STUDIES

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1. Influence of a NADH-containing nutrient combination on memory, concentration and prevailing mood.

   Author´s: Dr. Roesler et al 2008

INFLUENCE OF A NADH-CONTAINING NUTRIENT COMBINATION ON MEMORY, CONCENTRATION AND PREVAILING MOOD

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ABSTRACT

BACKGROUND/OBJECTIVE

Depression and dementia represent two of the most important diseases in advanced age. The positive influence of particular nutrients such as NADH, B-vitamins, and various trace elements is well documented in this connection. The aim of this study was to test the influence of a complex nutritional supplement containing such ingredients and a stabilized, gastric acid resistant oral form of NADH (PANMOL®-NADH) on memory, concentration and mood.

METHODS

Hamilton Depression Scale (HAMD-17) was used for investigating the parameter depression. In order to quantify dementia (divided into memory performance and attention), the Syndrome Short Test (SKT) was used. The study was designed as a double-blind, placebo-controlled, prospective trial.

RESULTS

Over three months 28 residents of similar nursing homes (24 women, 4 men) with an age range of 49-94 years (78.39 ± 9.19 years) were included in the study. The test product treatment group showed a significant improvement in depressive symptoms ($p = 0.049$) in comparison with the placebo group. A clear benefit in favour of the supplemented group was also observed for memory and attention parameters.

CONCLUSION

This study documents a beneficial effect of the multi-nutrient NADH-formula on the parameters dementia and depression.

KEY WORDS

depression, dementia, stabilized NADH, supplement

INTRODUCTION

Clinical and every day experience point to the importance of depressive mood as a co-morbidity factor in dementia. However, the literature is replete with references to the problem of making precise statements about prevalence secondary to the difficulties of comparing diverse psychometric methodologies [17, 18]. Jorm has also described in a review the role of depression as a causal risk factor in cognitive decline [10].

The elderly have a particularly high prevalence of both symptoms. This patient population also frequently suffers from nutritional deficiencies, which can result from medical (malabsorption, swallowing difficulties, immobility or a higher nutrient need on account of catabolic conditions) or social reasons (loneliness, low income, diminished alertness, alcohol and prescription medicine use) [1].

This work originated from acceptance that targeted orthomolecular supplementation can improve symptoms of dementia and depression secondary to improvements in neuron and neurotransmitter metabolism.

A recent methodologically adequate meta-analysis has underscored the beneficial effects of folic acid supplementation for patients with depression [16]. The link between depressive symptoms and folic acid or B vitamin deficiency is also well documented [2]. Likewise, the central importance of the B vitamins for neuronal metabolism is widely recognized [1]. Vitamin B12 intake, in particular, has been positively correlated with cognitive performance, and especially with respect to verbal and visual memory [3].

Vitamin D and, in a wider context, calcium intakes have also been shown to influence positively seasonal affective disorder (SAD). Moreover, zinc has been shown to play a major role in the metabolism of the neurotransmitters dopamine and noradrenaline and in the synthesis of glutamic acid and GABA [2].

Studies conducted at the University of Montreal, Canada, have recently led to suggestions that magnesium can exert a mood-stabilizing effect following observations on nine rapidly cycling manic-depressive subjects [5].

Further, several studies with nicotinamide adenine dinucleotide hybrid (NADH) have postulated beneficial effects on cognition, in both animals and humans. Birkmayer et al. showed in a placebo-controlled, double-blind study in 35 patients a significant improvement in cognitive performance after jetlag following intake of NADH [4]. In another study, NADH supplementation was associated with an improvement in mitochondria metabolism in patients with neurodegenerative diseases [11]. Rex et al. also showed in rats that NADH supplementation could significantly improve cognitive learning [13].

The present study was designed on the basis of the above observations to test the hypothesis that micronutrient supplementation can positively influence memory, concentration and prevailing mood in an elderly population.

METHODS

A multicenter, double-blind, placebo controlled study design was chosen to ensure the highest statistical power. To provide an ideal study setting we chose residents of nursing homes within a regional radius of about 20km. The advantage of this strategy was that these homes could provide very similar treatment conditions for all subjects and the nursing staff could ensure high compliance.

Two internationally validated psychometric tests were employed which allowed for quantification of cognitive deficit and depressive symptoms. The Syndrome Short Test (SKT) was used for evaluation of cognitive performance. This test uses a detailed playful scenario to screen for dementia using nine subtests. The testing process involves an assessment of memory and attention disturbances in subjects with conditions such as dementia, organic psychosis and cerebral insufficiency. For this study both total and specific scores for memory and attention were evaluated. International validation of these tests comprised investigations in over 15 countries [6]. Rothenhäusler et al. have reported that the test reliability ranges from 0.86 to 0.88 [14].

The Hamilton Depression Scale (HAMD-17) was used to quantify depression. This international psychometric test determines the stage of depressive symptoms by quantifying the cardinal symptoms. Gençöz et al. report that HAMD-17 has a test-retest coefficient >0.60 [8].

Table 1 Composition of the test product (daily dose)

Ingredient	Quantity per day	RDA*
PANMOL®-NADH (stabilized and gastric acid resistant)	10.0 mg	
Vitamin B1/thiamine	11.2 mg	800.0%
Vitamin B2/riboflavin	12.8 mg	800.0%
Niacin	144.0 mg	800.0%
Pantothenic acid	48.0 mg	800.0%
Vitamin B6/pyridoxine	16.0 mg	800.0%
Biotin	1.2 mg	800.0%
Folic acid	1.6 mg	800.0%
Vitamin B12/cyanocobalamine	0.008 mg	800.0%
Magnesium	117.0 mg	39.0%
Zinc	15.0 mg	
Iron	3.0 mg	21.4%
Manganese	0.5 mg	

Copper	0.15 mg	
Chromium	0.10 mg	
Selenium	0.03 mg	
Molybdenum	0.025 mg	

* RDA = RDA from EC-health authorities recommended daily quantity for adults

The test product was a micronutrient preparation comprising multivitamins and minerals and a stabilized, gastric acid-resistant NADH formulation, two capsules of which were to be taken each morning. The study ran for between 2-3 months, and daily intakes corresponded to the values depicted in Table 1.

Statistical evaluations were performed using SPSS (Version 11.0) for Windows©, an internationally recognized statistics application with modular construction [9].

Two study groups (placebo and treated) were formed and the respective results were initially evaluated descriptively. P-values were computed using the t-test for independent samples and the level of significance (alpha) set at alpha=0.05.

RESULTS

Study inclusion criteria were advanced age, symptoms of cognitive impairment and/or depressed mood and a personal desire to take part in the study.

Exclusion criteria were concurrent treatment with antiparkinson medications, advanced dementia, severe vision impairment, test product intolerance, and poor compliance (defined as an intake of less than 80% of the prescribed daily dose). A total of 28 subjects fulfilled the inclusion criteria. Two subjects did not fulfil the 80% daily intake compliance. A further two subjects left the study for personal reasons, and one participant degenerated cognitively to such an extent that she could no longer complete the final tests. These final tests were performed ten weeks after the study commenced.

The 28 subjects (24 women and four men) had an average age of 78.39 (± 9.19) years with a range of 49-94 years.

Subjects were allocated to placebo and treatment groups using a randomisation and blinding procedure based on envelope distribution by a third person not otherwise involved in the study. 15 subjects took a placebo and 13 took the test product.

Although the study groups were relatively small, the initial values were similar for all measured parameters. Noteworthy was that for each of the four tests and subtests, the magnitude of the scores correlated directly with the extent of the clinical condition. In comparison, the SKT memory scores at the beginning of the investigation gave a slight advantage to the placebo group, as illustrated in Table 2.

Table 2 Final mean values for placebo and active treatment groups

	Active treatment (n=13)		Placebo (n=15)	
	Mean	Standard deviation	Mean	Standard deviation
SKT total	14.23	5.37	16.07	6.31
SKT memory	4.54	2.76	4.20	2.37
SKT attention	9.69	3.57	11.87	4.93
Hamilton total	13.85	4.90	14.67	4.08

Results for each of the four main parameters (SKT total value, SKT memory, SKT attention and Hamilton total scores) were compared before and after consumption of the test product. The following results were obtained for the SKT tests (Table 3, Diagram 1):

Table 3/Diagram 1 Total values for cognition

SKT total	Mean (standard deviation)	
	Before treatment	After treatment
Placebo (n=15)	16.07 (±6.31)	12.93 (±7.55)
Active treatment (n=13)	14.23 (±5,37)	8.31 (±7.19)

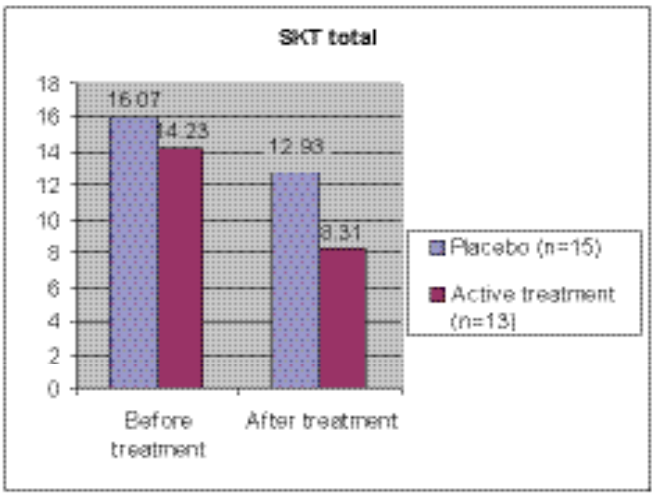


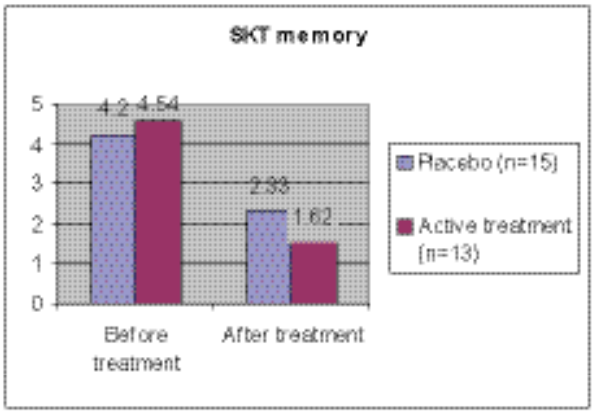
Diagram 1 shows psychometric test results before and after consumption of placebo or test product. There was a pronounced difference between these groups and this is discussed further in the discussion section below.

Results of the SKT, as mentioned above, could be subdivided into memory and attention subscores.

SKT for memory performance: initially it appeared that the placebo treatment was more effective; however, after continued consumption of the test product there was improved outcome in favour of the latter (Table 4, graphically displayed in Diagram 2).

Table 4/Diagram 2 Memory

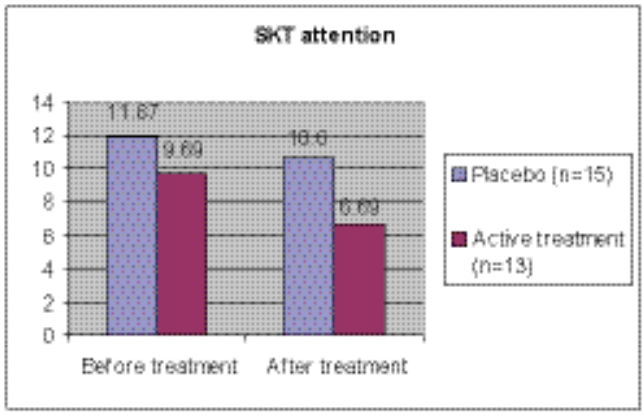
SKT memory	Mean (standard deviation)	
	Before treatment	After treatment
Placebo (n=15)	4.20 (±2.37)	2.33 (±3.20)
Active treatment (n=13)	4.54 (±2.76)	1.62 (±2.66)



SKT for attention: the second SKT subtest focused on attention and revealed initially a slight advantage in favour of the test product. After ten weeks of treatment the improvement was more strongly in favour of the test product compared with the placebo group. Detailed results are provided in Table 5 and Diagram 3.

Table 5/Diagram 3 Attention

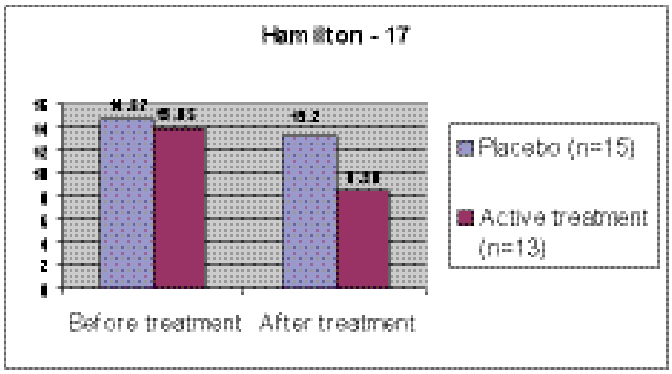
SKT attention	Mean (standard deviation)	
	Before treatment	After treatment
Placebo (n=15)	11.87 (±4.93)	10.60 (±5.44)
Active treatment (n=13)	9.69 (±3.57)	6.69 (±5.07)



The final aspect of the descriptive statistics comprised results of the Hamilton Depression Scale, which were as similarly pronounced as those previously mentioned. These results are reported in Table 6 and Diagram 4.

Table 6/Diagram 4 Hamilton-17 (depressive symptoms)

Hamilton-17	Mean (standard deviation)	
	Before treatment	After treatment
Placebo (n=15)	14.67 (±4.08)	13.20 (±5.14)
Active treatment (n=13)	13.85 (±4.90)	8.38 (±3.36)



Results of the t-test for independent samples revealed that the p-values of the three SKT results marginally failed to reach statistical significance (P>0.05). Taking an error probability of 5%, the p-value for the SKT total was 0.149, for the memory subscore p=0.206, while for attention p=0.177.

The outcome of the HAMD-17 test illustrated statistical significance (assuming an error probability of 5% with p=0.049), attesting to a significantly improved score for the test product group compared with the placebo group (see Table 7).

Table 7 Results of analytic statistics calculation (*denotes statistical significance)

Parameter	Difference between initial and final scores (placebo; n=15)	Difference between initial and final scores (active treatment; n=13)	Signifi-cance (p-value)
SKT total	3.13 (±4.73)	5.92 (±5.12)	0.149
SKT memory	1.87 (±2.20)	2.92 (±2.10)	0.206
SKT attention	1.27 (±3.01)	3.00 (±3.51)	0.177
Hamilton	1.47 (±5.62)	5.46 (±4.63)	0.049 *

DISCUSSION

The greatest advantage of this study was the setting of four nursing homes for the elderly, which ensured optimal subject compliance, a comparable participant population and a homogeneous group in near identical surroundings. The nursing staff supervised consumption of the test preparations and could thus help assure treatment compliance. One weakness in the study design may have been the short study duration of only ten weeks. The relative improvement in SKT over this period, even in the placebo group, may imply that at least in some subjects the proceedings of the cognition tests could have been remembered. The resulting learned effect may have contributed to the strong placebo effect, especially for memory, for which initial values were almost halved. Nevertheless, there was a tendency to a positive effect for the test product, although this, with p=0.206, was not statistically significant.

The influence of the test product on cognition was deemed positive, as illustrated in Diagrams 1-3. Further, this finding is supported by diverse references in the literature, which suggest a correlation between vitamin and/or trace element supplementation and improvement in cognitive performance.

For the parameters total cognition and attention, both initial and final scores for the test product group were twice those of the placebo group. Statistical significance was not achieved (p=0.149 and p=0.177 respectively), but suggested a tendency towards a positive effect of the preparation.

Claims by Birkmayer et al [4] and Rex et al [13], which attest to the positive effect of NADH on cognitive performance in subjects with jetlag and rats, suggest that in our study population the main cognitive benefit of this product could be mediated by these ingredients. Nevertheless, the possible central benefits of the B vitamins, especially vitamin B12, and zinc should not be underestimated.

The clearest effect of the test product was seen with symptoms of depression. The difference between initial and final test values of the Hamilton Depression Scale in the test product group were a factor of 3.7 times higher than seen with the placebo group. These differences were statistically significant (p=0.049). This result is noteworthy, when one takes into account the possibly sub optimal study duration. The study commenced in August, whereas the final tests were conducted at the beginning of November. Thus, the seasonal difference could have been responsible for introducing an element of SAD in some patients, masking or strengthening the classic depressive symptoms of SAD relative to the timing of the tests.

Literature references support the important role of the vitamins investigated. According to Taylor et al [16], following a meta-analysis, folic acid had a positive effect on depressive symptoms; whereas Bayer et al [1] attest to the central importance of the B vitamins on neuronal metabolism.

Endogenous synthesis of NAD+ and NADH requires the amino acid tryptophan. However, other substances such as riboflavin, as a component of the hydrogen transferring coenzyme FAD (flavine adenine dinucleotide) and magnesium are also necessary [12]. Moreover, recent findings suggest that endogenous NAD+ formation can be increased by dietary supplementation with nicotinic acid and nicotinamide and by sufficient dietary intake of tryptophan [15]. The test preparation is thus expected to contribute to increased NADH synthesis by its content of riboflavin, magnesium and niacin. In addition to direct supplementation with NADH, increased NADH synthesis from the other ingredients of the test product may represent additional reasons for the improved cognitive performance and prevailing mood. The importance of dietary zinc, which plays a regulatory role on noradrenaline and dopamine metabolism [2], and magnesium, which has been shown to have a stabilizing effect on mood [5], may also have contributed to the positive outcomes in the subjects examined.

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