

**LE Magazine December 1998**

## ABSTRACTS

### **Cognition Enhancing Supplements**

**Preventing or treating brain decline  
with vinpocetine.**

Life Extension magazine republishes abstracts on health and longevity topics in each issue, drawn from research papers originally published in science and medical journals throughout the world.

## Vinpocetine & brain disfunction

### ***A double-blind placebo controlled evaluation of the safety and efficacy of vinpocetine in the treatment of patients with chronic vascular senile cerebral dysfunction***

*J Am Geriatr Soc (1987 May) 35(5):425-30*

In a double-blind clinical trial, vinpocetine, a synthetic ethyl ester of apovincamine, was shown to effect significant improvement in elderly patients with chronic cerebral dysfunction. Forty-two patients received 10 mg vinpocetine three times a day for 30 days, then 5 mg three times a day for 60 days. Matching placebo tablets were given to another 42 patients for the 90-day trial period. Patients on vinpocetine scored consistently better in all evaluations of the effectiveness of treatment including measurements on the Clinical Global Impression (CGI) scale, the Sandoz Clinical Assessment- Geriatric (SCAG) scale, and the Mini-Mental Status Questionnaire (MMSQ). There were no serious side effects related to the treatment drug.

## Vinpocetine and the brain

### ***The effect of a cerebral vasodilator, vinpocetine, on cerebral vascular resistance evaluated by the Doppler ultrasonic technique in patients with cerebrovascular diseases***

*Angiology (1995 Jan) 46(1):53-8*

Changes in cerebral vascular resistance were examined in patients with cerebral circulatory diseases by the Doppler ultrasonic technique after administration of a cerebral vasodilator, vinpocetine, for two months. Continuous index (CI) and pulsatility index (PI) of the blood flow pattern in the internal carotid artery were used as objective parameters for changes in cerebral vascular resistance. 1. The CI and PI significantly after administration of the drug; i.e., the CI increased while the PI decreased. 2. An inverse correlation was noted between the rate of change of the CI (delta CI) and that of the PI (delta PI). 3. The results suggest that measurement of the CI and PI by the Doppler ultrasonic technique is useful in investigating the effect of drugs on the cerebral circulation.

## Alzheimer's and vinpocetine

### ***The safety and lack of efficacy of vinpocetine in Alzheimer's disease.***

*J Am Geriatr Soc (1989 Jun) 37(6):515-20*

Fifteen Alzheimer's patients were treated with increasing doses of vinpocetine (30, 45, and 60 mg per day) in an open-label pilot trial during a one-year period. Patients were assessed seven times both on and off drug with: the Buschke Selective Reminding Task, a letter fluency test, a category fluency test, the Boston Naming Test, a cognitive capacity screening examination, and a clinical global impression. Vinpocetine failed to improve cognition on psychometric testing or overall functioning, as measured by the clinical global impression, at any dose tested. Patients showed significant decline in most measures during the course of the study, at the same rate as a matched control group, consistent with progressive dementia. There were no significant side effects from drug therapy. We conclude that vinpocetine is ineffective in improving cognitive deficits and does not slow the rate of decline in individuals with Alzheimer's disease.

Vinpocetine, potassium, calcium

***Nootropic agent vinpocetine blocks delayed rectified potassium currents more strongly than high-threshold calcium currents***

*Neurosci Behav Physiol (1998 Mar-Apr) 28(2):116-20*

A two-microelectrode potential clamping method was used on isolated common snail neurons to measure high-threshold Ca<sup>2+</sup> and delayed rectified K<sup>+</sup> currents. Addition of the nootropic agent vinpocetine (VPC) to the bathing solution rapidly and reversibly inhibited both types of current. The effects of VPC were dose-dependent and were independent of the test stimulus voltage. Maximum blockade of the Ca<sup>2+</sup> current averaged 27% at a VPC concentration of 600 microM. Maximum blockade of the K<sup>+</sup> current averaged 76% at a VPC concentration of 30 microM. It is concluded that K<sup>+</sup> channels are more likely targets of VPC than Ca<sup>2+</sup> channels.

## Hydergine and the elderly

### ***Changes of pituitary secretion after long-term treatment with Hydergine, in elderly patients***

*Acta Endocrinol (Copenh) (1983 Mar) 102(3):332-6*

The aim of this study was to evaluate the effects of long-term treatment with an ergot derivative, dihydroergotoxine mesylates (Hydergine) 6 mg/day, on pituitary secretion on 10 elderly patients of both sexes. Samples were drawn at 120-minute intervals during a 24-hour period, before and after 1 month of therapy. Serum levels of Prolactin (Prl), Growth Hormone (GH), Luteinizing Hormone (LH), Follicle Stimulating Hormone (FSH), Thyroid Stimulating Hormone (TSH) and cortisol were measured by Radioimmunoassays (RIAs). Hydergine induced a significant increase in the nocturnal serum GH peak. Conversely, no appreciable changes in the pattern of the other hormones studied were found. The observed endocrine effects could be due to the chronic dopaminergic stimulation induced by Hydergine.

## Senile dementia

### ***Senile dementia: combined pharmacologic and psychologic treatment***

*J Am Geriatr Soc (1981 Apr) 29(4):164-71*

Either supportive counseling (SC) or cognitive training (CT) was used in an attempt to enhance the efficiency of a standard pharmacologic treatment for dementia, that is, dihydroergotoxine mesylate (DEM, Hydergine). DEM was administered orally to 21 moderately demented subjects, in a dosage of 1 mg three times daily; and SC or CT was conducted for one hour every two weeks for a total of 12 weeks. The CT was designed to enhance memory and other intellectual functions by the teaching of organizational schemes and mnemonic devices. Outcome measurements included the Sandoz Clinical Assessment-Geriatric (SCAG), a behavioral rating scale measuring selected symptoms and signs of dementia; the Hamilton Rating Scale for Depression (HRSD); and the Buschke Selective Reminding Scale (BSRT), a psychometric test of memory and learning. The DEM-plus-CT group of patients improved more than did the DEM-plus-SC group for the measures of memory and learning (BSRT). However, no differences between groups were noted for the HRSD or SCAG behavioral measures.

## Weight loss & ephedrine-caffeine

### ***Energy expenditure, body composition, and glucose metabolism in lean and obese rhesus monkeys treated with ephedrine and caffeine***

*Am J Clin Nutr* (1998 Jul) 68(1):42-51

The administration of ephedrine and caffeine (E plus C) has been proposed to promote weight loss by increasing energy expenditure and decreasing food intake. We tested this hypothesis in six lean (4-9% body fat) and six mildly-to-moderately obese (13-44% body fat) monkeys studied during a 7-week control period, an 8-week drug treatment period, and a 7-week placebo period. During the drug treatment period, the monkeys were given ephedrine (6 mg) and caffeine (50 mg) orally three times per day. At the end of each period, a glucose tolerance test was performed, energy expenditure was measured, and body composition was determined. Treatment with E plus C resulted in a decrease in body weight in the obese animals ( $P = 0.06$ ). This loss in weight was primarily the result of a 19% reduction in body fat. Drug treatment also resulted in a decrease in body fat in the lean group ( $P = 0.05$ ). Food intake was reduced by E+C only in the obese group ( $P < 0.05$ ). Nighttime energy expenditure was increased by 21% ( $P < 0.03$ ) in the obese group and 24% ( $P < 0.01$ ) in the lean group with E plus C treatment. Twenty-four-hour energy expenditure was higher in both groups during drug treatment. E plus C did not produce systematic changes in glucoregulatory variables, whereas plasma leptin concentrations decreased in both groups with drug treatment. Overall, these results show that E plus C treatment can promote weight loss through an increase in energy expenditure, or in some individuals, a combination of an increase in energy expenditure and a decrease in food intake.

## Weight maintenance

### **Randomized comparison of diets for maintaining obese subjects' weight after major weight loss: ad lib, low fat, high carbohydrate diet vs. fixed energy intake**

*BMJ (1997 Jan 4) 314(7073):29-34*

**Objectives:** To compare importance of rate of initial weight loss for long-term outcome in obese patients and to compare efficacy of two different weight maintenance programs. **Design:** Subjects were randomized to either rapid or slow initial weight loss. Completing patients were re-randomized to one year weight maintenance program of ad lib diet or fixed energy intake diet. Patients were followed up one year later. **Setting:** University research department in Copenhagen, Denmark. **Subjects:** 43 (41 women) obese adults (body mass index 27-40) who were otherwise healthy living in or around Copenhagen.

**Interventions:** 8 weeks of low-energy diet (2 MJ/day) or 17 weeks of conventional diet (5 MJ/day), both supported by an anorectic compound (ephedrine 20 mg and caffeine 200 mg thrice daily); one year weight maintenance program of ad lib, low fat, high carbohydrate diet or fixed energy intake diet (< or = 7.8 MJ/day), both with reinforcement sessions 2-3 times monthly. **Main outcome measures:** Mean initial weight loss and proportion of patients maintaining a weight loss of > 5 kg at follow up. **Results:** Mean initial weight loss was 12.6 kg (95% confidence interval 10.9 to 14.3 kg) in rapid weight loss group and 12.6 (9.9 to 15.3) kg in conventional diet group. Rate of initial weight loss had no effect on weight maintenance after 6 or 12 months of weight maintenance or at follow up. After weight maintenance program, the ad lib group had maintained 13.2 (8.1 to 18.3) kg of the initial weight loss of 13.5 (11.4 to 15.5) kg, and the fixed energy intake group had maintained 9.7 (6.1 to 13.3) kg of the initial 13.8 (11.8 to 15.7) kg weight loss group difference 3.5 (-2.4 to 9.3) kg. Regained weight at follow up was greater in fixed energy intake group than in ad lib group (11.3 (7.1 to 15.5) kg v 5.4 (2.3 to 8.6) kg, group difference 5.9 (0.7 to 11.1) kg,  $P < 0.03$ ). At follow up, 65% of ad lib group and 40% of fixed energy intake group had maintained a weight loss of > 5 kg ( $P < 0.07$ ).

**Conclusion:** Ad lib, low fat, high carbohydrate diet was superior to fixed energy intake for maintaining weight after a major weight loss. The rate of the initial weight loss did not influence long-term outcome.

## Smoking and weight

### ***The effect of ephedrine plus caffeine on smoking cessation and post-cessation weight gain***

*Clin Pharmacol Ther* (1996 Dec)60(6):679-86

**Objectives:** To evaluate the efficacy of a combination of ephedrine and caffeine on smoking cessation rates, post-cessation weight gain, and withdrawal symptoms and to examine changes in glycosylated hemoglobin (HbA1c) after smoking cessation. **Methods:** This randomized double-blind placebo-controlled study with a 1-year follow-up period was carried out at the Department of Pulmonary Medicine in Denmark. Study subjects were 225 heavy smokers who wanted to quit smoking without gaining weight. Two-thirds of the subjects were randomized to receive 20 mg ephedrine plus 200 mg caffeine three times a day; one-third of the subjects received placebo treatment. The dosage was gradually decreased from week 12 to discontinuation at week 39. Group support and control were performed at entry and after 1, 3, 6, 12, 26, 39, and 52 weeks. Main outcome measures were: (1) self-reported abstinence with validation by carbon monoxide in expired air and serum cotinine and (2) weight gain. **Results:** The success rates after 1 year were 17% in the group treated with ephedrine plus caffeine and 16% in the group treated with placebo; the success rates were not significantly different at any time. The success rates for the four counseling physicians varied between 7% and 27% after 1 year ( $p < 0.05$ ). The weight gain was significantly lower in the ephedrine plus caffeine-treated group during the first 12 weeks, but weight gains were similar after 1 year. No differences in the smoking withdrawal symptoms could be observed between the treatment groups. HbA1c was lower 6 weeks and 1 year after smoking cessation ( $p < 0.05$ ).

**Conclusions:** We found an effect of this combination of ephedrine and caffeine on weight gain during the first 12 weeks, but we found no effect on the success rates or craving for cigarettes.

## Ephedrine, obesity

### ***Ephedrine, caffeine and aspirin: safety and efficacy for treatment of human obesity***

*Int J Obes Relat Metab Disord (1993 Feb) 17 Suppl 1:S73-8*

The safety and efficacy of a mixture of ephedrine (75-150 mg), caffeine (150 mg) and aspirin (330 mg), in divided pre-meal doses, were investigated in 24 obese humans (mean BMI 37.0) in a randomized double-blind placebo-controlled trial. Energy intake was not restricted. Overall weight loss over 8 weeks was 2.2kg for ECA vs. 0.7 kg for placebo ( $p < 0.05$ ). Eight of 13 placebo subjects returned 5 months later and received ECA in an unblinded crossover. After 8 weeks, mean weight loss with ECA was 3.2 kg vs 1.3 kg for placebo ( $p = 0.036$ ). Six subjects continued on ECA for 7 to 26 months. After 5 months on ECA, average weight loss in 5 of these was 5.2 kg compared with 0.03 kg gained during 5 months between studies with no intervention ( $p = 0.03$ ). The sixth subject lost 66 kg over 13 months by self-imposed caloric restriction. In all studies, no significant changes in heart rate, blood pressure, blood glucose, insulin, and cholesterol levels, and no differences in the frequency of side effects were found. ECA in these doses is thus well-tolerated in otherwise-healthy obese subjects, and supports modest, sustained weight loss even without prescribed caloric restriction, and may be more effective in conjunction with restriction of energy intake.

## Ephedrine, caffeine

### ***The effect and safety of an ephedrine/caffeine compound compared to ephedrine, caffeine and placebo in obese subjects on an energy restricted diet. A double blind trial***

*Int J Obes Relat Metab Disord (1992 Apr) 16(4):269-77*

The sympathomimetic agent ephedrine has potent thermogenic and anti-obesity properties in rodents. The effect is markedly enhanced by caffeine, while caffeine given alone has no effect. This study was undertaken to find out if a similar weight-reducing synergism between ephedrine and caffeine is present in obese patients. In a randomized, placebo-controlled, double blind study, 180 obese patients were treated by diet (4.2 MJ/day) and either an ephedrine/caffeine combination (20 mg/200 mg), ephedrine (20 mg), caffeine (200 mg) or placebo three times a day for 24 weeks. Withdrawals were distributed equally in the four groups, and 141 patients completed the trial. Mean weight losses was significantly greater with the combination than with placebo from week 8 to week 24 (ephedrine/caffeine, 16.6 +/- 6.8 kg vs. placebo, 13.2 +/- 6.6 kg (mean +/- s.d.),  $P = 0.0015$ ). Weight loss in both the ephedrine and the caffeine groups was similar to that of the placebo group. Side effects (tremor, insomnia and dizziness) were transient and after eight weeks of treatment they had reached placebo levels. Systolic and diastolic blood pressure fell similarly in all four groups. We conclude, that in analogy with animal studies, the ephedrine/caffeine combination is effective, while caffeine and ephedrine separately are ineffective for the treatment of human obesity.

## Ephedrine/caffeine vs. dexfenfluramine

### **Comparison of an ephedrine/caffeine combination and dexfenfluramine in the treatment of obesity. A double-blind multi-center trial in general practice**

*Int J Obes Relat Metab Disord (1994 Feb) 18(2):99-103*

In previous separate studies, dexfenfluramine (DF) and ephedrine/caffeine (EC) have been shown to promote weight loss in obese patients as compared with placebo. In order to compare the efficacy and safety of these two anorectic drugs, 103 patients with 20-80% overweight were included in a 15-week double-blind study in general practice. Patients were randomized to either 15 mg DF twice daily (n = 53), or 20 mg/200 mg ephedrine/caffeine three times a day (n = 50), supplementary to a 5 MJ/day diet. Forty-three patients from the DF group and 38 from the EC group completed the study. After 15 weeks of treatment, the DF group (n = 43) had lost 6.9 +/- 4.3 kg and the EC group (n = 38) had lost 8.3 +/- 5.2 kg (mean +/- s.d., P = 0.12). In the subgroup of patients with BMI > or = 30 kg/m<sup>2</sup> (n = 59), the mean weight loss was 7.0 +/- 4.2 kg in the DF group (n = 29) and 9.0 +/- 5.3 kg in the EC group (n = 30), P < 0.05. Both systolic and diastolic blood pressures were reduced similarly during both treatments. Twenty-three patients in the DF group (43%) and 27 in the EC group (54%) complained of side effects. Central nervous system side-effects, especially agitation, were more pronounced in the EC group (P < 0.05), whereas gastro-intestinal symptoms were more frequent in the DF group (P < 0.05). The side effects declined markedly during the first month of treatment in both groups.

## Ephedrine, diabetes

### ***Ephedrine: a new treatment for diabetic neuropathic edema.***

*Lancet (1983 Mar 12) 1(8324):548-51*

Peripheral edema secondary to diabetic neuropathy is poorly understood and difficult to treat. Ephedrine markedly reduced neuropathic edema in four insulin-dependent diabetics. Mean weight-loss ( $p$  less than 0.05) after 7 days' treatment was  $7.43 \pm 4.51$  (SD) kg. The edema returned (mean weight increase  $6.33 \pm 1.73$  kg;  $p$  less than 0.01) when ephedrine was withdrawn but resolved (weight-loss  $4.85 \pm 1.57$  kg;  $p$  less than 0.01) when ephedrine treatment was repeated. In one patient mean 24-hour sodium excretion increased from  $177 \pm 5.20$  mmol before ephedrine to  $502 \pm 78$  mmol on ephedrine therapy ( $p=0.028$ ). Ephedrine also reduced excessive peripheral blood flow produced by the neuropathy; both arterial diastolic flow and arteriovenous shunting as demonstrated by Doppler blood velocity profiles were reduced and the pulsatility index increased from  $2.50 \pm 0.61$  to  $4.75 \pm 1.76$  ( $p$  less than 0.001). Ephedrine continues (12-15 months) to be an effective treatment for neuropathic edema in these four patients.

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