pm$  6.1 and 42.1 ± 11.8 years respectively. 86% of the subjects were males in both groups. Drug users were mainly multiple drug users (87.5%) and intravenous users (71.3%). The mean duration of heroin/alcohol use was  $5.8 \pm 4.3$  and  $21.4 \pm 11.7$  years respectively. In overall, a significantly higher number of substance abusers had been arrested/convicted during their lifetime than alcoholics ( $x^2 = 30.4 & 26.6$ , p < 0.000). This held true for all types of offences, although a differential distribution was observed between drug and alcohol abusers. Thus, drug addicts had been more frequently arrested/convicted for offences related to drugs and against property than alcoholics (p < 0.000). Instead, intra-group comparison showed that alcoholics were more often arrested/convicted for crimes of violence and other offences. The two groups differed significantly only in the mean number of arrests/convictions for offences against property (p < 0.0001 and p < 0.0005). Drug abusers had been first arrested at a much younger age than alcoholics. This difference was highly significant - over 10 years - and was present in almost all types of crime (crimes of violence: p < 0.0003; offences against property: p < 0.013; other offences: p < 0.004). The mean age when first convicted was similar for both groups, except for crimes of violence (p < 0.0002). Regarding their legal status, there was a much higher percentage of drug addicts with legal matters pending against them compared to alcohol users (24.6% vs 6.3%). Furthermore, in many cases, criminality of drug abusers seemed to pre-exist the age of onset of heroin abuse (21.4  $\pm$ 5.1 years).

Conclusion: A clear-cut differentiation in the criminal behaviour of drug abusers and alcoholics was observed in our sample. The two groups exhibited distinct characteristics regarding the number, type and age at onset of criminal activities. In general, substance abusers faced more legal problems than alcoholics and their deviant social behaviour started at an earlier age.

## P.5.006 The role of hyperbaric oxygenation in treatment of alcohol abuse and drug addiction

N. Epifanova, M. Romasenko, A. Koukchina, I. Epifanov. Sklifosovsky Research Institute for Emergency Medicine, Department of Psychosomatic Disorders, Moscow, Russia

Introduction: Long-term alcohol abuse and drug addiction are associated with homeostasis impairments and the development of a toxic encephalopathy and somatic pathology. In these conditions the treatments of a disease may be difficult due to restricting psychopharmacological agents. We have been investigated experimentally on toxic brain edema model with light mycroscopy, that hyperbaric oxygenation (HBO) activates the rhybonucleoproteids syntesis in the neurons, increasis in the

P.5 Addiction S283

proliferative glial reactions and thus improves the cerebral methabolism. In this connection, it is necessary to undertake a complex treatment aimed at correction of metabolism, improvement of CNS and visceral organ condition.

Methods: A comparative study including 552 patients randomized into two groups was undertaken. The 1st group included 367 patients (311 patients suffering from alcohol abuse and 56 patients with drug addiction) who received sessions of hyperbaric oxygenation (HBO) treatment: 100% oxygen in monoplace chambers under hyperbaric conditions (sessions for 40 minutes at 0.2-2.0 ATA maximal pressure). The 2nd group included 185 patients who received a standard pharmacological therapy. We performed the following investigations: KT, EEG, ECG, cerebral blood flow (CBF), biochemical studies (investigations of serum serotonin and lipid peroxidation).

Results: Besides eliminating hypoxia, HBO facilitates the correction of metabolic processes and the normalization of antioxidant system function, optimisation the immune processes the neurohormone levels influences. Experimental studies have demonstrated, that in rats with induced alcochol addiction, the HBO produces psychostimulating or antidepressive effects. In our series, a comparative clinico-psychopathological and functional studies of the patients in the HBO group and the control groups has shown that irrespective of the intoxication and abstinence types, the HBO effect manifested in a significantly accelerated reduction of somatovegetative, psychoneurological and asthenic disorders. In HBO group the period necessary for the control of withdrawal syndrome decreased average two times from 5 + 0.2 to 2 + 0.4 days (p < 0.001). The patients with drug and alcochol addiction has POL/AOS system dysbalance deteriorating with the increase of patient severiti. The use of HBO prevents the development of complications and contributes to normalizing neurochemical processes. The monitoring of systemic and cerebral hemodynamics, dation of lipid peroxidation undertaken within the course of treatment demonstrated their optimization under the effect of a HBO session and the total HBO course. A HBO session and course resulted in the elevation of serum serotonin level, that correlated with the subsiting of depression symptoms in the patients with alcohol and drug addiction. We also noted a stabilizing hypnotic and anxiolytic effect of HBO sessions.

Conclusions: The use of HBO posing detoxication, antihypoxic and metabolic effects in complex treatment of alcohol abuse and drug addiction is justified from the point of pathogenesis and allows to improve the outcomes. Thus, HBO may be used as a method of a methabolic brain protect.

# P.5.007 Cue exposure: A non-pharmacological intervention for the reduction of drug craving: A pilot study

I.H.A. Franken, V.M. Hendriks. RBC Institute, Research Department, Abuse Treatment Unit, PO Box 53002, 2505 AA The Hague, E-mail: ifranken@worldonline.nl, The Netherlands

This study has been conducted at the Psychiatric Centre Bloemendaal, The Hague, Substance Abuse Treatment Unit

Rationale: Cue reactivity to drug related stimuli is a frequently observed phenomenon in drug dependent subjects. Cue-reactivity refers to a classical conditioned response (CR) which occurs when a (post)addicted subject is exposed to drug-related stimuli (CS). This response is presumed to consist of physiological and/or subjective reactions. Craving, a subjective desire to use the drug of choice, is believed to play an important role in the occurrence of relapse in abstinent drug-addicted persons in their natural setting. Besides craving, other subjective cue elicited reactions have been reported, including subjective withdrawal symptoms, subjective drug agonistic effects, mood swings, and anxiety. Physiological reactions that have been investigated include skin conductance, heart rate, salivation and body temperature. The exact nature of the relation between subjective and physiological signs of reactivity is still subject of debate. Conditioned reactivity to substance related cues is believed to be an important factor within addictive use of alcohol, opiates, nicotine, and cocaine. Cue exposure therapy (CET) is a behavior therapy technique which aims at deconditioning of the

conditioned response by exposing the subject to the CS and preventing drug use.

Methods: The study designed to examine the occurrence and nature of cue reactivity in 16 subjects who have been treated for drug dependence in an intensive, drug-free inpatient treatment program for a minimal period of 12 months. At time of the study, the subjects participated in an outpatient resocialization program. It was hypothesized that cue reactivity, if present, would decrease in this population after a protocolized 9 session CET. Enduring effects of CET were studied by evaluating cue reactivity of the study subjects six weeks after the last exposure session.

Results: Results of the pilot study indicate that cue reactivity is still present among detoxified patients after 12 months of intensive inpatient treatment. When subjects are confronted with drug-related stimuli, there is an increase in craving, feelings of depression and anger. Given that subjects in the resocialization phase are likely to be confronted with these stimuli (in vivo) soon after treatment discharge, a reduction of cue reactivity may contribute to the prevention of relapse. In the present study, cue reactivity (feelings of depression, anger, tension, craving and physical symptoms) reduced after cue exposure therapy, and this effect maintained for (at least) 6 weeks after the last cue exposure therapy session. The implications for clinical practice are that cue exposure treatment can reduce self-reported craving in subjects who have been in a long term inpatient treatment program. Although many drug abuse treatment programs of drug dependence are focused on changing negative patterns of behavior and promoting a drug-free lifestyle, it may be beneficial to incorporate cue exposure as a non-pharmacological intervention for relapse prevention into these programs.

## P.5.008 Benzodiazepines' consumption in the contexts of poly-substance abuse and of impulse dyscontrol

E. Levarta, G. Forza, D. Da Ros\*, F. Schifano. Addiction Treatment Unit #1, Local Health Unit #16, Padova, Italy

The concern about benzodiazepines' (BDZs) abuse or dependence is growing. It is well known that positive reinforcement given by BDZ is more prevalent in former or present drug addicts than in the general population, but there are few data about the possible differences between addicted patients using BDZ and addicted patients who don't use these drugs. The aim of this study is to assess the issue of BDZ consumption in opiate-dependent patients.

Ninety-two out the 550 patients in methadone maintenance (range: 20-90 mg/die) for at least three months in Addiction Treatment Units #1 and #2 of Padua and Addiction Treatment Unit of Dolo (Venice) at the date of 1.1.97 were randomly assigned at the sample. They had been studied with the means of a clinical interview and a questionnaire (SCL-90) evaluating ten different dimensions of psychopathological suffering.

Fifty-eight patients (63.0%) reported a BDZ usage in 1996, with an average diazepam-equivalent daily dosage of 67.6 ± 95.5 mg. DSM-IV criteria defines abuse/dependence not only on a pharmacological basis; abuse/dependence entails a loss of control on the use of a substance. Consequently we defined as "problematic BDZ users" those patients who showed at least one of the following characteristics: 1) a reported daily diazepam-equivalent dosage larger than 60 mg (14 pts); 2) a use of BDZs to get the "high" or to "boost" the effects of methadone itself (17 pts); 3) a self-administration characterized by binges in some circumstances (7 pts); and 4) i.v. usage in some circumstances (4 pts). Due to the overlap of these criteria, we identified a subgroup of 26 patients (28.3% of the total sample, 44.8% of BDZ users) defined as "problematic" BDZ users. With respect to the others, these last pts showed a significant higher prevalence of concurrent administration of BDZs with alcohol (63.2% vs. 20.8%, p = 0.011) and/or with cocaine (26.3% vs. 0%, p = 0.011)0.011), and a significant higher lifetime prevalence of cocaine (69.6% vs. 43.3%, p = 0.049), amphetamine (52.2% vs. 3.4%, p < 0.001) and hallucinogens (34.8% vs. 5.0%, p = 0.001) abuse/dependence. On a toxicological basis, this group is therefore characterized by a polysubstance abuse/dependence. On a psychopathological basis, problematic BDZ users showed, with respect to the others, a profile more disturbed at the SCL-90 (GSI: 1.12  $\pm$  0.81 vs. 0.59  $\pm$  0.51, p = 0.003), in particular

N.M. Yepifanova.

HYPERBARIC OXYGENATION IN THE TREATMENT OF NARCOMANIACS, TOXICOMANIACS, AND ALCOHOLICS IN THE POSTINTOXICATION AND ABSTINENCE PERIODS.

HBO Department of the Scientific Research Institute of Emergency Medicine

N.V.Sklifosofsky.

The growing incidence of drug addiction and alcoholism in the working-age population is a mayor social and medical problem. [4.5.10.11]. Substance and alcohol abuse can produce rapid personality degradations.

One of the acute manifestations of this pathology is a withdrawal syndrome that develops in the intoxicated organism and is accompanied by metabolic abnormalities. tissue hypoxia [4.5.10.11.18.20], and cardiovascular disorders, more pronounced in the heart and brain vasculature [2.7.9.14.16.17]. The high incidence of complications due to psychopharmacologic therapy [4.8.10.19], and also the risk of addiction to prescribed drugs [4.5.10], requires new treatment methods, one of which is the hyperbaric oxygen therapy (HBOT).

For its known antihypoxic mechanism of action HBOT reduces the cerebral edema [12.15] leaving less memory and cognitive disturbances after the resolution of the psychotic state [3.8.12.13.15]. These studies have shown the effectiveness of HBOT in the treatment of alcoholic psychosis and the alcohol withdrawal syndrome [6.8].

The aim of the present study was the evaluation of the HBOT effectiveness in the treatment of patients with substance abuse and alcoholics in the post-intoxication and abstinence periods.

Materials and Methods. The study included 525 patients. The main group treated with HBOT consisted of 340 patients, among them: 223 patients with different severity degree of alcohol withdrawal syndrome (AWS) (I-II-III); 68 patients with substance abuse (drug abuse: 38; inhalants: 30); and 49 patients with opioids abuse. (Table 1).

The control group (not receiving HBOT treatment) consisted of 185 patients: 113 with AWS of I-III degree of severity; 50 patients with substance abuse (drugs: 35; inhalants: 15); and 22 patients with opioid abuse. These patients were treated only with pharmacologic agents: detoxifying agents, vitamins, neuroleptics, tranquilizers, and nootropic agents (depending on the abuse substance).

Both the HBOT group and the control group of patients were similar in age, gender, and main clinical features. However, the HBOT group included more patients with severe psychotic forms of AWS (III degree of severity: 27% vs. 7.1 % in the control group.) The HBOT was applied as part of the therapy or as the only method, generally initiated at the first day of admission.

HBOT sessions were given in monoplace chambers "OKA-MT". The protocol and the number of HBOT sessions were defined individually, and related to the severity of the

Similar to the abstract, but not the land.

patients' state and their physical and psychical evolution. The course of treatment consisted from 1 to 5 HBOT sessions (once or twice a day) with pO<sub>2</sub> 0.16-0.2 MPa.

Forty-two percent of the patients complained about middle ear congestion during the compression phase, because of rhinitis, which is typical for withdrawal syndrome; this required the prolongation of isopressure time (and the avoidance of using high pressure). Haemodynamics indexes were studied by tetrapolar rheography. A standard 12-Lead ECG was recorded for each patient.

#### Results and Discussion.

The therapeutic effect of HBOT in the treatment of post-intoxication and abstinence periods in patients with alcohol and substance abuse was evaluated by comparing the clinical features and instrumental testing on both, HBOT and the control groups.

Abuse substance	Main group (HBOT w/ pharmacologic treatment)	Control group (pharmacologic treatment)	
Opioids	49	22	
Sympathomimetics	12	10	
Benzodiazepines	20	15	
Cholinolytics	6	10	
Inhalants	30	15	
Alcohol	223	113	
Totals:	340	185	

Table 1. Distribution of patients by abuse substances and method of treatment

Among opioid users, 21 patients (42.9%) in the HBOT group and 9 patients (40.9%) in the control group consumed raw opium treated with acetic anhydride. These patients had more pronounced clinical features of toxic encephalopathy as a result of chronic opium intoxication. The clinical features of the withdrawal syndrome were more pronounced when the duration of the addiction was more than three years. The symptoms appeared 6-8 hours after the last narcotic application and were characterized by the asthenia (weakness, indisposition, drowsiness,) somatoautonomic, and psychoneurological alterations.

Somatoautonomic alterations depended upon the duration of the addiction and included: chills, salivation, tearing eyes, runny nose, cough, sensation of accumulated throat expectoration, pain in knees, ankles and elbows joints, and pain in arms, hands, feet, legs, back, and waist muscles. These pains caused half-bent body positions and the need to be in continuous movement. Dyspeptic disorders were presented by nausea, vomiting, gastrointestinal cramps, tenesms, and diarrhea. Psychoneurological alterations included: psychical discomfort, irritability, restlessness, melancholy, fearfulness, tension, inconsolable depressed mood, anxiety, sleep disturbances, fine nystagmus, muscle hypotension, and reduction of tendon reflexes.

Most of the patients suffering the disease during a relatively short time (less than three years) had the abortive form of this syndrome, while the others had the fully manifested form.

Personality disorders in patients that were relatively short-term opioid users were expressed in the acute manifestation of pre-morbid personality traits with progressive

formation of typical narcotics user's hysteric or explosive personality, whose severity was related to the length of the addiction.

In long-time drug users we observed a reaction to negate an unknown (by them) therapeutic method. These patients needed psychological therapy before HBOT application, and special attention during the first HBOT session.

The analysis of the clinical and psychopathological state of the patients showed that HBOT modifies the clinical course of the abstinent syndrome and of ECG tracings.

The study of the abstinent syndrome in the opioid users group demonstrated that the psychoneurological, somatoautonomical symptomatology and asthenia signs were reduced during  $3\pm0.1$  days in the HBOT group, while in the control group were reduced during  $5\pm0.2$  days (P<0.001).

uindowe

In general, practically all patients after the first HBOT session felt better, the degree of this improvement depended on their initial severity level of abstinence syndrome. All patients in stage I of abstinence syndrome severity, and most of the patients in stage II experienced the ending (or a significant reduction) of abstinence symptomatology after 2-3 HBOT sessions. A sedative (somnolence) effect was observed: patients get calm and sometimes need to sleep after the HBO session or fall asleep during the session. Only two patients with psychopathic traits showed increased irritability during the HBOT sessions, which they linked to the monotony of the treatment.

Psychoneurological and somatoautonomical symptomatology was reduced during the HBOT sessions. Patients experienced physical cheerfulness, an improvement in the associative activity of their minds, and showed a marked interest in the environment. To complete the process of night sleep normalization and to reduce the most persistent components of the abstinence syndrome, patients in stage II of severity syndrome needed 4-5 HBOT sessions. As a rule, the asthenia symptomatology also disappeared at that time.

The clinical evolution of the opioid abstinence syndrome within the stage II of severity showed that 7 patients (14.3%) experienced a subjective discomfort during the first HBOT session because their typical body pain symptoms required movement and the patients wished to change position continuously, and wished to stretch their back, neck, legs and arms. These unpleasant feelings disappeared, as a rule, after the first session, but went back after some hours (unstable prolonged effect). They were probably linked with metabolic acidosis produced by cellular hypoxia, resulting from low pO2 in blood [1.4.5.10]. In this condition anaerobic glycolysis is activated, which leads to the accumulation of pyruvic, lactic and acetoacetic acids [4.5]. It is obvious that one HBOT session is not enough to stop the opioid abstinence syndrome (degree II). The following sessions led to the disappearance of hypoxia and to the correction of metabolic disorders, clinically manifested as a prolonged therapeutic effect. Some patients that received only pharmacological therapy, showed asthenia symptomatology all the time until discharge from the hospital, which is in accordance with bibliographic data [4.5.10] and can be explained by the persistence of the metabolic acidosis and the hypoxemia as a secuelae of a chronic opioid intoxication of these patients.

The patients with inhalants intoxication (toluene) were admitted while in the final intoxication stage. Some of them still suffered dissociative disorders, such as derealization and depersonalization. The adolescents referred that the environment looked "unreal," felt their legs weak, and made comments such as "my legs are going by themselves." Others suffered time and space disorientation, felt dazed but conscious about their own personality with a slowdown in their processes of mental association, with difficulty to comprehend questions and experiencing a delay in answering, and high asthenization of the thinking processes with difficulty in concentration and a high level of involuntary distraction.

The patients presented oculostatic and psychovestibular symptoms: coordination disorders, locomotion disturbances, dizziness, nausea, vomiting, muscle ataxia, disarthria, horizontal and vertical nystagmus, convergence weakness, augmentation of the periostal reflexes with enlarging of the reflex zone. The vascular disorders consisted in paleness of the teguments, acrocyanosis, bradicardia, instable arterial tension (AT) with tendency to arterial hypotony (AT 105/70 mm Hg), anorexia, and urine retention.

The ECG of some patients showed incomplete bundle branch block, signs of overloaded left ventricle, and moderate myocardial alterations. Taking into account the young age of these patients, one can suppose that these changes are bound to the cardiotoxic effect of the inhalants.

Dazed feelings, weakness, and motor and speech disturbances persisted in some patients for 72 hours, but, in most cases, the cognitive function was recovered earlier. Patients had forgotten the acute period of intoxication (a kind of amnesia), being able to recall only partially some events that occurred before the last inhalation experience. Fixation amnesia, with inability to concentrate and maintain attention, persisted much longer. The intoxication ended with a somatic asthenia in favourable cases. In less favourable cases the intoxication led to CNS affectation: toxic encephalopathy, and psychoorganic syndrome with disturbances of memory, attention, and other cognitive functions.

In this group of patients HBOT produced two main effects. Ten patients experienced a tranquilizing and sedative action. These patients had a residual premorbid psychoorganic symptomatology with exciting traits. Their acute intoxication ran with the psychomotor excitement. During HBOT sessions they fell asleep (it was a physiological sleep that lasted after the conclusion of the HBOT with a complete recovery of consciousness later.)

Twenty patients presented psychomotor weakness (slowdown), and dizziness. During HBOT sessions they experienced a stimulating effect that was perceived as a feeling of physical cheerfulness, fresh surge of energy, "clearing up" of the mind, and ability to think.

A stable therapeutic effect after the first session was observed in 15 patients. An "exposition" effect (favourable effect that lasted only during the HBOT session itself) was manifested in 7 patients. Non-stable prolonged effect was observed in 8 patients (a favourable effect that lasted some hours after the HBOT session, and then ceased).

The HBOT session promoted the recuperation of consciousness earlier than in the control group. The behaviour of these patients became adequate in the first 24 hours.

The natural rhythm of sleep and wakefulness was recuperated, fixation amnesia and concentration disturbances practically were not observed. The clinical comparison between the HBOT treated and the control groups showed an acceleration in psychoneurological and somatoautonomic recuperation, which occurred 1-2 days earlier in the HBOT treated group.

During HBOT treatment weakness, dizziness, and headaches disappeared, teguments became of a normally pink colour, and blood pressure normalized, as well as did gastrointestinal functions and appetite. There was noticeable regression in neurological symptomatology: disappeared nystagmus, altered convergence was recuperated, coordination tests were fulfilled better, and locomotor ataxia disappeared.

The favourable effect of HBOT on the patients with acute inhalants intoxication is probably linked with the antihypoxic and desintoxication action of hyperbaric oxygen.

The clinical comparison between patients who suffered addiction to prescribed drugs also demonstrated two types of HBOT action. Twelve patients (8 with sympathomimetics and 4 with cholinolytic intoxication), who showed a psychomotor excitement during the acute stage of intoxication, underwent a tranquilizing and sedative effect with the HBOT. Twenty-six patients with lethargy antecedents, weakness, and sluggishness, showed a stimulating HBOT effect. The exposition effect of the first session was observed in 8 patients, and the unstable prolonged effect in 16 patients. A stable prolonged effect was seen in 6 patients after the first HBOT session, in 12 patients after the second session, and in 14 patients after the fourth session.

The HBOT application during the acute intoxication prevented the development of the acute psychoorganic syndrome in the somatogenic phase of poisoning.

The effect of HBOT in patients with alcohol withdrawal syndrome (AWS) was mostly seen in those within the II and III degree of severity of abstinent syndrome, because they showed more pronounced somatoautonomic and psychoneurological disorders. As result of this treatment, patients in the main group experienced the ceasing of AWS twofold faster than those in the control group (see table 2). Also compulsive alcohol attraction was reduced and then disappeared.

Groups of patients	Duration of recovery from abstinence syndrome (in days)			
	Severity degree of abstinence syndrome			
	I	II	III	
HBOT and pharmacological treatment	1.6±0.1	2.4±0.1	2.4±0.1	
	(N=25)	(N=60)	(N=21)	
HBOT only	1.4±0.1	2.0±0.1	2.5±0.1	
	(N=14)	(N=25)	(N=22)	
Control group	3.5±0.2*	5.2±0.2*	5.6±0.4*	
	(N=24)	(N=70)	(N=3)	

Table 2. Duration of the recovery from abstinence syndrome in main and control groups of patients (Mean  $\pm$  SE). N = number of patients, \* - P<0.001.

The control group of patients suffered asthenia and emotional abnormalities with the predominance of dysphoria for a longer time period, with lack of affects and frequent conflicts with the people around them. Additionally, 7% of the control group of patients developed complications such as alcohol delirium and epileptic syndrome, although both groups were similar in the sense of the risk factors for developing these complications.

The study of the AWS in the group of patients that used alcohol surrogates was important. 50% of these patients had psychopathological disorders (AWS within the III degree of severity) superimposed upon somatoautonomic and neurological symptomatology. HBOT sessions were initiated within the first 24 hours after admission in 96% of the cases, 28% of them within the first three hours after admission. In cases of patients that used alcohol surrogates, 31% tolerated the first half of the first HBOT session with some subjective difficulties. There were no recordings of any changes in their physical state, and their complaints were poorly defined. As a result of the HBOT treatment this group also showed a significant reduction in the time necessary to recover from the AWS: from  $5.0 \pm 0.9$  to  $2.3 \pm 0.2$  days. (P<0.001)

It is well known that patients with AWS show deterioration in their cardio-vascular system. The analysis of the central haemodynamics data showed that with the progression of the disease the hyperkinetic and eukinetic types of circulation were changed to hypokinetic. Some authors [9.10.16.17] refer that it could be explained by the excessive sympathetic tone and compensatory hyperkinetics of the myocardium, because of the hypoxia in AWS. The HBOT session corrected significantly the haemodynamics of the heart (see figure), which could be explained by the adrenolytic action of the hyperbaric oxygen and the correction of tissue metabolism. This HBOT effect prevents the development of cardiovascular decompensation in patients with the abstinent syndrome. These haemodynamic changes were conserved until the release of the patients from the hospital.

<sup>&</sup>lt;sup>1</sup> [Translator's note: In Russia it is common to substitute standard alcoholic beverages with surrogates (any substance that contains alcohol)]

The pharmacologic therapy didn't change the hyperkinetic type of circulation. The cardiac index was high.

[Translator's note: This table does not appear in the original paper-Its sole purpose is to better explain the diagram.]

	Before HBO	3-7 days	8-14 days
Hyperkinetic type	49.2%	12.7%	9.5%
Eukinetic type	44.5%	85.7%	87.3%
Hypokinetic type	6.3%	1.6%	3.2%
	Before		
1	pharmacologic	3-7 days	8-14 days
	treatment		
Hyperkinetic type	37.5%	40.6%	50%
Eukinetic type	59.1%	56.3%	43.7%
Hypokinetic type	3.1%	3.1%	6.3%

Figure. Comparison between types of central haemodynamics in patients with abstinence syndrome during the treatment. [Translator notes—Horizontal hatching: hyperkinetic type; vertical hatching: eukinetic type; without hatching: hypokinetic type. Upper line of circles: treatment with HBOT; lower line of circles: pharmacological treatment. First column: before the treatment; second column: 3-7 days of treatment; third column: 8-14 days of treatment.]

At the same time, 42% of patients experienced an improvement in the myocardium, manifested with a normalization of the T wave and ST segment. In the control group improvement in ECG was noted in only 25% of the patients during the treatment and in 18% of the patients at the time of release. In other cases haemodynamics returned to the previous state. This data correlated with the number of patients that initially presented hyperkinetic type of haemodynamics. This is interpreted as a compensatory reaction to the persisting tissue hypoxia in the group that received only pharmacological treatment.

The comparison of data showed the favourable effect of HBOT upon the tone and perfusion of the cerebral vasculature. The patients that received only the pharmacologic therapy continued with a high tone of cerebral vasculature. Compensation of cerebral blood flow occurred at the expense of the activation of the central haemodynamics, forming the hyperkinetic type of circulation.

So, the clinical, psychopathological and functional study of the HBOT and control groups of patients showed that HBOT accelerated the reduction of the somatoautonomic, psychoneurological disturbances and asthenia signs. Probably, it is due to antihypoxic, desintoxication and bioenergic effects of hyperbaric oxygen. Obviously, HBOT is not a specific nosological method of therapy, nevertheless, it becomes a pathogenically based therapeutic method in the treatment of patients with drugs, substance, and alcohol abuse, and those suffering post-intoxication and withdrawal syndromes.

#### Conclusion:

1. The inclusion of HBOT in the scheme of pharmacological treatment of patients suffering post-intoxication and withdrawal syndromes of substance abuse, and the use of HBOT as the unique method of therapy (without pharmacological treatment) accelerates the process of regression of somatoautonomic and psychoneurological symptomatology and asthenia signs, with a twofold decrease in the recovery time from abstinence syndrome, while preventing the development of complications.

2. Alcohol surrogate abuse produces, in 50% of the cases, psychotic forms of the withdrawal syndrome and the abstinence syndrome within the III degree of severity. HBOT application in these patients shows the same effectiveness as

in the treatment of users of standard alcoholic beverages.

3. The withdrawal syndrome in users of raw opium, treated with the acetic anhydride, produces a very complex state of the disease that includes cognitive and affective disorders; asthenia; somatoautonomic alterations; and sensory components. The reduction of these manifestations is accelerated with HBOT application.

4. The progression of the severity of the withdrawal syndrome augments the disorders of the central haemodynamics causing their hyperkinetic or hypokinetic types. HBOT reduces the tissue oxygen deficit and promotes the normalization of the myocardium function, while pharmacological treatment alone contributes to the appearance of the hyperkinetic type of haemodynamics, increasing the number of patients with this type of haemodynamics.

5. Application of HBOT produced improvement of the myocardium tissue, of the tone of the cerebral vasculature, and in the perfusion of the brain; while in the group of patients treated with pharmacological method alone, this effect was

significantly less.

6. The protocol of treatment of the substance withdrawal syndrome should consist of 1-5 HBOT sessions (once or twice with pO<sub>2</sub> 0.16-0.2 MPa).

Bibliography:

1. Aksenov V.S., Pagosov A.V., Niyasi G.O. Important problems of psychiatry and narcology. Dushanbe, 1991, p. 123-126.

2. Hyperbaric medicine. Moscow, 1983, vol. I (Russian)

3. Gorgaslidse A,G., Sayfulaeva M.A., Kuz'mina M.M. All Russia IV Congress of Cardiology: Abstracts. Pensa, 1991. pp. 44-45.

4. Gulyamov M.G., Pagosov A.V. Narcomania problems. 1992, p. 25.

Gulyamov M.G., Pagosov A.V. Narcomania. Dushanbe, 1987.

6. Epifanova N.M., Isakov Yu.V., Churkin E.L. Journal of Neuropathology and Psychiatry. (Russian). 1988 N.2, pp. 78-81.

Kekhonez C., Levenez B.A., Bondarenko V.V. et al., Allunion 8<sup>th</sup> Congress of Neuropathology, Psychiatry and Narcology. Moscow, 1988.

pp. 366-368.

8. Kondrashenko V.T. 2<sup>nd</sup> Congress of Neuropathology and Psychiatry of Belorussia. Proceedings. Minsk. 1980, pp. 218-220.

9. Levenez P.V. Clinics and therapy of patients with alcoholism and of different haemodynamic types. Graduate thesis in medical sciences.

Moscow, 1987.

10. Paukov V.S., Ugriumov A.I., Belyaeva I.Yu., et al. Alcoholism's problems: clinics, pathogenesis, therapy. Moscow, 1986. pp. 48-54.

Pyatnizkaya N.N. Narcomanias. M, 1994. 11.

Romasenko M.V. Central nervous system and post-resuscitation 12. pathology of the organism. Moscow, 1989, pp. 288-289.

Hyperbaric oxygenation manual. Yefuni S.N., Ed. Moscow, 1986. pp. 5-13. 35.

Smetnev S.S., Ivanov A.I., Gorgaslidse A.G. et al. Cardiologia. 1990. N. 14. 8. pp. 34-36. (Russian)

Sukoff M.K. // Hyperbaric medicine. Moscow, 1983, vol. 1, pp. 156-162. 15.

(Russian)

Angehrn, Swiss Med 1984. Bd. 6, N. 7a, S. 59-61. 16.

- Burton M, Alfura Ph.D., Bella T. Alcoholism. Clin. Exp. Res. 1987. vol. 17. 11. N. 2. pp. 549-559.
- Dagnestanl A.N. Postgrad. Med. 1987. vol. 81, N. 6. pp. 116-118. 18.

Lechaf P, Fontagne J. Therapie. 1974. Vol. 29, N. 1, pp. 5-21. 19.

Simmel B. Advanc. Alcohol Subst. Abuse. 1985. vol. 5. N. 11. pp. 121-20. 133.

Entered 25.01.1995.

### Hyperbaric Oxygen Therapy

Brain healing and function restored

Prepared by Kent MacLaughlin Waterloo, Wisconsin 7 April 2007

## Lost without Hope?

Or hopelessly lost?

#### There is a difference

- · 9+ years of doctor supervised drug dependence
- 3 months of reduction
- 5 months of severe physical withdrawal
- · Short term disability from work
- Completely worthless for spouse and family
- Was my life hopelessly lost?
- HBOT the turning point
- Don't give up on what society views as hopelessly lost

# 9+ years of doctor supervised dependence

- 1998 18 credits + full time management position family and home
- · Panic Attack near Christmas time
- Visit to Psychiatrist (big mistake)

   prescribed extended use benzodiazepine (Industrial strength Valium) disregarding manufacturers label
- Dose increased over time as brain became accustomed to med – inter-dose withdrawal increased
- · Became more sick as time went on
- Misdiagnosed with Fibromyalgia in 2006 Lyme disease?
- Discovered that my drug could be my problem

#### 3 months of reduction

- Doctor said to reduce over 3 weeks failed miserably
- Found info on internet that guided me to reduce slowly using water titration
- €3 months later April 13, 2007 finished
- Not that bad and feeling a little better

# 5 months of severe physical withdrawal

- April 15<sup>th</sup> the physical withdrawal began
- Inability to sleep
- · Severe palpitations
- Severe Headache
- · De-realization, de-personalization
- · Inability to concentrate
- Twitching muscles
- · Complete exhaustion
- Depression, anxiety at new levels

### Short term disability from work

- It became so bad that my doctor removed me from work on a 6 month short term disability – July 24, 2007
- Suicide was real- life was too hard, prayed that God would take me home
- Worst time was between midnight and 6am
- Surviving somewhere between zombie and death

# Completely worthless for spouse and family

- · Basically laid on couch and did nothing
- Lost 15 lbs
- No interest in family
- · Life was chore not worth the time

#### Was my life was hopelessly lost?

- ◆ I began to wonder would I recover, or was my life lost
- Began considering returning to the drug for relief
- Actually took a dose, but saw almost no relief – almost no options
- Considered taking a large dose daily to try and reinstate

### HBOT - the turning point!

- Had studied Hyperbaric Oxygen and had considered using it because of it's proven use to ameliorate brain injury
- Looked for a doctor to help
- Very angry that I could not find a doctor who knew about my condition or how to help
- Cost for HBOT was a major concern... would it be better to go back on the drug?
- Finally found hope with Sunny Sonnenrein and Steve Reimers
- They told me of a doctor very experienced with dependency and withdrawal as well as HBOT

### HBOT - the turning point, cont'd

- This physician explained that benzo and alcohol work on the same GABA receptors in the brain
- Doctor prescribed 2, one hour treatments per day at 2.4 ATA
- · Was there hope? I would try it
- For me relief began on the first treatment and by the third, I began getting 3 hours of sleep, which was a gift I am eternally grateful for
- By the end of 40 treatments I was well enough that my doctor approved my return to work

# Don't give up on what society views as hopelessly lost

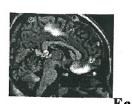
- The most frustrating part of this for me was that the doctors that I talked to did not understand why I was having problems although there are many documented cases of protracted withdrawal and even suicide attributed to it.
- They could not help and could offer nothing besides drugs... the same drugs that caused the condition in the first place
- This caused me to loose hope and loss of hope makes you wonder if you can ever live normal again

# Don't give up on what society views as hopelessly lost

- · HBOT was the last hope for me
- HBOT repairs and ameliorates Brain injury
- · HBOT uses a very safe drug Oxygen
- Risk of unintended bad consequences is very, very low.
- I felt better after the third treatment

# Don't give up on what society views as hopelessly lost

- I wish that all people that suffer from withdrawal from drugs could at least try HBOT
- If it only helps 25 -50% that is a huge success
- I can not express in words the gratitude that I have for the chance to try HBOT
- I truly believe it saved me from a life of addiction to prescription drugs... I could not take the withdrawal without hope for another day.
- $\odot$  I was not hopelessly lost- I was lost without hope and HBOT gave me the hope I needed



as of 2006;

1.4 million people in all Adicted to moth.

Early Methamphetamine Abstinence: fMRI and Cognition

Methamphetamine (MA) abuse is a national public health concern. People who are dependent on MA have problems with mental functions (e.g., learning, remembering, focusing attention, solving problems). Such problems can interfere with their treatment for MA abuse, and thereby may promote continued drug use. While the effects of MA have been studied in rodents and non-human primates, its effects on the human brain have not been well characterized.

This project aims to identify the brain regions and pathways that show dysfunction contributing to the problems of MA abusers in performing mental tasks. We are using functional magnetic resonance imaging (fMRI), a noninvasive brain imaging procedure, to study brain function while research participants perform tests of memory and concentration. We are comparing brain activity in regular users of MA with activity in a comparison group of participants who do not use MA.

MA abusers must abstain from illicit drugs during the study. We use fMRI to measure their brain activity at 4 - 7 days after they stop MA use, and again at about one month later. Knowledge of the pattern of cerebral deficits in MA abusers during drug abstinence can guide development of treatments aimed at reversing or compensating for those deficits.

Our first results, published in the Archives of General Psychiatry (link to paper), showed that, compared to normal non drug-using controls, methamphetamine abusers show regional cerebral metabolic rate (rCMRglc) deficiencies in several executive functioning regions of their brains, namely the medial orbitofrontal cortex, anterior cingulate, etc.

### Effects of Methamphetamine Abuse on Cerebral Glucose Metabolism

Abuse of the psychomotor stimulant methamphetamine (METH) is a national public health concern. Although the effects of METH have been extensively studied in animal models, long-term effects of METH on the human brain have not been well characterized. The rate at which a brain area uses glucose, the primary source of energy for the brain, is proportional to the functional activity of that region. Positron emission tomography (PET), a nuclear medicine procedure, will be used with 2-deoxy-2[F-18]fluoro-D-glucose (FDG), a radioactive tracer, to measure the rates at which glucose is used in different regions of the brain. This study has shown that local rates at which the brain uses glucose are abnormal in humans after prolonged METH use and abstinence.

## Nicotine Withdrawal, Smoking, and Cognition: An fMRI Study

This study evaluates the effects of smoking nicotine cigarettes on memory, concentration, and brain function during performance of cognitive tasks. The study has two parts: part A involves memory and concentration tests, and part B involves brain scanning with functional magnetic resonance imaging (fMRI). The fMRI procedure can takes pictures of the brain at work by measuring blood flow to different regions of brain as indicated by

http://london.npih.ucla.edu/vereacon.htm

increases or decreases in local signal intensity resulting from changes in blood oxygen levels.

#### Genetics of Alcohol Effects on Brain Functioning

Nearly half of Americans over 12 years of age drink alcohol, yet only 5.6% drink heavily. It is important to know why only some people become alcohol-dependent. Alcoholism has a genetic component. The D2 dopamine receptor gene (DRD2) exists in two forms (alleles): A1 and A2. Carriers of the A1 allele are more susceptible to alcoholism. In this study of social drinkers, we will compare carriers and non-carriers of the DRD2 A1 allele, with respect to the effect of alcohol challenge on mood and associated regional brain function. Positron emission tomography (PET), a nuclear medicine procedure, will be used with 2-deoxy-2[F-18]fluoro-D-glucose (FDG), a radioactive tracer, to measure the rates at which glucose is used in different regions of the brain.

#### **Recent Journal Articles**

Horti A, Chefer S, Mukhin A, Koren A, Gündisch D, Links J, Kurian V, Dannals R, London E. 6-[18F]fluoro-A 85380, a novel radioligand for in vivo imaging of central nicotinic ACh receptors. Life Sci 2000; 667:463-69.

Bartzokis G, Lu PH, Beckson M, Rapoport R, Grant S, Wiseman EJ, London ED. Abstinence from cocaine reduces high-risk responses on a gambling task. Neuropsychopharmacology 2000;22:102-103.

Grant S, Contoreggi C, London ED. Drug abusers show impaired performance in a laboratory test of decision making. Neuropsychologia 2000;38:1180-1187.

Mukhin AG, Gündisch D, Horti AG, Koren AO, Tamagnan G, Kimes AS, Chambers J, Vaupel DB, King SI, Picciotto MR, Innis RB, London ED. 5-Iodo-A-85380, an 4 2 subtype-selective ligand for nicotinic acetylcholine receptors. Mol Pharmacol 2000;57:642-649.

Koren AO, Horti AG, Mukhin AG, Gündisch E, Dannals RF, London ED. Synthesis and initial in vitro characterization of 6-[18F]fluoro-3-(2(s)-azetidinylmethoxy)-pyridine, a high-affinity radioligand for central nicotinic acetylcholine receptors. J Labelled Compounds & Radiopharmaceuticals 2000;43:413-423.

Ernst M, Matochik J, Heishman S, Van Horn J, Jons P, Henningfield J, London E. Acute and chronic nicotine effects on brain activation during performance of a working memory task. Proc Natl Acad Sci USA 2001;98:4728-4733.

Ernst M, Heishman SJ, Spurgeon L, London ED. Smoking history and nicotine effects on cognitive performance. Neuropsychopharmacology 2001;25:313-319.

Mintzer MZ, Griffiths RR, Contoreggi C, Kimes AS, London ED, Ernst M. Effects of triazolam on brain activity during episodic memory encoding: a PET study. Neuropsychopharmacology 2001;25:744-756.

Ernst M, Bolla K, Mouratidis M, Contoreggi C, Matochik JA, Kurian V, Cadet JL, Kimes AS, London ED. Decision-making in a risk-taking task: A PET study. Neuropsychopharmacology 2002;26:682-691.

Bonson KR, Grant SJ, Contoreggi CS, Links JM, Metcalfe J, Weyl HL, Kurian V, Ernst M, London ED. Neural systems and cue-induced cocaine craving.

- Neuropsychopharmacology 2002;26:376-386.
- Brody A, Mandelkern m, London E, Childress AR, Lee GS, Bota R, Ho M, Saxena S, Baxter L, Madsen D, Jarvik M. Brain metabolic changes during cigarette craving. Arch Gen Psychiatry 2002;59:1162-1172.
- Rose JE, Behm FM, Westman EC, Mathew RJ, London ED, Hawk TC, Turkington TG, Coleman RE. Nicotinic influences on neural systems: PET studies in cigarette smokers. Am J Psychiatry 2003; 60:323-33.
- Bolla KI, Eldreth DA, London ED et al. Orbitofrontal cortex dysfunction in abstinent cocaine abusers performing a decision-making task: NeuroImage 2003;19:1085-1094.
- Chefer S, London E, Koren A, Pavlova OA, Kurian V, Kimes AS, Horti AG, Mukhin AG. Graphical analysis of 2-[18F]FA binding to nicotinic acetylcholine receptors in rhesus monkey brain. Synapse 2003; 48:25-34.
- Kimes AS, Horti AG, London ED et al. 2-[18F]F-A85380: PET imaging brain nicotinic acetylcholine receptors and whole body distribution in humans: FASEB J 2003;10:1331-1333.
- London E, Simon S, Berman S et al. Regional cerebral dysfunction associated with mood disturbances in abstinent methamphetamine abusers. Arch Gen Psychiatry 2004;61:73-84.
- Brody A, Mandelkern M, Jarvik M, Lee G, Smith E, Huang J, Bota R, Bartzokis G, London E. Differences between smokers & non-smokers in regional gray matter volumes & densities. Biol Psych 2004;55:77-84.
- Bolla K, Ernst M, Kiehl K, Mouratidis M, Eldreth D, Contoreggi C, Matochik J, Kurian V, Cadet J, Kimes A, Funderburk F, London E. Prefrontal cortical dysfunction in abstinent cocaine abusers. Neuropsych Clin Neurosci, 2004; 16:4. Brody A, Olmstead R, London E, Farahi J, Meyer J, Grossman P, Lee GS, Huang J, Hahn E, Mandelkern, MA. Smoking-induced ventral striatal dopamine release. Am J Psychiatry 2004;161:1211-1218.
- Brody A, Mandelkern M, Lee G, Smith E, Sadeghi M, Saxena S, Jarvik M, London E. Attenuated cue-induced cigarette craving and anterior cingulate cortex activation in bupropion-treated smokers: a preliminary study. Psych Res Neuroimaging, 2004;130:269-281.
- Thompson P, Hayashi K, Simon S, Geaga J, Hong M, Sui Y, Lee J, Toga AW, Ling W, London ED. Structural abnormalities in the brains of human subjects who use methamphetamine. J Neurosci 2004; 24:6028-6036.
- JR. Monterosso, AR. Aron, Xl Cordova, J Xu, ED London, (in press) Impaired Response Inhibition Associated With Chronic Methamphetamine Abuse Drug and Alcohol Dependence Drug and Alcohol Dependence.
- J Xu, A Mendrek, MS Cohen, J Monterosso, P Rodriquez, SL Simon, A Brody, M Jarvik, CP Domier, R Olmstead, M Ernst, ED London (in press). Brain activity in cigarette smokers performing a working memory task: Effects of smoking. Biol. Psychiatry
- B Voytek, SM. Berman, BD Hassid, SL. Simon, MA Mandelkern, AL. Brody, J Monterosso, W Ling, ED. London (in press). Differences in regional brain metabolism associated with marijuana abuse in methamphetamine abusers. Synapse.

#### Stephen D. Reimers

From: sunny124ny@aol.com

**Sent:** Saturday, April 19, 2008 7:14 PM

To: sreimers@reimerssystems.com

Subject: Re: Need Reference

Hi Steve,

got it from this website:

http://london.npih.ucla.edu/research.html

Also, saw statistics last night that as of 2006, 1.4 million people are meth addicted in the US

Hi Sunny

The attached paper is very useful to our argument. Do you have the source for it? If so, please advise.

**Thanks** 

Sunny www.hyperbaric-clearinghouse.com www.ReimersSystems.com

----Original Message----

From: Steven Reimers <steve171@sprintpcs.com>

To: Sunny124NY@aol.com Sent: Sat, 19 Apr 2008 6:56 pm

Subject: Need Reference

Hi Sunny

The attached paper is very useful to our argument. Do you have the source for it? If so, please advise.

**Thanks** 

Stephen D. Reimers, PE President Reimers Systems, Inc. 8210-D Cinder Bed Road Lorton, VA www.reimerssystems.com

Phone: 703-952-0240