Study Name / Link
Early intervention of intravenous KB220IV--neuro-adaptagen amino-acid therapy (NAAT) improves behavioral outcomes in a residential addiction treatment program: a pilot study. https://www.ncbi.nlm.nih.gov/pubmed/23457891
Abstract
Substance use disorders (SUD) are inheritable and the culprit is hypodopaminergic function regulated by reward genes. We evaluated a natural dopaminergic agonist; KB220 intravenous (IV) and oral variants, to improve dopaminergic function in SUD. Our pilot experiment found a significant reduction of chronic symptoms, measured by the Chronic Abstinence Symptom Severity (CASS) Scale.
Key Points
● In 129 patients a combination of IV and oral NAAT therapy (generic KB220) were assessed for Chronic Abstinence Symptom Severity (CASS) Scale over a 30 day period. ● Three scales were constructed based on this factor analysis: Emotion, Somatic, and Cognitive. ● All three scales showed significant improvement (p=.00001) from pre- to post-treatment: t=19.1 for Emotion, t=16.1 for Somatic, and t=14.9 for impaired - Cognitive. ● A two year follow-up in a subset of 23 patients showed: 21 (91%) were sober at 6 months with 19 (82%) having no relapse; 19 (82%) were sober at one year with 18 (78%) having no relapse; 21 (91%) were sober at two-years post-treatment with 16 (70%) having no relapse.

Study Name / Link
Enkephalinase inhibition: Regulation of ethanol intake in mice. Blum K, Wallace JE, Trachtenberg MC. Briggs AH, Dellallo L. Alcohol: 4; 449-456 https://www.ncbi.nlm.nih.gov/pubmed/2829941
Abstract
This is the first report of alteration in alcohol intake in mice with a genetic

predisposition to alcohol preference and known to have innate brain enkephalin deficiencies. We have been able to significantly attenuate both volitional and forced ethanol intake respectively by acute and chronic treatment with hydrocinnamic acid and D-phenylalanine, known carboxypeptidase (enkephalinase) inhibitors. Since these agents, through their enkephalinase inhibitory activity, raise brain enkephalin levels, we propose that excessive alcohol intake can be regulated by alteration of endogenous brain opioid peptides.

Key Points

- Mice genetically predisposed to like alcohol have a measured deficiency in enkephalin.
- D-phenylalanine and its metabolite hydrocinnamic acid are substances known to stop the breakdown of enkephalin in the brain -the amount of enkephalin available in the brain increases.
- When the amount of enkephalin available in the brain increases both voluntary and forced intake of alcohol decreases.
- D-phenylalanine is one of the ingredients in NAAT.

Study Name / Link

Acute intravenous synaptamine complex variant KB220™ (“NAAT”) "normalizes" neurological dysregulation in patients during protracted abstinence from alcohol and opiates as observed using quantitative electroencephalographic and genetic analysis for reward polymorphisms: part 1, pilot study with 2 case reports.

https://www.ncbi.nlm.nih.gov/pubmed/21084795

Abstract

It is well established that in both food- and drug-addicted individuals, there is dopamine resistance due to an association with the DRD2 gene A1 allele. Evidence is emerging whereby the potential of utilizing a natural, nonaddicting, safe, putative D2 agonist may find its place in recovery from reward deficiency syndrome (RDS) in patients addicted to psychoactive chemicals. Utilizing quantitative electroencephalography (qEEG) as an imaging tool, we show the impact of Synaptamine Complex Variant KB220™ as a putative activator of the mesolimbic system. We demonstrate for the first time that its intravenous administration reduces or "normalizes" aberrant electrophysiological parameters of the reward circuitry site. For this pilot study, we report that the qEEGs of an alcoholic and a heroin abuser with existing abnormalities (ie, widespread theta and widespread alpha activity, respectively) during protracted abstinence are significantly normalized by the administration of 1 intravenous dose of Synaptamine Complex Variant KB220™. Both patients were genotyped for a number of neurotransmitter reward genes to determine to what extent they carry putative dopaminergic risk alleles that may predispose them for alcohol or heroin dependence, respectively. The genes tested included the

dopamine transporter (DAT1, locus symbol SLC6A3), dopamine D4 receptor exon 3 VNTR (DRD4), DRD2 TaqIA (rs1800497), COMT val158 met SNP (rs4680), monoamine oxidase A upstream VNTR (MAOA-uVNTR), and serotonin transporter-linked polymorphic region (5HTTLPR, locus symbol SLC6A4). We emphasize that these are case studies, and it would be unlikely for all individuals to carry all putative risk alleles. Based on previous research and our qEEG studies (parts 1 and 2 of this study), we cautiously suggest that long-term activation of dopaminergic receptors (ie, DRD2 receptors) will result in their proliferation and lead to enhanced "dopamine sensitivity" and an increased sense of happiness, particularly in carriers of the DRD2 A1 allele. This is supported by a clinical trial on Synaptamine Complex Variant KB220™ using intravenous administration in > 600 alcoholic patients, resulting in significant reductions in RDS behaviors. It is also confirmed by the expanded oral study on Synaptose Complex KB220Z™, published as part 2 of this study. Future studies must await both functional magnetic resonance imaging and positron emission tomography scanning to determine the acute and chronic effects of oral KB220™ on numbers of D2 receptors and direct interaction at the nucleus accumbens. Confirmation of these results in large, population-based, case-controlled experiments is necessary. These studies would provide important information that could ultimately lead to significant improvement in recovery for those with RDS and dopamine deficiency as a result of a multiple neurotransmitter signal transduction breakdown in the brain reward cascade.

Key Points

- Combination of both IV –NAAT and oral forms
- Two case reports of an alcoholic and heroin addict
- Both patients were genotyped for a number of neurotransmitter reward genes to determine to what extent they carry putative dopaminergic risk alleles that may predispose them for alcohol or heroin dependence, respectively.
- The genes tested included the dopamine transporter (DAT1, locus symbol SLC6A3), dopamine D4 receptor exon 3 VNTR (DRD4), DRD2 TaqIA (rs1800497), COMT val158 met SNP (rs4680), monoamine oxidase A upstream VNTR (MAOA-uVNTR), and serotonin transporter-linked polymorphic region (5HTTLPR, locus symbol SLC6A4).
- Both patients showed prevalence of at least one risk allele.
- qEEG analysis revealed dys-regulation in the PFC-Cingulate Gyrus in both addicts.
- IV-NAAT and oral produced a regulation of widespread theta activity
- These results have relevance for relapse prevention because of its effect on the part of brain involved in relapse (PFC-Cingulate Gyrus).

Study Name / Link

Kenneth Blum, Thomas J.H. Chen, B.W. Downs, Brian Meshkin, Seth H. Blum, Manuel Martinez Pons, Julie F. Mengucci, Roger L. Waite, Vanessa Arcuri, Michael Varshofsiky and Eric R. Braverman, 2007. Synaptamine (SG8839),™ An Amino-Acid

Enkephalinase Inhibition Nutraceutical Improves Recovery of Alcoholics, A Subtype of Reward Deficiency Syndrome (RDS). Trends in Applied Sciences Research, 2: 132-138.

http://scialert.net/abstract/?doi=tasr.2007.132.138

Abstract

The present research was conducted to test the hypothesis that manipulation of the reward neural circuitry by utilization of oral and intravenous amino-acid–enkephalinase therapy would improve both the emotional and behavioral symptomology of recovering 600 alcoholics in an open trial clinical study. Our findings suggest that the combination of both oral and intravenous administration of SG8839 significantly improved both the emotional and behavioral recovery of the alcoholic subjects when compared to pre and post administration scores, including reduction of craving ($p<0.001$), reduced depression ($p<0.001$), reduced anxiety ($p<0.001$), anger ($p<0.001$), fatigue ($p<0.001$), lack of energy ($p<0.001$) and crisis ($p<0.001$). Mean reductions for anxiety (53.8±10.2%), craving (76.3±3.1%), depression (61.0±6.3%), fatigue (76.9±3.1%) and crisis (53.8±5.5%) were all significantly greater than 50% ($p<0.001$). This is the first study combining both oral and intravenous solutions suggesting clinical improvement.

Key Points

- In an open clinical study Intravenous plus oral Amino-Acid Enkephalinase Inhibition Nutraceutical improved symptomatology of 600 recovering Alcoholics.
- Emotional and behavioral recovery scores significantly improved after administration of oral and intravenous Synaptamine (NAAT).
- Mean reductions for craving, depression, anxiety, anger, fatigue, lack of energy and crisis were all significantly greater than 50% ($p<0.001$)

Study Name / Link

Neuronutrient effects on weight loss in carbohydrate bingers: an open clinical trial.

https://www.cabdirect.org/cabdirect/abstract/19931458707

Abstract

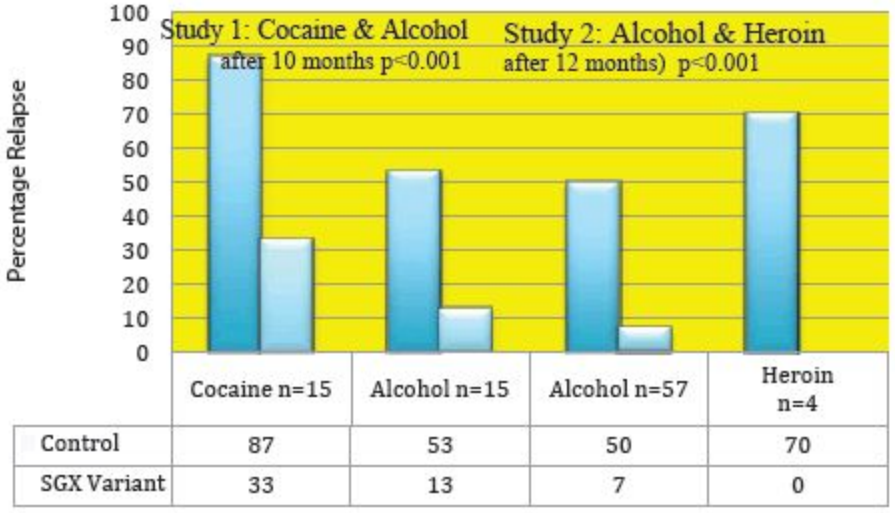
The effects of precursor amino acid loading and enkephalinase inhibition on compulsive eating and weight loss were studied in a controlled-diet clinical setting. In a 90-day open trial, the effect of the experimental neuronutrient PCAL-103 on weight loss, uncontrollable carbohydrate binging and relapse rates was studied in 27 outpatients attending a supervised diet-controlled treatment programme. The patients were assigned, retrospectively, to 2 matched treatment groups: those receiving the neuronutrient (experimental group of 16 (EG)) and those not receiving the

neuronutrient (control group of 11 (CG)). EG patients exhibited facilitated withdrawal from carbohydrates compared with the CG patients. The EG group lost an average of 26.96 ± 2.7 lb; the CG group only 10.0 ± 2.1 lb. Only 18.2% of the EG group relapsed in contrast to 81.8% of the CG group. Use of the amino acid supplement PCAL-103 by chronic carbohydrate bingers allowed overweight subjects to lose 2.7 times as much weight as patients without benefit of this product.

Key Points

- Examine the effects of PCAL-103 (NAAT) on compulsive eating and weight loss in 27 outpatients attending a supervised diet-controlled treatment program.
- The PCAL-103 average weight loss was 26.96 lbs vs 10.2 lbs in the control group. Relapse 18.2% in the PCAL-103 group vs 81.8% in the control group.

Relapse Prevention Studies: Controls Compared to NAAT Oral (depicted as SGX).



	Cocaine n=15	Alcohol n=15	Alcohol n=57	Heroin n=4
Control	87	53	50	70
SGX Variant	33	13	7	0

(Modified from Blum et al. [66] and Blum et al. [75]).

Figure 11: Relapse Prevention Studies: Controls Compared to NAAT Oral (depicted as SGX).