A multicomponent medication enhances cognitive function in vivo

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INTRODUCTION

A characteristic feature of patients with dementia is neuronal degeneration of hippocampal cholinergic neurons leading to a marked decline in cognitive function. This loss of cholinergic neurons might result in a deficiency of acetylcholine in specific brain regions that mediate learning and memory. Acetylcholine inhibitors such as Donepezil and Galantamine are approved drugs with noticeable effects on the symptoms of dementia. However, strong side effects and low efficacy limit their clinical benefit. To date a disease modifying drug is not available.

HE-300 is a multi-component medication consisting of different natural sources. Thus the efficacy arises from different biochemical levels. It was already observed that HE-300 changes gene expression in AD specific genes, affects synaptic plasticity, neuronal outgrowth and APP processing. These data suggest that HE-300 exhibits potential to support cognitive functions by targeting several cellular networks. The treatment with such a multi-component/multi-target drug depicts a new and innovative approach for a beneficial treatment of this complex and chronic disease.

OBJECTIVE

In the present study, we assessed the effect of HE-300, a multicomponent medication derived from natural sources on cognitive function using two different in vivo animal models. HE-300 was tested in (1) the T-maze continuous alternation task in mice with scopolamine-induced learning deficit, (2) the novel object recognition test in mice, investigating the natural forgetting behaviour.

MATERIALS & METHODS

T-maze assay: The percentage of alternation of 14 free-choice trials was determined for each mouse and was used as an index of working memory performance. This percentage was defined as entry in a different arm of the T-maze over successive trials. Drug-induced reversion was calculated by considering the saline/vehicle group as 100% and scopolamine/vehicle group as 0%. Mice were treated with 10 mg/kg Scopolamine. HE-300 was administrated acutely or during 3 consecutive days prior to the trial.

RESULT: HE-300 IMPROVES NATURAL MEMORY PROCESSES IN THE NOVEL OBJECT RECOGNITION TEST

A significant decrease in the recognition index was observed 24 h after the acquisition trial (black column) indicating natural forgetting. The novel forgetting was reversed by the treatment with Donepezil (0.3 mg). Donepezil increased contact (a) and time (b) recognition index significantly.

RESULT: HE-300 REVERSES SCOPOLAMINE INDUCED DEFICITS IN THE T-MAZE CONTINUOUS ALTERNATION TASK MODEL

The t-maze is based on the natural behavior to explore new environments. It is the innate tendency of healthy rodents to alternate freely both sides in a T-maze over a series of successive runs (spontaneous alternations). This sequential procedure relies on working memory and is sensitive to various pharmacological manipulations affecting memory processes.

The experiment consisted of one single session, which started with a "free-choice" trial followed by "fix-alternating" trials. A novel object (NO) was introduced to the open-field in addition to the familiar one. NO were removed from the maze as soon as 14 free-choice trials have been performed or after 10 minutes.

The time spent exploring each of the 2 objects during the retention trial was recorded. Recognition index was as follow: RI = tNO/(tFO+ tNO) x 100, where t denotes time. Recognition index was also expressed as the number of visit (contacts) to the novel object in % and was calculated as follow RI = nNO/(nFA + nNO) x 100, where n denotes number of contacts.

Statistical analysis: Statistical analysis of variance (ANOVA) was performed followed by Fisher’s Protected Least Significant Difference for pair wise comparison. All values are presented as mean ± standard error of mean (SEM) and differences are considered statistically significant at p<0.05.

REFERENCES: